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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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MEMORANDUM

September 22, 2011

Subject: Registration Review: Preliminary Problem Formulation for Environmental Fate and Ecological Risk, Endangered Species, and Drinking Water Assessments for Metsulfuron-methyl (Case 7205)

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The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the environmental fate and ecological risk, endangered species, and drinking water assessments to be conducted as part of the Registration Review of the herbicide metsulfuron-methyl (metsulfuron, also known as DPX-T6376; PC Code 122010). Only metsulfuron is associated with registered end use products. 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 metsulfuron and its degradates. It also describes the preliminary ecological risk hypothesis and analysis plan for evaluating and characterizing risk to non-target species and the environment in support of registration review.

Data Gaps

The available environmental fate and transport data are considered incomplete and inadequate for the purposes of risk assessment. The following data gaps exist:

- Photolytic degradation in water (OPPTS guideline # 835.2240). Two studies are currently in review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- Photolytic degradation in soil (OPPTS guideline # 835.2410). One study is currently in review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- There are no acceptable data for aerobic soil metabolism (OPPTS guideline # 835.4100). The guideline stipulates that results from at least four relevant soils of different organic carbon content, pH, clay content, and microbial biomass must be submitted in order to characterize the variability in aerobic biodegradation of metsulfuron in the environment.
- Anaerobic soil metabolism (OPPTS guideline # 835.4200). There is currently one study in review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- There is no acceptable aerobic aquatic metabolism study (OPPTS guideline # 835.4300). This study is necessary in order to describe the fate of metsulfuron in surface water. The guideline stipulates that at least two different sediment:water systems be submitted that are similar to the potential use sites in the United States.
- Submission of an acceptable anaerobic aquatic metabolism (OPPTS guideline # 835.4400) study is necessary to understand the degradation of metsulfuron in oxygen-limiting environments.
- There is currently one adsorption/desorption batch equilibrium study (OPPTS guideline # 835.1240) under review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. This study is necessary to understand the mobility and sorption characteristics of metsulfuron.
- An acceptable aquatic field dissipation study (OPPTS guideline # 835.6200) is required for all pesticides with use patterns for aquatic food and nonfood applications.
- Supplemental to the aquatic field dissipation and terrestrial field dissipation studies are the independent laboratory method validation, and environmental chemistry methods used for the field study.

The available effects dataset is considered incomplete for the purposes of risk assessment. The following data gaps exist:

- 850.1300. A daphnid lifecycle study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- 850.2100. **An avian acute oral study with a passerine using TGAI is necessary for risk assessment.** Additionally, an acute oral study with mallard duck is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- 850.4100 (850.4225). A seedling emergence study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.

- 850.4150 (850.4250). A vegetative vigor study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.
- Non-guideline. **Terrestrial Plant Reproduction Study using TGAI** will be necessary for risk assessment (See Appendix A for justification and an example DCI for the special study).
- **Seedling emergence and aquatic plant toxicity data necessary for degradate IN-A4098 (2-amino-4-methoxy-6-methyl 1, 3, 5-triazine).**

Additional detail on the current data gaps for environmental fate and effects for metsulfuron is provided in Section 8.0.

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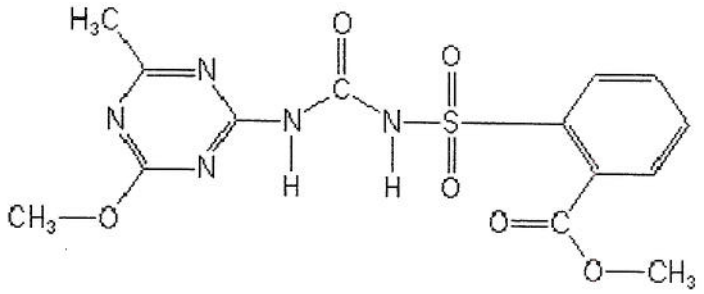
Problem Formulation for the Environmental Fate and Ecological Risk, Endangered Species, and Drinking Water Assessments in Support of the Registration Review of Metsulfuron-methyl



methyl 2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoate
CAS Registry Number: 74223-64-6
PC Code: 122010

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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 and ecological effects of the registered uses of metsulfuron-methyl (metsulfuron; PC Code 122010). While a widely used active ingredient, metsulfuron is also a major degradate of iodosulfuron-methyl sodium (PC code 122021). Iodosulfuron is scheduled for Registration Review in 2013, therefore a problem formulation will be completed for iodosulfuron at that time. Metsulfuron belongs to the sulfonylurea class of herbicides and it is applied for selective control of annual and perennial broadleaf weeds and certain monocots in agricultural noncrop and industrial areas, pasture and rangeland, turf, golf course and ornamental grasses, forestry and marshes and wetland areas. Crop uses include barley, sugar cane, triticale, and wheat. This herbicide can be applied as pre-and post-emergence treatments and may be used on established plantings. In addition, several labels allow for uses in aquatic systems. Metsulfuron is an acetolactate synthase (ALS) inhibitor. ALS is an important enzyme for the synthesis of branched chain amino acids. This metabolic pathway is present only in plants. Metsulfuron is absorbed by the foliage and roots in plants. This document will provide a plan for analyzing data relevant to metsulfuron and for conducting environmental fate and ecological risk, endangered species, and drinking water assessments for its registered uses. Additionally, this problem formulation is intended to identify data gaps, uncertainties, and potential assumptions used to address those uncertainties relative to characterizing the ecological risk associated with the registered uses of metsulfuron.

2. Problem Formulation

2.1. Nature of Regulatory Action

Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), all pesticides distributed or sold in the United States generally must be registered by the Environmental Protection Agency (EPA). As part of determining whether a pesticide can be registered in the U.S., the Agency evaluates its safety to non-target species based on a wide range of environmental and health effects studies. In 1996, FIFRA was amended by the Food Quality Protection Act, and the Agency was mandated to implement a new program for the periodic review of pesticides, *i.e.*, Registration Review (http://www.epa.gov/oppsrrd1/registration_review/). The Registration Review program is intended to ensure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health and the environment. Changes in science, public policy, and pesticide use practices occur over time. Through the new Registration Review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely.

As part of the implementation of the Registration Review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the Agency is beginning its evaluation of metsulfuron to determine whether it continues to meet the FIFRA standard for registration. This problem formulation for the environmental fate, ecological risk, endangered

species, and drinking water assessment chapter in support of the Registration Review will be posted in the initial docket, which will open the public phase of the review process.

2.2. Previous Risk Assessments

In 1983, the Agency granted an Experimental Use Permit (EUP) for metsulfuron on wheat, barley and fallow fields. In 1984, the Agency produced a hazard assessment for the full registration of metsulfuron for use as selective weed control in small-grain cereals and reduced-tillage fallow systems. At the time, the acute toxicity data were considered complete. However there were no chronic data and concerns about chronic exposure were identified. In 1985, the Agency expanded an EUP application for use in forestry applications. Specific listed plant species were identified as associated with this permit. In 1986, a hazard assessment for an EUP for use on rangeland and pasture grass was issued.

In 1989, the Agency reviewed an emergency exemption (Section 18) for use as a harvest aid on wheat in Oklahoma and Kansas. Potential hazard to Federally listed plant species via offsite movement was identified. In 1990, a Section 18 for the same use in Texas was reviewed; the Agency noted its concern for the potential for drift from aerial application and the potential for metsulfuron to leach, especially from sandy soils.

In 1992 a tank mix with 2,4-D was added to the Section 3 registration for preharvest uses on wheat; the hazard assessment stated that this use would be added to a general herbicide consultation with the Services 'at some point in the future'.

In 1996, a risk assessment was conducted for the addition of sorghum to a product label. The assessment identified concerns for plants, but no exceedances of the Levels of Concern (LOC) for aquatic or terrestrial animals were noted (RQs <0.01). In 1998, a Tier 1 drinking water assessment for sorghum uses was conducted. In 1999, an assessment for a Section 18 use on sorghum in Oklahoma was conducted, including a drinking water assessment. In 2002, a review of data gaps associated with the sorghum use was conducted and several ecotoxicity studies were identified as necessary for further risk assessment, especially regarding metsulfuron degradates.

In 2002, a combined drinking water assessment for iodosulfuron (PC Code 122021) and metsulfuron (which is a degradate of iodosulfuron) was conducted.

3. Stressor Source and Distribution

3.1. Mechanism of Action

Metsulfuron's mode of action is the inhibition of amino acid synthesis in plants through inhibition of acetolactate synthase (ALS). ALS is the first common enzyme in the biosynthesis of branched-chain amino acids (valine, leucine and isoleucine). ALS inhibition in plants adversely affects plant growth and reproduction. Although acetolactate is present in mammals, the biosynthesis of branch chain amino acids occurs only in plants. Chlorsulfuron (PC Code

118601), the most studied pesticidal SU, does not affect acetolactate forming enzymes in mammalian cells (Nakata, 1991). SUs in general are less toxic to animals than plants.

3.2. Overview of Pesticide Use and Usage

Metsulfuron belongs to the sulfonylurea class of herbicides and it is applied for selective control of annual and perennial broadleaf weeds and certain monocots in agricultural noncrop and industrial areas, pasture and rangeland, turf, golf course and ornamental grasses, forestry, and marshes and wetland areas. Crops uses include barley, sugar cane triticale and wheat. This herbicide can be applied as pre-and post-emergence treatments and may be used on established planting. In addition, several labels allow for uses in aquatic systems. According to the Biological and Economic Analysis Division's (BEAD) Screening Level Usage Analysis (SLUA; USEPA 2011), roughly 20,000 lbs of metsulfuron is applied annually on wheat, while about 17,000 lbs are used on pasture and pasturelands.

Metsulfuron does not appear to be co-formulated with any other active ingredients and it is unclear if it can be tank mixed with other products. There is evidence that a tank mix with at least 2,4-D was permitted in the past. Metsulfuron is generally formulated as a dry flowable intended for tank mixing with water. The application rate varies with use site, stage of weed growth and application timing, but the maximum single application is 0.15 lbs a.i./A. A summary of general use patterns is provided in **Table 2**. Maximum annual rate is specified on some labels and not others. Metsulfuron, in theory, may be applied on some sites in unlimited quantity. Unless these issues are resolved before the risk assessment, conservative assumptions will need to be employed regarding annual application rates. This herbicide can be applied aerially, via ground spray, back pack sprayers, tree injection, and other methods. There are currently 43 Section 3 registrations and six SLN registrations. Many of the Section 3 registrations have geographical restrictions (*e.g.* off label in CA, *etc.*). For further information, see 'BEAD Chemical Profile for Registration Review: Metsulfuron-methyl (122010)' (March, 2011).

Table 2. Summary of use sites and application rates for metsulfuron.

Site	Use Group	AI%	Formulation	A. I. Max App Rate	A. I. Conv Seasonal Max Dose/Year	Application Method	Application Method	Application Timing
AIRPORTS/LANDING FIELDS	TERRESTRIAL NON-FOOD CROP	7.3	DF	0.091 lb / a	0.091 lb / a	Broadcast	Aerial	When needed.
AGRICULTURAL UNCULTIVATED AREAS	TERRESTRIAL NON-FOOD CROP	60	DF	0.15 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
BARLEY	TERRESTRIAL FOOD + FEED CROP	48	DF	0.008 lb / a	0.063 lb / a	Broadcast	Aerial	Foliar.
BARLEY	TERRESTRIAL FOOD + FEED CROP	15	DF	0.004 lb / a	NS	Broadcast	Aerial	Foliar.
BERMUDAGRASS	TERRESTRIAL FEED CROP	15	DF	0.014 lb / a	0.023 lb / a	Broadcast	Aerial	Established plantings.
BERMUDAGRASS	TERRESTRIAL NON-FOOD CROP	9.5	DF	0.024 lb / a	NS	Broadcast	Ground.	Dormant.

FORESTRY	FORESTRY	60	DF	0.15 lb / a	0.15 lb / a	Broadcast	Aerial	Foliar.
FORESTRY	FORESTRY	9.5	DF	0.113 lb / a	NS	Broadcast	Aerial	Established plantings.
COMMERCIAL/ INDUSTRIAL LAWNS	TERRESTRIAL NON-FOOD CROP	60	DF	0.075 lb / a	0.15 lb / a	Broadcast	Aerial	Foliar.
DRAINAGE SYSTEMS	AQUATIC NON-FOOD INDUSTRIAL	9.5	DF	0.15 lb / a	NS	Broadcast	Aerial	When needed.
GOLF COURSE TURF	TERRESTRIAL NON-FOOD CROP	60	DF	0.038 lb / a	NS	Broadcast	Ground.	Foliar.
INDUSTRIAL / CONSTRUCTION AREAS (OUTDOOR)	TERRESTRIAL NON-FOOD CROP	60	DF	0.075 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
INDUSTRIAL / CONSTRUCTION AREAS (OUTDOOR)	TERRESTRIAL NON-FOOD CROP	60	DF	0.113 lb / a	0.15 lb / a	High volume spray (dilute).	Ground.	When needed.
INTERMITTENTLY FLOODED AREAS/WATER	AQUATIC NON-FOOD OUTDOOR	9.5	DF	0.15 lb / a	NS	Broadcast	Aerial	When needed.
INTERMITTENTLY FLOODED AREAS/WATER	AQUATIC NON-FOOD OUTDOOR	60	DF	0.15 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
NONAGRICULTURAL RIGHTS-OF-WAY/FENCEROWS/HEDGEROWS	TERRESTRIAL NON-FOOD + OUTDOOR RESIDENTIAL	60	DF	0.15 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
NONAGRICULTURAL RIGHTS-OF-WAY/FENCEROWS/HEDGEROWS	TERRESTRIAL NON-FOOD CROP	9.5	DF	0.15 lb / a	NS	Broadcast	Aerial	When needed.
ORNAMENTAL GRASSES	TERRESTRIAL NON-FOOD CROP	60	DF	0.038 lb / a	0.15 lb / a	Broadcast	Aerial	Established plantings.
ORNAMENTAL LAWNS AND TURF	TERRESTRIAL NON-FOOD CROP	60	DF	0.038 lb / a	NS	Broadcast	Ground.	Foliar.
PASTURES	TERRESTRIAL FEED CROP	20	DF	0.015 lb / a	NS	Broadcast	Aerial	Foliar.
PASTURES	TERRESTRIAL NON-FOOD CROP	60	DF	0.038 lb / a	0.15 lb / a	Broadcast	Aerial	Established plantings.
RANGELAND	TERRESTRIAL FEED CROP	48	DF	0.038 lb / a	0.063 lb / a	Broadcast	Aerial	Established plantings.
RANGELAND	TERRESTRIAL FEED CROP	20	DF	0.015 lb / a	NS	Broadcast	Aerial	Foliar.
RESIDENTIAL	TERRESTRIAL NON-FOOD CROP	12.6	DF	0.091 lb / a	0.091 lb / a	Broadcast	Aerial	When needed.
RECREATIONAL AREAS	TERRESTRIAL NON-FOOD CROP	7.3	DF	0.091 lb / a	0.091 lb / a	Broadcast	Aerial	When needed.
SEWAGE DISPOSAL AREAS	TERRESTRIAL NON-FOOD CROP	60	DF	0.075 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
SUGARCANE	TERRESTRIAL FOOD + FEED CROP	20	DF	0.125 lb / a	NS	Broadcast	Aerial	Preemergence.
SWAMPS/MARSHES/WETLANDS/STAGNANT WATER	AQUATIC NON-FOOD OUTDOOR	9.5	DF	0.15 lb / a	NS	Broadcast	Aerial	When needed.
TRITICALE	TERRESTRIAL FOOD + FEED CROP	20	DF	0.004 lb / a	NS	Broadcast	Aerial	Foliar.
UTILITY POLES / RIGHT-OF-WAY	TERRESTRIAL NON-FOOD CROP	60	DF	0.075 lb / a	0.15 lb / a	Broadcast	Aerial	When needed.
UTILITY POLES / RIGHT-OF-WAY	TERRESTRIAL NON-FOOD CROP	60	DF	0.113 lb / a	0.15 lb / a	Broadcast	Ground.	When needed.
WHEAT	TERRESTRIAL FOOD + FEED CROP	12.5	DF	0.004 lb / a	NS	Broadcast	Aerial	Preemergence.

3.3. Environmental Fate and Transport

The herbicidal active ingredient metsulfuron is also a transformation product of a widely used SU active ingredient iodosulfuron-methyl sodium (PC Code 122021). Iodosulfuron does not persist long in soil, but its major and rapidly forming transformation product is metsulfuron. Metsulfuron is more persistent than iodosulfuron. It is water soluble with a relatively low octanol/water partition, and it is relatively stable to hydrolysis and photolysis. Metsulfuron has been described as mobile in sandy soils with low organic content (based on the FAO Soil Mobility Classification Guidance; the lowest K_{oc} equal to 46). Metsulfuron is not likely to bioaccumulate in aquatic organisms. Metsulfuron is stable to hydrolysis, however some amount of degradation was observed in the laboratory studies conducted at pH 5 resulting in a half-life of approximately three weeks. Therefore, aquatic concentrations are likely to remain relatively stable for one or two weeks and longer for aquatic systems with pH levels higher than five.

Table 3.4 presents the general physical and chemical properties, as well as the available environmental fate properties of metsulfuron.

Table 3.4. General Chemical Properties and Environmental Fate Properties of Metsulfuron.

Parameter	Value	Reference (MRID #) /Comment
Physical/Chemical Parameters		
Molecular mass	381.4 g/mol	ACC 072767
Vapor pressure (20°C)	2.5×10^{-12} torr	ACC 072767
Henry's Law Constant	2.35×10^{-16}	EPISuite v4.0
Water solubility (25°C)	109 mg/L (in water)	Solubility significantly increases with increasing pH. ACC 072767
Octanol-water partition coefficient (K_{OW})	0.018	ACC 072767
Dissociation Constant (pKa)	3.5	ACC 072767
Mobility		
Soil Partitioning Coefficient (Koc, 1/n) †	214, 134, 226, and 46 mL/goc 0.84, 0.78, 0.84, and 0.87 (1/n values)	44143301 Note: data are from a supplemental study, and should not be use quantitatively. EPISuite calculated value is 22 mL/g oc.
Persistence in Water		
Hydrolysis half-life (25°C, pH 5, 7, & 9) †	Stable	ACC 072767
Aqueous photolysis half-life (25°C)†	Stable	ACC 072767
Aerobic aquatic metabolism half-life	No available data	--
Anaerobic aquatic metabolism half-life	35 - 365 days	ACC 260973 41395501
Persistence in Soil		
Soil photolysis†	No available data	--

Parameter	Value	Reference (MRID #) /Comment
Aerobic soil metabolism half-life (25°C)	54.2 days 25.9, and 28 days	44491201 ACC 071434
	Triazine amine‡: 240 days	40340317
Anaerobic soil metabolism†	No available data	--
Field Dissipation		
Terrestrial field dissipation half-life (DT_{50})†	1 – 10.5 months	42016507 Note: sampling/depth of analysis was insufficient to define the extent of leaching (35 cm).
Aquatic Bioconcentration		
Bioconcentration Factor (BCF) in fish	Low Kow indicates low potential to bioaccumulate.	ACC 072767

‡ Major degradate of metsulfuron
† At least one study is currently under review by the Agency.

Metsulfuron is not volatile, having a vapor pressure of 2.5×10^{-12} torr. It is stable to hydrolysis at pH 7 and 9, but at pH 5 some amount of degradation was observed with a reported half-life of about 3 weeks (ACC 072767, 252492). It is also stable to photolysis. The K_{ow} is low and does not indicate a potential to bioaccumulate. The product chemistry data for metsulfuron reports that metsulfuron is a weak acid, with a pKa of 3.5 (ACC 072767). However, data in other submitted studies, as well as open literature data, indicate the dissociation constant is strongly pH dependent. Sulfonylurea herbicides, including metsulfuron, tend to have pK_a values below 6. At pHs of 6 and above, the concentration of the anionic species increases and mobility is expected to increase.

The mobility of metsulfuron varies with soil types, with a strong correlation between the adsorption and organic matter ($r^2 = 0.993$). Adsorption is also correlated with CEC ($r^2 = 0.982$), and clay content ($r^2 = 0.999$). Metsulfuron will have a tendency to leach in sandy, non-clayey inorganic soils. It is important to note that this data was reported in a supplemental study and will only be used qualitatively for risk assessment (see Section 8).

The half-life of metsulfuron in aerobic soil ranged from 25 to 54 days; metsulfuron is considered moderately persistent in soil (ACC 071434, MRID 44491201). Data for one of the major transformation products, 2-amino-4-methoxy-6-methyl 1,3,5-triazine (IN-A4098), show that the transformation product is persistent and will remain in the soil after the parent has degraded (half-life of 240 days; MRID 40340317). Other major transformation products observed in the aerobic soil metabolism study include methyl 2-(aminosulfonyl)benzoate (IN-D5803), and 2-(aminosulfonyl)benzoic acid (IN-581), both of which are hydrolytic degradation products. Two degradates, IN-B5067[1] (major) and IN-F5438[2] (minor), maintain the dual phenyl/triazine ring structure which suggests similar toxicity to the parent. Additional major degradates observed in the laboratory study include carbamoyl guanidine (IN-NC148), and an unidentified compound IN-581. A proposed metabolic pathway is included in **Appendix B**.

[1] Chemical name: (methyl 2-[[[[(4-hydroxy-6-methyl- 1,3,5-triazine-2-yl)amino]carbonyl]amino] sulfonyl]benzoate
[2] Chemical name: 2-[[[[(4-methoxy-6-methyl-1 ,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoic acid

There are no available data for anaerobic metabolism in soil; in the absence of data the compound will be assumed stable to anaerobic metabolism for the purposes of risk assessment.

Metabolic degradation of metsulfuron in aquatic systems is uncertain due to the lack of data for aerobic systems. Data on the anaerobic aquatic metabolism of metsulfuron is variable with half-lives ranging from 35 to 365 days (MRID 41395501 and ACC 260973).

Supplemental terrestrial field dissipation data reported variable results with dissipation half-lives ranging from 1 to 10.5 months (30 – 320 days) for samples taken from 0 to 35 cm (MRID 42016507). It is important to note that the depth of sampling was insufficient to define the extent of leaching for metsulfuron. The compound may leach in low organic matter soils (which is consistent with other sulfonylurea herbicides), however adequate field dissipation data are not available to characterize the extent of potential ground water contamination.

3.3.5. Bioaccumulation

Available data for the bioconcentration potential of metsulfuron in fish indicate a low potential for bioconcentration (ACC 00073657), further the low K_{ow} (0.018; ACC 072767) also indicates a low potential for bioaccumulation.

4. Receptors

Consistent with the process described in the Overview Document (USEPA 2004), the risk assessment for metsulfuron 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 registrant, along with the available open literature, will be used to evaluate the potential direct and indirect effects of metsulfuron 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 identified through EPA's ECOTOXicology (ECOTOX) database, which employs a literature search engine for locating chemical toxicity data for aquatic and terrestrial plants and wildlife, will be considered for the risk assessment. The evaluation of both sources of data may also provide insight into the direct and indirect effects of metsulfuron usage on biotic communities from loss of species that are sensitive to the chemical and from changes in structure and functional characteristics of the affected communities.

A brief summary of the aquatic and terrestrial toxicity data available for the species most sensitive to metsulfuron is provided in Sections 4.1 and 4.2, respectively. A more complete summary of the available data is presented in **Appendix C**. In addition, a summary of ecological incidents associated with metsulfuron and a description of ecosystems potentially at risk are

provided in Sections 4.3 and 4.4, respectively. As noted previously, data on the formation and decline of metsulfuron degradates are minimal, but there are also no data on the potential toxicity of any degradates.

Toxicity to fish and aquatic invertebrates is categorized using the system shown in **Table 4.1** (US EPA, 2004). Toxicity to terrestrial fauna (birds and mammals) is categorized using the system shown in **Table 4.2**. Toxicity categories for plants have not been defined.

Table 4.1. Categories of Acute Toxicity for Aquatic Animals

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

Table 4.2. Categories of Acute Toxicity for Terrestrial Animals

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

4.1. Effects to Aquatic Organisms

The most sensitive of the available aquatic toxicity data from registrant-submitted studies are provided in **Table 4.3**. Any studies available in ECOTOX will be reviewed for the risk assessment. There are no data for estuarine/marine organism, although the lack of toxicity to freshwater organisms suggests these data are not necessary for risk assessment; however, the daphnid lifecycle study is still under review. Based on the available information, metsulfuron is classified as practically nontoxic to fish and invertebrates on an acute exposure basis. Available data indicate both vascular and nonvascular aquatic plants are affected by metsulfuron.

- 850.1300. A daphnid lifecycle study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.

Table 4.3. Aquatic Wildlife Toxicity Profile for Metsulfuron

Taxonomic Group	Species (Common Name)	Endpoint (mg ai/L)	Acute Classification	Reference (MRID)
Freshwater Fish	*Lepomis macrochirus* (Bluegill sunfish)	LC_{50}>150	Practically nontoxic	00125817
	Oncorhyncus mykiss (rainbow trout)	NOAEC=4.5	--	44122801
Freshwater Invertebrates	*Daphnia magna* (Water flea)	LC_{50}>150	Practically nontoxic	00125818

	Chronic data unavailable	NOAEC=na	--	--
Estuarine/marine Fish	No data	--	--	--
Estuarine/marine Invertebrates	No data	--	--	--
Vascular plants	*Lemna minor* (duckweed)	EC_{50}=0.00036 NOAEC=0.00016	--[a]	41773902[b]
Nonvascular plants	*Pseudokirchneriella subcapitata*	EC_{50}=0.031 NOAEC=0.005	--[a]	40639302[b]

[a] Toxicity categories for plants have not been defined.
[b] appears to be most sensitive pending review of other studies

4.2. Effects to Terrestrial Organisms

Table 4.3 summarizes the most sensitive terrestrial toxicity endpoints for metsulfuron, based on an evaluation of the submitted data. If open literature studies are identified through ECOTOX, they will be reviewed for the risk assessment. Metsulfuron is classified as practically nontoxic to terrestrial birds on a subacute dietary exposure basis; acute oral data for mallard are under review and a passerine study is necessary for risk assessment. Metsulfuron is classified as practically nontoxic to mammals on an acute oral exposure basis. Metsulfuron is classified as practically nontoxic to honey bees (*Apis mellifera*) on an acute contact exposure basis.

As an herbicide, metsulfuron is expected to have adverse effects on plants. The required seedling emergence and vegetative vigor studies have been submitted and are in the review process. Until the studies are reviewed, the Agency cannot determine if the data are adequate for risk assessment purposes. However, a cursory review of the studies revealed undefined NOAECs for several species, suggesting possible problems with the studies.

- 850.2100. **An avian acute oral study with a passerine is necessary for risk assessment.** Additionally, an acute oral study with mallard duck is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- 850.4100. A seedling emergence study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.
- 850.4150. A vegetative vigor study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.
- Non-guideline. **Terrestrial Plant Reproduction Study** will be necessary for risk assessment.
- **Seedling emergence and aquatic plant toxicity data necessary for degradate IN-A4098 (2-amino-4-methoxy-6-methyl 1,2,5-triazine).**

Table 4.3 Terrestrial Organism Toxicity Profile for Metsulfuron

Taxonomic Group	Surrogate Species (Common Name)	Endpoint	Acute Classification/ Chronic effect	Reference (MRID)
Birds	*Anas platyrhynchos* (Mallard duck)	LD_{50}>2150 mg ai/kg-bw[a]	Practically nontoxic[a,b]	00125819[a]
	Colinus virginianus (Bobwhite quail)	LC_{50}>5620 mg ai/kg diet	Practically nontoxic	00125821
	Anas platyrhynchos (Mallard duck)	NOAEC=209 mg ai/kg-diet	--	44115702
Mammals	*Rattus norvegicus* (Laboratory rat))	LD_{50}>5000 mg ai/kg-bw	Practically non toxic	47018706
	Laboratory rat	LOAEL=5000 mg ai/kg-diet NOAEC=500 mg ai/kg-diet	Adult body weight gain	00151028
Terrestrial Invertebrates	*Apis mellifera* (Honey bee)	LD_{50}>25 µg/bee	Practically nontoxic	0012210
Seedling emergence	--	--[a]	--	42690101[a]
Vegetative vigor	--	--[a]	--	42690102[a]

[a]data under review (provisional data reported here)
[b]data are incomplete pending passerine submission

Although avian subacute and mammalian acute endpoints are nondefinitive values, preliminary calculation of RQs (not shown) indicate that the highest dose tested (*e.g.* 5000 mg ai/kg-bw) are sufficiently higher than the EECs that further data are not needed at this time.

4.3. Incident Database Review

A review of the Ecological Incident Information System (EIIS) database for incidents involving metsulfuron was conducted on May 24, 2011. Eighteen incidents are reported in the database (Appendix D). Of these, 16 are plant incidents that occurred from use on agricultural areas (including barley and wheat), and uses on conservation reserve, home, and rights of way sites; the incidents ranged in certainty from 'possible' to 'highly probable'. The magnitude of the incidents varied from 50-75 trees to 1400 acres. In addition to the plant incidents, there is one incident with a certainty of 'possible' that reports mortality to algae, 32 bluebirds, 5 Carolina chickadees, 35 unknown birds and an unknown fish in Aiken County SC. Additionally, there is an incident involving 3000 unknown fish, although the certainty that metsulfuron was responsible is 'unlikely.'.

Similarly, a search of the Avian Incident Monitoring System (AIMS; http://www.abcbirds.org/abcprograms/policy/toxins/aims/aims/index.cfm) was conducted. AIMS is a database administered by the American Bird Conservancy that contains publicly

available data on reported avian incidents involving pesticides. The only incident in this database is the one from Aiken County SC reported above.

Pesticide registrants report certain types of incidents to the Agency as aggregate counts of incidents occurring per product per quarter. Seventeen aggregated plant incidents have been reported to the Agency associated with metsulfuron since 1998 and five wildlife incidents (species unknown) have also been reported. Unless further information regarding these aggregate incidents is discovered, it will be assumed that they resulted from registered uses.

4.4. Ecosystems Potentially at Risk

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

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

5. Assessment Endpoints

Assessment endpoints are defined as "explicit expressions of the actual environmental value that is to be protected."[3] Selection of the assessment endpoints is based on valued entities (*e.g.*, fish, birds), the ecosystems potentially at risk (*e.g.*, waterbodies, riparian vegetation, and upland habitats), the migration pathways of metsulfuron (*e.g.*, runoff, drift, *etc.*), and the routes by which ecological receptors are exposed to metsulfuron (*e.g.*, direct contact, *etc.*).

Assessment endpoints for metsulfuron include direct toxic effects on the survival, reproduction, and growth of the receptors, as well as indirect effects, such as reduction of the prey base or modification of habitat. Each assessment endpoint requires one or more "measures of ecological effect," defined as changes in the attributes of an assessment endpoint or changes in a surrogate entity or attribute in response to exposure to a pesticide. Specific measures of ecological effect are generally evaluated based on acute and chronic toxicity information from registrant-submitted guideline tests that are performed on a limited number of organisms. Additional ecological effects data from the open literature will also be considered.

[3] From U.S. EPA (1992). *Framework for Ecological Risk Assessment.* EPA/630/R-92/001.

6. Conceptual Model

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

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

Based on the available data, metsulfuron is water soluble showing increasing solubility with increasing pH. It is stable in neutral to alkaline water, and is also stable to photolytic degradation. Metsulfuron is moderately persistent in soil under aerobic conditions, but assumed to be stable in soil and sediment under anaerobic conditions until data are available. It is mobile in soil and is not volatile. Metsulfuron appears to have the potential to leach into ground water or move offsite into surface water. Given its relatively low K_{ow}, metsulfuron is not expected to bioaccumulate in aquatic or terrestrial food chains.

6.1. Risk Hypothesis

A risk hypothesis describes the predicted relationship among the stressor, exposure, and assessment endpoint response along with the rationale for their selection. For metsulfuron, the following ecological risk hypothesis will be employed for the national-level ecological risk assessment:

Given the uses of metsulfuron and its environmental fate properties, there is a likelihood of exposure to non-target terrestrial and aquatic organisms. When used in accordance with the label, metsulfuron may result in potential adverse effects upon the survival, growth, and reproduction of non-target terrestrial and aquatic organisms.

Additionally, SU herbicides are known to be very toxic to non-target plants. When used in accordance with the label, metsulfuron may move off the site of application by spray drift and/or runoff. This may result in potential risk to the reproduction in terrestrial non-target plants inhabiting adjacent or nearby acreage.

6.2. Conceptual Diagram

The conceptual model used to depict the potential ecological risk associated with the use of metsulfuron (the stressor) assumes that as a pesticide, metsulfuron can adversely affect terrestrial and aquatic organisms (the receptors) if environmental concentrations exceed toxic thresholds as a result of application according to the label directions (**Figures 1 and 2**). Ecological receptors

that may potentially be exposed to metsulfuron include terrestrial and semi-aquatic wildlife (*e.g.*, mammals, birds, terrestrial-phase amphibians and reptiles), terrestrial and semi-aquatic plants, and terrestrial invertebrates (*e.g.*, honey bees). Additionally, given the mobility of metsulfuron, aquatic organisms (*i.e.*, freshwater and estuarine/marine fish and invertebrates, aquatic-phase amphibians, and aquatic plants) are potential receptors in adjacent water bodies through off-site transport of metsulfuron from the application site through runoff, erosion, and spray drift.

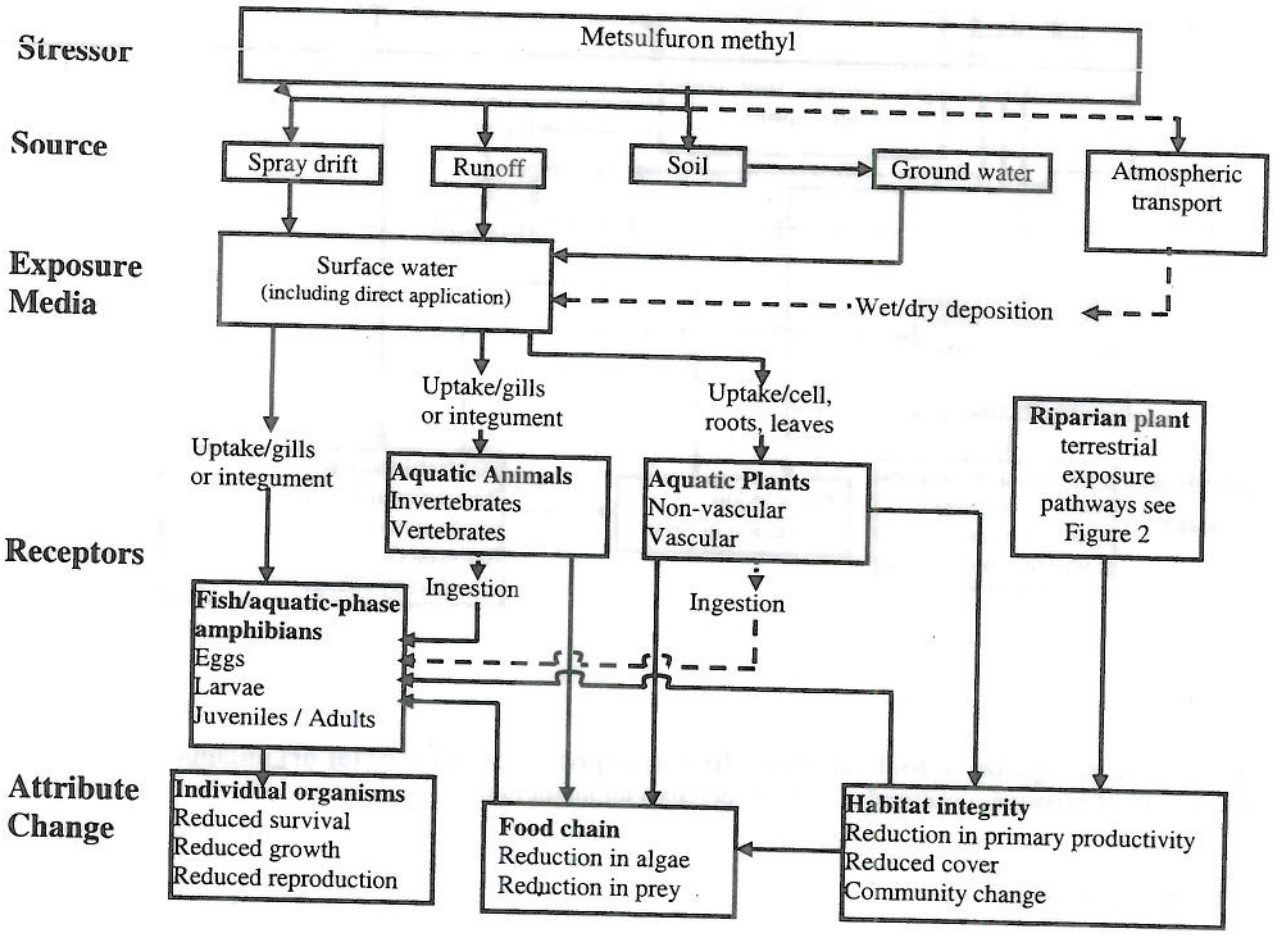


Figure 1. Conceptual model for metsulfuron exposure to aquatic organisms. Dashed lines indicate route of exposure considered of lower importance for metsulfuron.

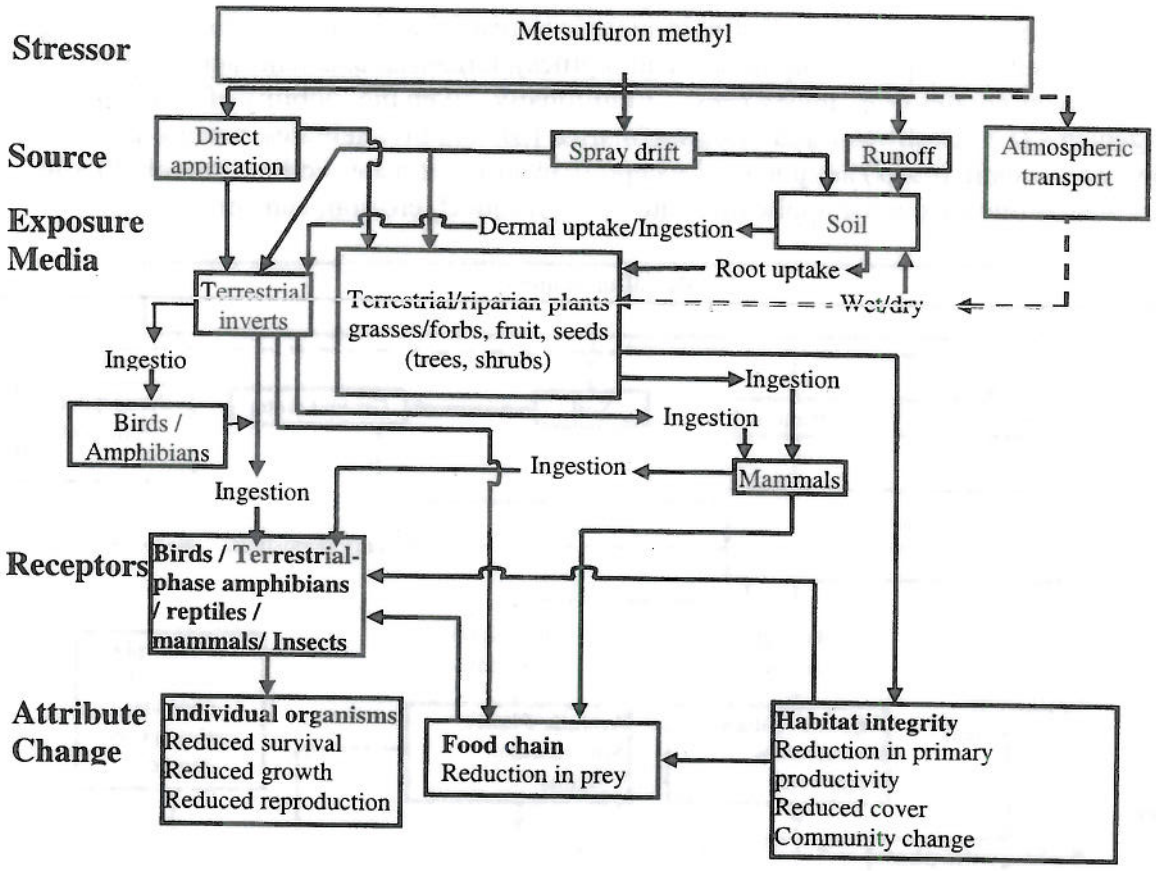


Figure 2. Conceptual model for metsulfuron exposure to terrestrial organisms. Dashed lines indicate route of exposure considered of lower importance for metsulfuron.

7. Analysis Plan

In order to address the risk hypothesis, the potential for adverse effects on the environment will be estimated. The use, environmental fate, and ecological effects of metsulfuron will be characterized and integrated to assess the risks. 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 and/or magnitude of an adverse effect. However, as outlined in the Overview Document (USEPA 2004), the likelihood of effects to individual organisms from particular uses of metsulfuron may be estimated using the probit dose-response slope and either the level of concern (discussed below) or the actual calculated risk quotient value.

This analysis plan will be revisited and may be revised depending upon the information submitted by the public in response to the opening of the Registration Review docket for metsulfuron.

7.1. Stressors of Concern

The stressor of concern in the assessment will be metsulfuron. There are no products of specific mixtures of metsulfuron with other active ingredients registered. The Agency does not routinely include an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator's tank. In the case of the product formulations of active ingredients (that is, a registered product containing more than one active ingredient), each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product containing more than one active ingredient, the data may be used qualitatively or quantitatively in accordance with the Agency's Overview Document and the Services' Evaluation Memorandum (USEPA, 2004; Williams and Hogarth, 2004).

7.2. Measures of Exposure

In order to estimate risks of metsulfuron exposures in aquatic and terrestrial environments, exposure modeling will be based on maximum application rates and methods cited in **Table 3.2.** Measures of exposure are based on aquatic and terrestrial models that predict estimated environmental concentrations (EECs) of metsulfuron. The models used to predict aquatic EECs are the Pesticide Root Zone Model coupled with the Exposure Analysis Modeling System (PRZM/EXAMS). The model used to predict terrestrial EECs on food items is the Terrestrial Residue Exposure model (T-REX). The model used to derive EECs relevant to terrestrial plants is TerrPlant. These models are parameterized using relevant reviewed environmental fate data from registrant submissions and the literature. Model input values will be consistent with the most recent version of the input parameter guidance (Version 2.1; USEPA 2009).

PRZM (v3.12.2; 5/15/05) and EXAMS (v2.98.04.06; 4/25/05) are simulation models coupled with the linkage program shell: PE5 (PRZM EXAMS Model Shell; v5.0; 11/15/06), which incorporates the standard scenarios developed by EFED. The models generate daily exposures and calculated 1-in-10 year EECs of metsulfuron and possibly (depending on the outcome of environmental fate studies) toxicologically significant degradatation products. PRZM simulates pesticide fate and transport as a result of leaching, direct spray drift, runoff and erosion from an agricultural field, and EXAMS estimates environmental fate and transport of pesticides in a surface water body for a 30-year period. The combined model is designed to estimate pesticide concentrations found in water (standard pond) at the edge of the treated field. As such, it provides high-end values of the pesticide concentrations that might be found in ecologically sensitive environments following pesticide application. The location of the field is specific to the crop being simulated using site-specific information on the soils, weather, cropping, and management factors associated with the scenario. The crop/location scenario is intended to represent a high-end exposure site on which the crop is normally grown. Based on historical rainfall patterns, the receiving water body receives multiple runoff events during the years simulated. Weather and agricultural practices are simulated for 30 years so that the 10-year exceedance probability at the site can be estimated. The simulation is generated using 30 years

of meteorological data, encompassing the years from 1961 to 1990. Additional information on these models can be found at: http://www.epa.gov/oppefed1/models/water/index.htm.

The standard scenarios used for ecological pesticide assessments assume application to a 10-hectare agricultural field that drains into an adjacent 1-hectare water body that is 2 meters deep (20,000 m^3 volume) with no outlet. PRZM/EXAMS is used to estimate screening-level exposure of aquatic organisms to metsulfuron. The measure of exposure for aquatic species is the 1-in-10 year return peak or rolling mean concentration. The 1-in-10 year peak is used for estimating acute exposures of direct effects to aquatic organisms. The 1-in-10-year 60-day mean is used for assessing chronic exposure to fish and aquatic-phase amphibians. The 1-in-10-year 21-day mean is used for assessing chronic exposure to aquatic invertebrates.

Exposure estimates for terrestrial organisms assumed to be in the target area or in an area exposed to off-site deposition are derived using the T-REX model (version 1.4.1, 10/09/2008). This model incorporates the Kenaga nomograph, as modified by Fletcher *et al.* (1994), which is based on a large set of field residue data. The upper limit values from the nomograph represent the upper bound of residue values from actual field measurements (Hoerger and Kenaga 1972). The Fletcher *et al.* (1994) modifications to the Kenaga nomograph are based on measured field residues from 249 published research papers, including information on 118 species of plants, 121 pesticides, and 17 chemical classes. Based on these data, T-REX assumes a 35-day foliar dissipation half-life in the absence of other data.

In order to determine if more data are necessary, the Screening Tool for Inhalation Risk (STIR v.1.0) was used to calculate an upper bound estimate of exposure using metsulfuron's vapor pressure and molecular weight for vapor phase exposure as well as the maximum application rate and method of application for spray drift. STIR incorporates results from several toxicity studies including acute oral and inhalation rat toxicity endpoints obtained from the "six-pack" of core studies, which are a series of six guideline studies that are submitted to the Registration Division of the Office of Pesticide Programs for technical and formulated products of a pesticide as well as the most sensitive acute oral avian toxicity endpoint. Based on the results of the STIR model, inhalation exposure alone was not determined to be a potential pathway of concern for avian or mammalian species on an acute exposure basis.

Inhalation exposure via spray drift and/or vapor-phase of the pesticide alone does not appear to be of concern. The analysis of the inhalation route of in STIR does not consider that aggregation with other exposure pathways such as dietary, dermal, or drinking water may contribute to a total exposure that has a potential for effects to non-target animals. However, the Agency does consider the relative importance of other routes of exposure in situations where data indicate that pesticide exposures through other routes may be potentially significant contributors to wildlife risk (USEPA, 2004). The risk assessment will discuss the impact of consideration of other routes of exposure that have been identified as potentially important and the degree of certainty associated with screening-level risk assessment conclusions. Detailed information about STIR v.1.0, as well as the tool, can be found on the EPA's website at:http://www.epa.gov/pesticides/science/models_pg.htm#terrestrial.

The Screening Imbibition Program (SIP v.1.0) was used to calculate an upper bound estimate of exposure using metsulfuron's solubility, the most sensitive acute and chronic avian and mammalian toxicity endpoints. Drinking water exposure alone was determined to be a potential pathway of concern for both avian (and surrogates) and mammalian species on an acute and chronic exposure basis. This route of exposure will be considered further in the risk assessment.

This pathway will be explored further with the development of SIP v.2.0 in the risk assessment for metsulfuron. Detailed information about the SIP v.1.0, as well as the tool, can be found on the EPA's website at http://www.epa.gov/pesticides/science/models_pg.htm#terrestrial.

EECs for terrestrial plants are derived using TerrPlant (v.1.2.2). This model uses estimates of pesticides in runoff and in spray drift to calculate EECs. EECs are based upon solubility, application rate and minimum incorporation depth.

The AgDRIFT (v2.01; May 2001) or AgDISP (v. 8.15) spray drift model may be used to assess exposures of organisms to metsulfuron deposited on terrestrial habitats by spray drift.

7.3. Measures of Effect

Ecological effects data are used as measures of direct and indirect effects to biological receptors. Effects data are obtained from registrant-submitted studies or from literature studies identified by the ECOTOX database.

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

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

In the absence of taxon-specific data, the assessment of risk for direct effects to non-target organisms makes the assumption that toxicity of metsulfuron to birds is similar to terrestrial-phase amphibians and reptiles. The same assumption is made for fish and aquatic-phase

amphibians. In the absence of data for either acute or chronic effects, the conservative assumption will be to presume that metsulfuron is toxic.

7.4. Integration of Exposure and Effects

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

7.5. Deterministic and Probabilistic Assessment Methods

The quantitative assessment of risk will primarily depend on the deterministic point-estimate (RQ) based approach described in the risk assessment. An effort will be made to further qualitatively describe risk using probabilistic tools that the Agency has developed. These tools have been reviewed by FIFRA Scientific Advisory Panels (http://www.epa.gov/scipoly/sap/index.htm) and have been deemed as appropriate means of refining assessments where deterministic approaches have identified risks. Newer tools may be available to assess the routes of exposure (*e.g.* TIM and SWAMP models) and will be applied as appropriate in Registration Review.

7.6.. Endocrine Disruptor Screening Program

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (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.

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. This list of chemicals was selected based on the potential for human exposure through pathways

such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Metsulfuron is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

7.7. Endangered Species Assessment

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

The assessment of effects associated with the registration of metsulfuron is based on an action area. The action area is considered to be the area directly or indirectly affected by the federal action, as indicated by the exceedance of Agency Levels of Concern (LOCs) used to evaluate direct or indirect effects. The Agency's approach to defining the action area under the provisions of the Overview Document (USEPA 2004) considers the results of the risk assessment process to establish boundaries for that action area with the understanding that exposures below the Agency's defined LOCs constitute a no-effect threshold. For the purposes of this assessment, attention will be focused on the footprint of the action (*i.e.*, the area where metsulfuron application occurs), plus all areas where offsite transport (*i.e.*, spray drift, runoff, *etc.*) may result in potential exposure that exceeds the Agency's LOCs. Specific measures of ecological effect that define the action area for listed species include any direct and indirect effects and/or potential modification of its critical habitat, including reduction in survival, growth, and reproduction as well as the full suite of sublethal effects available in the effects literature. Therefore, the action area extends to a point where environmental exposures are below any measured lethal or sublethal effect threshold for any biological entity at the whole organism, organ, tissue, and cellular level of organization. In situations where it is not possible to determine the threshold for an observed effect, the action area will initially be assumed to include all counties where metsulfuron is used in the United States.

7.8. Drinking Water Assessment

The 1998 Tier I drinking water assessments for metsulfuron using GENEEC (surface water) and SCI-GROW (groundwater) resulted in estimated drinking water concentrations (EDWCs) of 0.083 ug/L and 0.012 ug/L, respectively for use on sorghum at a rate of 0.019 lbs a.i./A. Further, a 2002 revised drinking water assessment for metsulfuron use on turf using PRZM-EXAMS

(surface water) and SCI-GROW (groundwater) reported acute surface water concentrations of 1.37 ug/L, chronic surface water concentrations of 0.332 ug/L, and 0.104 ug/L in groundwater.

In order to bring the drinking water exposure assessment up to date with current data, models and simulation model guidance, a new drinking water assessment will be conducted to support future human health dietary risk assessments of metsulfuron. The drinking water exposure assessment will be conducted for the maximum labeled use in support of the human health dietary risk assessment. The drinking water assessment will incorporate model estimates of metsulfuron alone in surface water and ground water including any residues that are determined to be of toxicological concern. Concentrations of metsulfuron in surface waters will be estimated using PRZM/EXAMS (see description above) using the Index Reservoir scenario to estimate environmental concentrations in drinking water rather than the standard pond used with aquatic exposure assessment.

An EDWC of metsulfuron in ground water will be estimated using EFED's Tier I aquatic model SCIGROW (Screening Concentration in Ground Water, version 2.3; 8/8/2003). SCIGROW is a regression model used as a screening tool to estimate pesticide concentrations found in ground water used as drinking water. The output of SCIGROW represents the concentrations that might be expected in shallow unconfined aquifers under sandy soils, which is representative of the ground water most vulnerable to pesticide contamination likely to serve as a drinking water source.

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

7.9. Environmental Monitoring Data

A query of the United States Geological Survey's (USGS) National Water Quality Assessment Program (NAWQA) for detections of metsulfuron in surface water returned 89 detections out of 2,573 samples analyzed (concentrations ranging from 0.004 to 6.72 ug/L; detection frequency of 3.5 %). For groundwater, 10 detections were reported out of 2,441 samples analyzed for metsulfuron (concentrations ranging from 0.003 to 0.23 ug/L; detection frequency of <1 %). Although the detection frequencies are low for surface water and groundwater, these detections illustrate that the potential exists for both surface water and groundwater contamination resulting from metsulfuron use. All monitoring data will be considered to characterize the modeling results and risk estimations for metsulfuron in the environment. States, Tribal Organizations, and other government and non-government organizations are encouraged to submit additional surface water and groundwater monitoring data for metsulfuron.

8.0. Preliminary Identification of Data Gaps

8.1. Environmental Fate

The studies submitted to fulfill environmental fate data requirements for metsulfuron are not sufficient to conduct an exposure assessment; nine data requirements have not been met as stipulated by 40 CFR part 158 Subpart N §158.1300 for all pesticides with use patterns for terrestrial and aquatic food and nonfood applications:

- Photolytic degradation in water (OPPTS guideline # 835.2240). Two studies are currently in review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- Photolytic degradation in soil (OPPTS guideline # 835.2410). One study is currently in review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- There are no acceptable data for aerobic soil metabolism (OPPTS guideline # 835.4100). The guideline stipulates that results from at least four relevant soils of different organic carbon content, pH, clay content, and microbial biomass must be submitted in order to characterize the variability in aerobic biodegradation of metsulfuron in the environment.
- Anaerobic soil metabolism (OPPTS guideline # 835.4200). Currently, there are no available data.
- There is no acceptable aerobic aquatic metabolism study (OPPTS guideline # 835.4300). This study is necessary in order to describe the fate of metsulfuron in surface water. The guideline stipulates that at least two different sediment:water systems be submitted that are similar to the potential use sites in the United States.
- Submission of an acceptable anaerobic aquatic metabolism (OPPTS guideline # 835.4400) study is necessary to understand the degradation of metsulfuron in oxygen-limiting environments.
- There is currently one adsorption/desorption batch equilibrium study (OPPTS guideline # 835.1240) under review by the Agency. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. This study is necessary to understand the mobility and sorption characteristics of metsulfuron.
- An acceptable aquatic field dissipation study (OPPTS guideline # 835.6200) is required for all pesticides with use patterns for aquatic food and nonfood applications.
- Supplemental to the aquatic field dissipation and terrestrial field dissipation studies are the independent laboratory method validation, and environmental chemistry methods used for the field study.

Table 8.1 identifies studies by MRID that offer data for each guideline requirement, as well as study classifications and whether or not further data are needed in order to support risk assessment (*i.e.*, whether there is a data gap).

Table 8.1. Summary of available environmental fate data.

Guideline	Study Title	MRID / ACC No.	Classification	Data Gap?	Comments
835.2120	Hydrolysis	00125823	**Acceptable**	No	This study is acceptable. No hydrolysis observed at pH 7 and 9, long half-life (>30 days) was observed for pH 5. Recommended additional study to describe the hydrolytic fate of the triazine fragment of metsulfuron.

Guideline	Study Title	MRID / ACC No.	Classification	Data Gap?	Comments
		46763805	Under review		Hydrolysis as a function of pH. Study is currently under review by the Agency.
835.2240	Photodegradation in Water	00141831	**Unacceptable**	Yes	Test substance was not incubated at a buffered, constant pH and under sterile conditions.
		00147909	Under review		Aqueous photolysis. Study is currently under review by the Agency.
		46763805	Under review		Direct photolysis rate in water by sunlight. Study is currently under review by the Agency.
		074003	Under review		Study is currently under review by the Agency.
835.2410	Photodegradation on Soil	00141832	**Unacceptable**	Yes	Previous reviews indicated that this study was unacceptable. HPLC data submitted by the registrant upgraded the study to supplemental. However study conditions were not kept constant (e.g., temperature), as well as data are needed addressing the photodegradation of the triazine moiety on soil.
		00153322 ACC 074003	Under review		Study is currently under review by the Agency.
835.4100	Aerobic Soil Metabolism	00125824	**Supplemental**	Yes	This study inadequately identified the metabolism of metsulfuron methyl because there was no monitoring of the triazine moiety.
		00125825	**Unacceptable**		Controls were not provided. Experimental temperatures were not reported. No monitoring was done for the triazine fragment of the parent.
		40340317	**Supplemental**		Study conducted on a major degradate of metsulfuron (triazine moiety). This study satisfies the need for an aerobic soil metabolism study for the triazine amine.
		44491201	**Supplemental**		Duplicate samples were not analyzed at each sampling interval.
835.4200	Anaerobic Soil Metabolism	No data	No data	**Yes**	No data available.
835.4300	Aerobic Aquatic Metabolism	No Data	**No Data**	**Yes**	No data available.
835.4400	Anaerobic Aquatic Metabolism	00141833	**Acceptable**	Yes	Study lacks information on the fate of the triazine moiety. However, ACC 260973 provides supplemental information on triazine moiety. Therefore this study was upgraded from Supplemental to Acceptable.
		41395501	**Supplemental**		Data was missing on the microbial counts before and after the study was conducted. It is uncertain if samples were incubated under dark conditions. It is uncertain if anaerobic conditions were sustained throughout the study.
		42016506	**Unacceptable**		Deficiencies are recorded in the Data Evaluation Record.
		ACC 260973	**Supplemental**		Study does not fulfill guidance. Half-lives should not be used in risk assessment. Study provides supplemental information for the fate of the triazine moiety. Degradates were not studied or quantified.

Guideline	Study Title	MRID / ACC No.	Classification	Data Gap?	Comments
835.1240	Mobility - Adsorption / Desorption	00141834	**Supplemental**	**Yes**	Soil column leaching study. Additional characterization for aged soils is needed. Further mobility on the triazine moiety is needed to characterize the mobility of the parent and major degradates.
		ACC 072767	**Unacceptable**		Friedman (1984) characterization of soils, and detailed analytical methods were missing from original study.
		ACC 072767	**Unacceptable**		Chrzanowski (1984) insufficient procedural and analytical information, further raw data was not included to verify adsorbtion/desorbtion calculations.
		44143301 46155802	**Supplemental**		Data should not be used quantitatively. Study partially fulfills data requirement. Desorption test was only studied at a single application rate, precluding the calculation of valid desorption coefficients. Soils were not properly characterized, and method detection limits were not reported.
		46155803	Under review		Study is currently under review by the Agency.
835.6100	Terrestrial Field Dissipation	42016507	**Ancillary**	**Yes**	Classified ancillary because the study provides some information about the dissipation of metsulfuron at different sites, however the depth of sampling was insufficient, analysis was only done on the parent and total residues (no information was provided on transformation products), and no data was provided on the frozen storage stability of metsulfuron and the major transformation products.
		44854001 44826201	Under review		Study is currently under review by the Agency.
		ACC 260974	**Supplemental**		Cited in R2016052 that E. Regelman reviewed on 7/12/84, further on 10/17/84.
850.1730	Fish Accumulation	00149407	**Acceptable**	No	Low potential for bioconcentration
Environmental Chemistry Methods	ECM Soil	45108502	**Acceptable**	No	ECM for soil.
	ECM Water	47148301	**Acceptable**		ECM and ILV.

8.2. Effects

The available ecological effects data for metsulfuron are largely complete. There are no data on the effect of metsulfuron on estuarine/marine species, although the lack of toxicity to freshwater species suggests that these data are not necessary. However, the chronic daphnid study is still under review; EFED will not know until the review is complete if the data are sufficient for risk assessment. There are no data for acute oral effects on avian species; a study with a passerine is necessary for risk assessment and study with mallard duck is under review. The data for terrestrial plants (seedling emergence and vegetative vigor) are under review and until the review is complete, EFED will not know if the data are sufficient for risk assessment. However, a cursory look at the studies suggests that valid no-effect levels were not achieved for several

species, suggesting problems with the studies. The available effects studies for metsulfuron are presented in **Tables 8.2-8.4.**

Seedling emergence and aquatic plant toxicity data necessary for IN-A4098 (a triazine amine). Existing data on saccharin will be used to estimate toxicity of 2-(aminosu1fonyl)benzoic acid (IN-581). The remaining degradates (**Appendix B**) retain the sulfonyl urea moiety and will be consider equally toxic to the parent unless data are submitted.

Terrestrial plants are typically very sensitive to sulfonylurea urea herbicide exposure. There is evidence[4] to suggest plant reproduction may be affected by sulfonylurea herbicides at levels below effects on vegetative growth or visual injury (Fletcher *et al.*, 1993). Uncertainty regarding the potentially greater sensitivity of terrestrial plant reproduction has been discussed extensively in the environmental fate and effects RED assessment for chlorsulfuron (D330621). Therefore, to the extent that terrestrial plant reproduction are more sensitive to metsulfuron than growth endpoints, risks to terrestrial plants may be underestimated in this risk assessment. Additional information on the reproductive toxicity of metsulfuron to terrestrial plants would help address this uncertainty.

- 850.1300. A daphnid lifecycle study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- 850.2100. **An avian acute oral study with a passerine** using TGAI is necessary for risk assessment. Additionally, an acute oral study with mallard duck is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment.
- 850.4100 (850.4225). A seedling emergence study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.
- 850.4150 (850.4250). A vegetative vigor study is under review. Until the review is complete, EFED cannot be certain the data are sufficient for risk assessment. However, provisional review suggests there may be issues with the study.
- Non-guideline. **Terrestrial Plant Reproduction Study** using TGAI will be necessary for risk assessment.
- **Seedling emergence and aquatic plant toxicity data necessary for degradate IN-A4098 (2-amino-4-methoxy-6-methyl 1, 3, 5-triazine).**

TABLE 8.2. Available ecological effects data for terrestrial animals exposed to metsulfuron

Guideline	Description	MRID/ Accession	Classification	Data Gap?	Comments
850.2100	Avian oral toxicity	00125819	Under review	Yes*	*Avian acute oral toxicity data are not available for passerine species. Mallard data are under review.
850.2200	Avian dietary toxicity	00125820 00125821	Acceptable Acceptable	No	
850.2300	Avian reproduction	44115701 44115702	Acceptable Acceptable	No	

[4] Snipes *et al.* 1992, Bansal *et al.* 1999; Fletcher *et al.* 1993, 1995,1996; Bhatti *et al.* 1995; Al-Khatib *et al.* 1992; Boutin *et al.* 2000; Asghari and Evans 1992

Guideline	Description	MRID/ Accession	Classification	Data Gap?	Comments
850.3020	Honeybee acute contact toxicity	00122010	Acceptable	No	

TABLE 8.3. Available ecological effects data for aquatic animals exposed to metsulfuron.

Guideline	Description	MRID/ Accession	Classification	Data Gap?	Comments
850.1075	Freshwater fish – Acute toxicity	00125816	Acceptable	No	Although estuarine/marine data are unavailable for metsulfuron, the lack of toxicity in the freshwater organisms suggests these data are unnecessary for the risk assessment. However, if the review of the daphnid lifecycle study indicates potential toxicity, estuarine/marine data may be necessary. An ACR will be used to determine if data are needed.
		00125817	Acceptable		
		45791501	Under review		
850.1075	Saltwater fish – Acute toxicity	None		Yes	
850.1010	Freshwater invertebrates – Acute toxicity	40977602	Acceptable	No	
		00098507	Acceptable		
850.1025 850.1035	Saltwater invertebrates –Acute toxicity	00098508	Acceptable	No	
		00098509	Acceptable		
		41000701	Supplemental		
850.1300	Freshwater invertebrate – life cycle test	44704901	Under review	**Yes**[a]	
850.1350	Saltwater invertebrates – life cycle test	None	--	Yes	
850.1400	Freshwater fish – early life stage test	44122801	Acceptable	No	
850.1400	Saltwater fish – early life stage test	--	--	Yes	

[a]data are necessary pending review

TABLE 8.4. Available ecological effects data for plants exposed to metsulfuron.

Guideline	Description	MRID	Classification	Data Gap?	comments
850.4100 (850.422)	Terrestrial Plant toxicity: Tier II seedling emergence	44050301	Under review	**Yes**[a]	The terrestrial plant studies under review appear to have deficiencies; however, until the review is complete, EFED will not know if the data are
850.4150 (850.225)	Terrestrial Plant toxicity: Tier II vegetative vigor	44050301	Under review	**Yes**[a]	

Guideline	Description	MRID	Classification	Data Gap?	comments
850.5400	Aquatic Plant Growth: algae	40639302 45109108 45109109 44244001 44244002 44420901 44650101 45791504 46319201	Acceptable Acceptable Acceptable Acceptable Acceptable Under review Under review Under review Under review	No	sufficient for risk assessment. Additionally, a number of aquatic plant studies are under review.
850.4400	Aquatic Plant Growth: vascular plants	41773902 45791503 45791505	Supplemental Under review Under review	No	

[a]data are necessary pending review

8. References

Open Literature Citations

Fletcher, J.S., J.E. Nellessen, and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. Environ. Tox. Chem. 13:1383-1391.

Hoerger, F., and E.E. Kenaga. 1972. Pesticide residues on plants: Correlation of representative data as a basis for estimation of their magnitude in the environment. In F. Coulston and F. Korte, *eds*., Environmental Quality and Safety: Chemistry, Toxicology, and Technology, Georg Thieme Publ, Stuttgart, West Germany, pp. 9-28.

Nakata, M. 1991. The mode of action of chlorsulfuron in culture cells of tobacco and hamster. J. Pest. Sci. 16:583-590

U.S. Fish and Wildlife Service (USFWS) and National Marine Fisheries Service (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.

USEPA. 2004. 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.

USEPA. 1998. Guidelines for Ecological Risk Assessment. Risk Assessment Forum, Office of Research and Development, Washington, D.C. EPA/630/R-95/002F. April 1998. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=30759

Willis, G.H. and L.L. McDowell. 1987. Pesticide Persistence on Foliage in Reviews of Environmental Contamination and Toxicology. 100:23-73.

Submitted Fate Studies

161-1 Hydrolysis

MRID	Citation Reference
125823	Friedman, P. (19??) Hydrolysis of 14C-Phenyl-DPX-T6376: Document No. AMR-62-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-I)

835.2110 Hydrolysis as a function of pH

MRID	Citation Reference
46763805	Wasser, C. (2003) Laboratory Abiotic Transformation Studies Rotam Metsulfuron-methyl Technical: (Final Report). Project Number: A/1147, A1147/10, A1147/18. Unpublished study prepared by Anadiag S.A. 131 p.

161-2 Photodegradation-water

MRID	Citation Reference
141831	Friedman, P. (1984) Aqueous Photolysis of [carbon radiolablled]- DPX-T6376. Unpublished study prepared by E. I. du Pont de Ne- mours and Co., Inc. 19 p.
147909	Harvey, J. (1981) Phytolysis of [Carbon 14]-DPX-5648: [Metsulfu- ron]: Document No. AMR-03-81. Unpublished study prepared by E. I. du Pont de Nemours & Co., Inc. 14 p.
153321 Accession No. 074003	McFetridge, R.D. and G.E. Cadwgan (1985) Photodegradation of [triazine-2-14C]metsulfuron methyl in water. Document No. AMR-451-85. E.I. du Pont de Nemours and Company, Wilmington, DE. Acc. No. 074003. (Exhibit 1).

835.2210 Direct photolysis rate in water by sunlight

MRID	Citation Reference

46763805	Wasser, C. (2003) Laboratory Abiotic Transformation Studies Rotam Metsulfuron-methyl Technical: (Final Report). Project Number: A/1147, A1147/10, A1147/18. Unpublished study prepared by Anadiag S.A. 131 p.

161-3 Photodegradation-soil

MRID	Citation Reference
141832	Friedman, P. (19??) Photodegradation of [carbon radio labelled]-Phenyl-DPX-T6376 on Soil. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 13 p.
153322 Accession No. 074003	Buchta, R.C. (1985) Photodegradation of [triazine-2-14C]metsulfuron methyl on Soil. Document No. AMR-450-85. E.I. du Pont de Nemours and Company, Wilmington, DE. Acc. No. 074003. (Exhibit 2).

162-1 Aerobic soil metabolism

MRID	Citation Reference
125824	Friedman, P. (19??) Aerobic Soil Metabolism of 14C-Phenyl-labeled-DPX-T6376: Document No. AMR-75-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-J)
125825	Chrzanowski, R. (1982) 14C-DPX-T6376 Aerobic Soil Dissipation Study in the Greenhouse: Document No. AMR-89-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-K)
146613	Rhodes, B. (1985) Aerobic Soil Metabolism of [2-(Carbon 14)] 4-Methoxy-6-methyl-1, 3, 5-Triazin-2-Amine: (Interim Report): Report No. AMR-408-85. Unpublished study prepared by E. I. du Pont de Nemours & Co., Inc. 19 p.
40340317	Rhodes, B. (1986) Aerobic Soil Metabolism of [2-Carbon 14] 4-Methoxy-6-methyl-1,3,5-triazin-2-amine: Rept. No. AMR-408-85. Unpublished study prepared by E.I. du Pont de Nemours & Co., Inc. 26 p.
44491201	Gorman, M.; Haney, P.; Li, Y. (1997) Aerobic Soil Metabolism of (carbon 14)-DPX-T6376: Lab Project Number: AMR 3768-96: 43232. Unpublished study prepared by ABC Labs., Inc. and DuPont Agricultural Products. 146 p.

162-2 Anaerobic soil metabolism

MRID	Citation Reference

147907	E. I. du Pont de Nemours & Co., Inc. (1985) Metasulfuron Methyl Environmental Fate Data Review. Unpublished study. 41 p.

162-3 Anaerobic aquatic metab.

MRID	Citation Reference
141833	Friedman, P. (19??) Anaerobic Aquatic Metabolism of (carbon radio labelled)-Phenyl-Metsulfuron Methyl. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 23 p.
41395501	Swanson, M. (1988) Anaerobic Aquatic Metabolism of ?Triazine-2-Carbon 14|Metsulfuron Methyl: Lab Project Number: AMR-1140-88. Unpublished study prepared by E. I. du Pont de Nemours & Co., Inc. 61 p.
42016506	Swanson, M. (1988) Anaerobic Aquatic Metabolism of ?Triazine-2-Carbon 14|-Metsulfuron Methyl: Lab Project Number: AMR-1140-88. Unpublished study prepared by E.I. du Pont de Nemours and Co., Inc. 61 p.
Accession No. 260973	Chrzanowiski, R.L. (1984a) Degradation of 14C-DPX-W4189 in Anaerobic Aquatic Environments. Document No. AMR-38-81. E.I. du Pont de Nemours and Company, Wilmington, DE. Acc. No. 260973.

163-1 Leach/adsorp/desorption

MRID	Citation Reference
141834	Chrzanowski, R. (19??) Soil Column Leaching Studies with [carbon radio labelled]-DPX-T6376. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 19 p.
141835	Friedman, P. (1981) Adsorption of (Carbon radiolabelled)-DPX-T6376 on Soil. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 7 p.
147907	E. I. du Pont de Nemours & Co., Inc. (1985) Metasulfuron Methyl Environmental Fate Data Review. Unpublished study. 41 p.
44143301 or 46155802	Li, Y.; McFetridge, R. (1996) Batch Equilibrium (Adsorption/Desorption) Study of a Metabolite, Triazine Amine (IN-A4098), of DPX-T6376 on Soil: Lab Project Number: AMR 3656-95. Unpublished study prepared by DuPont Agricultural Products. 59 p.
46155802	Li, Y.; McFetridge, R. (1996) Batch Equilibrium (Adsorption/Desorption) Study of a Metabolite, Triazine Amine (IN-A4098), of DPX-T6376 on Soil. Project Number: AMR/3656/95. Unpublished study prepared by E.I. du Pont de Nemours and Company. 59 p.
46155803	Yeomans, P.; Swales, S. (2000) (Carbon 14) IN-A4098:

Adsorption/Desorption in Soil. Project Number: DUPONT/3832, 3832, 550/80. Unpublished study prepared by Covance Laboratories, Ltd. 52 p.

164-1 Terrestrial field dissipation

MRID	Citation Reference
131086	E.I. du Pont de Nemours & Co., Inc. ?Environmental: DPX-T6376 DF Weed Killer|. (Compilation; unpublished study received Jul 8, 1983 under 352-EX-11; CDL:071766-A)
147910	Anderson, J.; Harvey, J. (1984) Field Soil Dissipation Study of DPX-T6376 in Delaware, North Carolina, Florida, and Mississippi: [Metsulfuron]: Document No. AMR-117-83. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 28 p.
42016507	Rapisarda, C.; Scott, M. (1986) Field Soil Dissipation of ?Phenyl (U)-Carbon-14|-Metsulfuron Methyl on United States and Canadian Soils: Lab Project Number: AMR-476-86. Unpublished study prepa- red by E.I. du Pont de Nemours and Co., Inc. 46 p.
44826201	McMillan, J. (1999) Field Soil Dissipation of (carbon-14) Metsulfuron Methyl Following Application of Ally Herbicide: Lab Project Number: AMR 3299-95: 960019. Unpublished study prepared by E.I. du Pont de Nemours and Company and Harris Laboratories, Inc. 161 p.
44854001	McMillan, J. (1999) Field Soil Dissipation of (carbon-14)Metsulfuron Methyl Following Application of Ally Herbicide: Revision No. 1: Lab Project Number: AMR 3299-95: 960019. Unpublished study prepared by DuPont Agricultural Products, and Harris Laboratories, Inc. 161 p.
ACC 260974	Han, J.C.Y. (1981) 14C-DPX-W4189 Soil Disappearance Studies in the Field: Document No. AMR-54-81. (Unpublished study received Nov 13, 1981 under 352-404; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, Del.; CDL:070470-M) **This is study done with 118601 Chlorsulfuron**

164-2 Aquatic field dissipation

MRID	Citation Reference
141833	Friedman, P. (19??) Anaerobic Aquatic Metabolism of (carbon radio labelled)-Phenyl-Metsulfuron Methyl. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 23 p.

164-5 Long term soil dissipation

MRID	Citation Reference
145009	Anderson, J.; Harvey, J. (19??) Field Soil Dissipation study of DPX-T6376 in Delaware, North Carolina, Florida, and Mississippi. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc. 28 p.

165-4 Bioaccumulation in fish

MRID	Citation Reference
149407	Han, J.; Anderson, J. (1984) Residue Studies with [Carbon-14] Metsulfuron Methyl in Bluegill Sunfish: Document No. **AMR-81-82**. Unpublished study prepared by E. I. du Pont de Nemours & Co. 29 p.
138701	Han, J. (1982) Residue Studies with (14C)-DPX-T6376 in Bluegill Sunfish: Document No. **AMR-81-82**. (Unpublished study received Feb 17, 1984 under 352-EX-111; submitted by E. I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:252492-A)

Non Guideline Selections

45108502	Wrede, A. (2000) Enforcement Method for Soil by LC-MS/MS: Metsulfuron-methyl (AE F075736) and Iodosulfuron-Methyl-Sodium (AE F115008): Lab Project Number: C006394: EM F13/99-0. Unpublished study prepared by Hoechst Schering AgrEvo GmbH. 38 p.
47148301	Yang, J. (2007) Preliminary Analysis and Enforcement Analytical Method of Metsulfuron-methyl TGAI- Validation of Analytical Methodology for the Assay of Active Ingredient and Related Significant Impurities of Metsulfuron-methyl TGAI and Subsequent 5-Batch Analysis of Metsulfuron-methyl TGAI . Project Number: NC/2007/007, NC2007007B, NC2007007A. Unpublished study prepared by Arysta Life Sciences North America Corporation. 96 p.

Submitted Effects Studies

71-1 Avian Single Dose Oral Toxicity

MRID	Citation Reference

125819	Under review	Fink, R.; Beavers, J.; Brown, R.; et al. (1981) Acute Oral LD50-- Mallard Duck: H-14,028: Project No. 112-125; HLO-359-81. Final rept. (Unpublished study received Feb 14, 1983 under 352-EX- 111; prepared by Wildlife International Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL: 071434-E)

71-2 Avian Dietary Toxicity

MRID		Citation Reference
125820 ACC 71434	2016059	Fink, R.; Beavers, J.; Brown, R.; et al. (1981) Eight-day Dietary LC50-- Mallard Duck: H-14,028: Project No. 112-124; HLO-455-81. Final rept. (Unpublished study received Feb 14, 1983 under 352- EX-111; prepared by Wildlife International Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL: 071434-F)
125821 ACC 71434	2016060	Fink, R.; Beavers, J.; Brown, R.; et al. (1981) Eight-day Dietary LC50-- Bobwhite Quail: H-14,028: Project No. 112-123; HLO-460-81. Final rept. (Unpublished study received Feb 14, 1983 under 352- EX-111; prepared by Wildlife International Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL: 071434-G)

71-4 Avian Reproduction

MRID		Citation Reference
44115701	2016080	Beavers, J.; Foster, J.; Mitchell, L. et al. (1996) DPX-T6376-141 (Metsulfuron Methyl): A Reproduction Study with the Northern Bobwhite (Colinus virginianus): (Final Report): Lab Project Number: 112-413: AMR 3412-95: CHR27. Unpublished study prepared by Wildlife Int'l. Ltd. 169 p.
44115702	2016082	Beavers, J.; Foster, J.; Mitchell, L. et al. (1996) DPX-T6376-141 (Metsulfuron Methyl): A Reproduction Study with the Mallard (Anas platyrhynchos): (Final Report): Lab Project Number: 112-414: AMR 3413-95: CHR27. Unpublished study prepared by Wildlife Int'l. Ltd. 171 p.

72-1 Acute Toxicity to Freshwater Fish

MRID		Citation Reference
125816	2016056	Muska, C.; Hall, C. (1982) 96-hour LC50 to Rainbow Trout: Haskell Laboratory Report No. 515-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-B)
125817	2016057	Phillips, F.; Hall, C. (1982) 96-hour LC50 to Bluegill Sunfish: Haskell

		Laboratory Report No. 154-82. (Unpublished study re- ceived Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-C)
45791501	Under review	Hoke, R. (1999) IN-F5438: Static, Acute, 96-Hour Limit Test to Rainbow Trout, Oncorhynchus mykiss: Lab Project Number: 12948: 228: DUPONT-3227. Unpublished study prepared by E.I. duPont de Nemours and Company. 29 p.

72-2 Acute Toxicity to Freshwater Invertebrates

MRID		Citation Reference
125818	2016058	Phillips, F.; Hall, C. (1982) 48-hour LC50 to Daphnia magna: Has- kell Laboratory Report No. 157-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-D)
45791502	Under review	Hoke, R. (1999) IN-F5438: Static, Acute, 48-Hour Limit Test to Daphnia magna: Lab Project Number: 12948: 241: DUPONT-3228. Unpublished study prepared by E.I. duPont de Nemours and Company. 29 p.

72-4 Fish Early Life Stage/Aquatic Invertebrate Life Cycle Study

MRID		Citation Reference
44122801	2016072	Kreamer, G. (1996) Early Life-Stage Toxicity of DPX-T6376-141 (Metsulfuron Methyl) to Rainbow Trout, (Oncorhynchus mykiss): Lab Project Number: HLR 182-96: 10352: 182-96. Unpublished study prepared by DuPont Haskell Lab for Toxicology and Industrial Medicine. 400 p.
44704901	Under review	Drottar, K.; Krueger, H. (1998) DPX-T6376: A Semi-Static Life-Cycle Toxicity Test with the Cladoceran (Daphnia magna): Final Report: Lab Project Number: 5025-98: 112A-176. Unpublished study prepared by Wildlife International Ltd. 76 p.

122-2 Aquatic plant growth

MRID		Citation Reference
40639302	2016065	Forbis, A. (1987) Acute Toxicity Screen of Metsulfuron Methyl to Selenastrum capricornutum Printz: ABC Final Report #35848. Un- published study prepared by Analytical Bio-Chemistry Laborator- ies, Inc. 17 p.
41773902	2016066	Douglas, M.; Handley, J. (1988) An Assessment of the Inhibitory Ef- fect of DPX-T6376 Technical on the Growth of Duckweed (Lemna minor):

		Lab Project Number: DPT 186(B)/881173. Unpublished study prepared by Huntingdon Research Centre Ltd. 20 p.
44244001	2016068 2016076	Hicks, S. (1997) DPX-T6376: Influence on Growth and Reproduction of Anabaena flos-aquae: (Final Report): Lab Project Number: AMR 3838-96: 43308: AMR 3840-96. Unpublished study prepared by ABC Labs., Inc. 65 p.
44244002	2016069 2016077	Hicks, S. (1997) DPX-T6376: Influence on Growth and Reproduction of Skeletonema costatum: (Final Report): Lab Project Number: AMR 3840-96: 43306: ABC 43306. Unpublished study prepared by ABC Labs., Inc. 65 p.
44650101	Under review	Sloman, T.; Leva, S. (1998) Metsulfuron Methyl 60 DF: Influence on Growth and Growth Rate of the Green Alga Selenastrum Capricornutum: Lab Project Number: AMR 4464-97: MR 12119. Unpublished study prepared by E.I. du Pont de Nemours and Company. 45 p.
45088212	Open lit	Fairchild, J.; Ruessler, D.; Haverland, P. et al. (1996) Comparative Sensitivity of Selenastrum capricornutum and Lemna minor to Sixteen Herbicides. **Archives of Environmental Contamination and Toxicology 32:353-357.**
45791504	Under review	Sloman, T. (1999) IN-F5438: Influence on Growth and Growth Rate of the Green Alga Selenastrum capricornutum: Lab Project Number: 12948: 280: DUPONT-3156. Unpublished study prepared by E.I. duPont de Nemours and Company. 39 p.
46319201	Under review	Ferrell, B. (2004) **IN-B5067**: Influence on Growth and Reproduction of Lemna gibba G3. Project Number: DUPONT/12740, 14650. Unpublished study prepared by Dupont Haskell Laboratory. 35 p.

123-1 Seed germination/seedling emergence and vegitative vigor

MRID		Citation Reference
44050301	Under review	Heldreth, K.; McKelvey, R. (1996) Influence of Metsulfuron Methyl (DPX-T6376) on Seedling Emergence and Early Growth and Vegetative Vigor of Several Terrestrial Plants: Lab Project Number: AMR 3242-94: MR 10180. Unpublished study prepared by E.I. du Pont de Nemours and Co. 413 p. {Relates to L0000011}.
45213701	Under review	Heldreth, K. (2000) Metsulfuron Methyl/Thifensulfuron Methyl (DPX-E8698) 75WG (1:10): A Greenhouse Study to Investigate the Effects on Several Terrestrial Plants Following Foliar Exposure: Lab Project Number: 3757. Unpublished study prepared by DuPont Agricultural Products. 84 p. {OPPTS 850.4250}

123-2 Aquatic plant growth

MRID		Citation Reference

41773902	2016066	Douglas, M.; Handley, J. (1988) An Assessment of the Inhibitory Ef- fect of DPX-T6376 Technical on the Growth of Duckweed (Lemna minor): Lab Project Number: DPT 186(B)/881173. Unpublished study prepared by Huntingdon Research Centre Ltd. 20 p.
44420901	Under review	Hicks, S. (1997) DPX-T6376: Influence on Growth and Reproduction of Navicula pelliculosa: Lab Project Number: AMR 3841-96: 43307: ABC 43307. Unpublished study prepared by ABC Laboratories, Inc. 59 p.
45791503	Under review	Sloman, T. (1999) IN-F5438: Influence on Growth and Reproduction of Lemna gibba G3: Lab Project Number: 12948: 328: DUPONT-3252. Unpublished study prepared by E.I. duPont de Nemours and Company. 38 p.
45791505	Under review	Sloman, T. (2000) IN-00581: Influence on Growth and Reproduction of Lemna gibba G3: Lab Project Number: 13141: 328: DUPONT-3551. Unpublished study prepared by E.I. duPont de Nemours and Company. 45 p.
45109112	2016073	Sowig, P. and O. Weller (1998) AE F075736 (Metasulfuron-methyl) Substance, Technical, Metabolite of AE F115008, Code: AE F075736 00 1C92 0001, Duckweed (Lemna gibba G3) Growth Inhibition Test. Laboratory: Hoechst Schering AgrEvo GmbH, Umweltforschung Oekobiologie, D-65926 Frankfurt am Main. Sponsor: Aventis CropScience USA LP (Formerly AgrEvo USA Co.) Little Falls Centre One, 2711 Centerville Road, Wilmington, DE 19808.
45109108	2016074	Heusel, R., O. Weller and H. Gosch (1998) AE F075736 (Metasulfuron-methyl) Substance, Technical, Metabolite of AE F115008, Code: AE F075736 00 1C92 0001, Algal Growth Inhibition Pseudokirchnerielia subcapitata; Hoechst Schering AgrEvo GmbH, Umweltforschung Oekobiologie, D-65926 Frankfurt am Main. Federal Republic of Germany. Sponsor: Aventis CropScience USA LP (Formerly AgrEvo USA Co.) Little Falls Centre One, 2711 Centerville Road, Wilmington, DE 19880-0402.
45109109	2016075	Sowig, P., O. Weller and H. Gosch (1998) AE F075736 (Metasulfuron-methyl) Substance, Technical, Metabolite of AE F115008, Code: AE F075736 00 1C92 0001, Algal Growth Inhibition; Navicula pelliculosa. Hoechst Schering AgrEvo GmbH, Umweltforschung Oekobiologie, D-65926 Frankfurt am Main, Federal Republic of Germany. Sponsor: Aventis CropScience USA LP (Formerly AgrEvo USA Co.) Little Falls Centre One, 2711 Centerville Road, Wilmington, DE 19880-0402.
47954502	Open lit	Ma, J.; Liang, W.; Xu, L.; et al. (2000) Acute Toxicity of 33 Herbicides to the Green Alga Chlorella pyrenoidosa. Bulletin of Environmental Contamination and Toxicology 66:536-541.
47954503	Open lit	Ma, J. (2001) Differential Sensitivity to 30 Herbicides Among Populations of Two Green Algae Scenedesmus obliquus and Chlorella pyrenoidosa. Bulletin of Environmental Contamination and Toxicology 68:275-281.
47954505	Open lit	Ma, J.; Lin, F.; Wang, S.; et al. (2004) Acute Toxicity Assessment of 20 Herbicides to the Green Alga Scenedesmus quadricauda (Turp.) Breb. Bulletin of Environmental Contamination and Toxicology 72: 1164-1171.

141-1 Honey bee acute contact

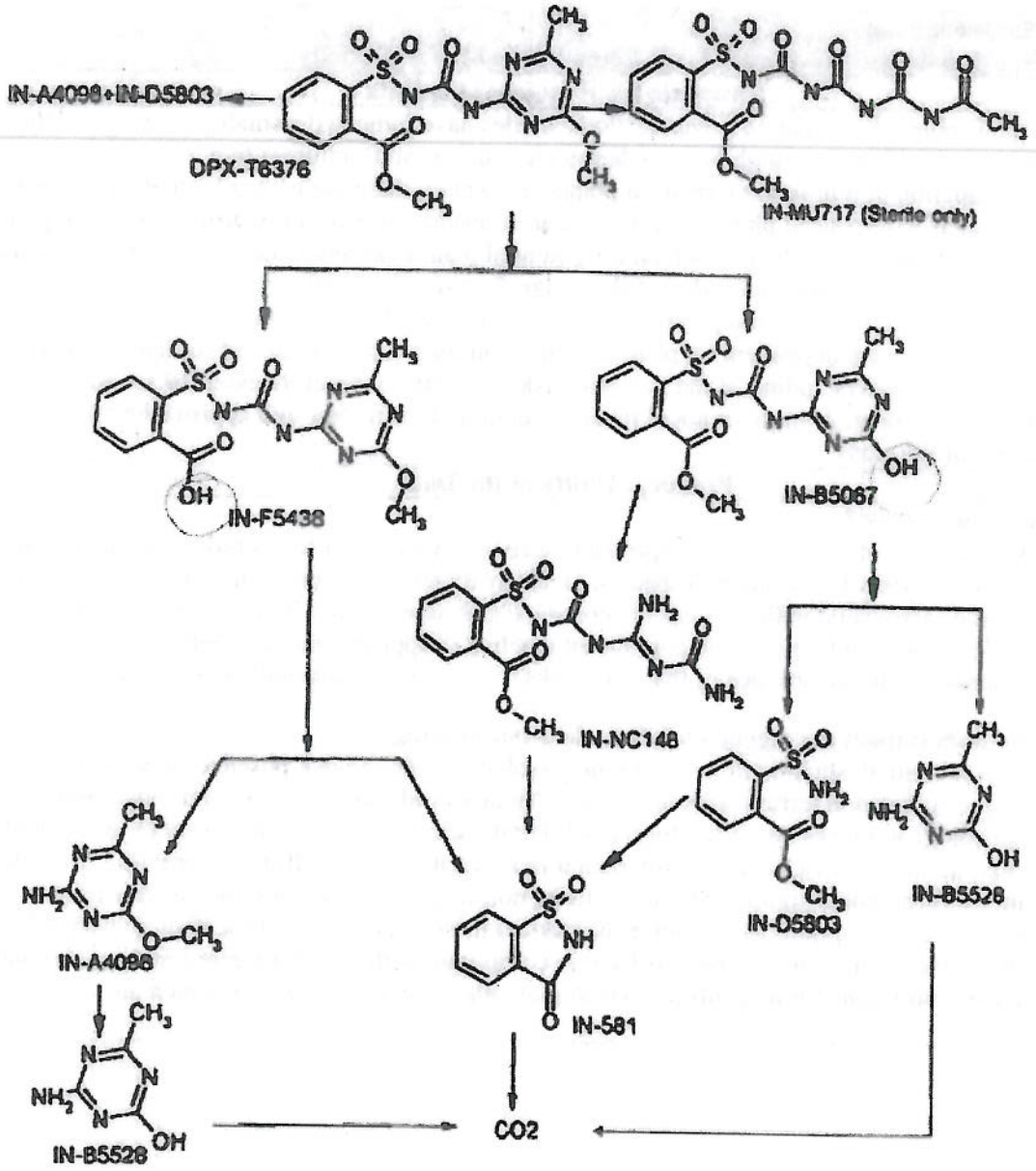
MRID		Citation Reference
141829	2016061	Meade, A. (1984) Acute Contact LD50 Study In Honey Bees (Apis-Mellifera L.) With INT 6376: Final Report: Project No. ABM-84-4. Unpublished study prepared by E. I. Du Pont De Nemours and Co., Inc. 11 p.

Appendix A. Justification for Special Study

Guideline Number: none Study Titles: Special Study for Non-Target Plant Reproductive Toxicity
Rationale for Requiring the Data
As stated in the Problem Formulation, investigations/studies have indicated a small percentage of the label application rate of low dose high potency herbicides such as sulfonylureas (e.g. metsulfuron) may impact the reproduction of non-target terrestrial plants. However, there are no available data on adverse reproductive impacts to terrestrial plants from metsulfuron residues due to spray drift. Terrestrial plant reproductive toxicity data would help to screen for potential plant risks associated with metsulfuron use. Plants form the basis of most habitats and contribute significantly to overall environmental quality. The loss of plant reproductive output could potentially have an adverse effect on animals, both invertebrates and vertebrates, as many are dependent on plant reproduction for a food source and for habitat quality and structure. A solid understanding of the potential risks to plants is therefore essential for sound environmental management. A study protocol must be submitted for review and approved by the Agency prior to initiation of the study.
Practical Utility of the Data
How will the data be used? The data will be used to estimate potential reproductive risks to non-target terrestrial plants, including the likelihood of potential risks to endangered species, either by direct effects or by indirect effects, and to reduce uncertainties associated with the current ecological risk assessment. By refining the assessment, the Agency will be able to determine whether current labeling is appropriate and whether further mitigation is necessary. In the absence of this data, risks to terrestrial plants will be presumed. **How could the data impact the Agency's future decision-making?** These data, once submitted, should allow the Agency to characterize the risk posed to plant reproductive processes from metsulfuron in terrestrial ecosystems. Primary producers (*i.e.* plants) provide food and habitat vital to ecological processes. Therefore, a solid understanding of the potential risks to non-target plants is essential in order to assess the environmental risks the use of metsulfuron may pose. If the data indicate that metsulfuron poses significant risks to these non-target plant species, the Agency may explore additional decision options to minimize the risks to these species. The lack of these data will limit the flexibility the Agency and registrants have in complying with the Endangered Species Act and could result in use restrictions for metsulfuron which may otherwise be avoided, or which are unnecessarily severe.

Appendix B. Proposed Metabolic Pathway

Proposed Metabolic Pathway of DPX-T6376 in Aerobic Soil



Appendix C. Summary of available effects studies

I. Aquatic

A. Fish

i. Freshwater

Acute

A 96-hr acute exposure study (MRID 00125816; acceptable) was conducted with rainbow trout (*Onchorhynchus mykiss*; formerly *Salmo gardneri*). Ten fish each were exposed to nominal concentrations of 0 (control and 0.5 ml DMF/L solvent control), 5, 10, 25 50, 100 and 150 mg ai/L. No mortalities were observed at test concentrations up to 150 mg/L during the 96-hr exposure period. At the 150 mg/L test concentration, three of the fish showed erratic swimming, rapid breathing and were lying on the bottom of the test container 24 hours after the test was initiated. At 48 hours two of the three fish had completely recovered; the third fish was affected throughout the entire study. The LD_{50} for rainbow trout from acute exposure to metsulfuron methyl is >150 mg/L. Metsulfuron methyl is classified as practically non-toxic to fish.

A 96-hr acute exposure study (MRID 00125817; acceptable) was conducted with bluegill sunfish (*Lepomis macrochirus*). Ten fish each were exposed to nominal concentrations of 0 (control and 0.5 ml DMF/L solvent control), 5, 10, 25 50, 100 and 150 mg ai/L. No mortalities were observed at test concentrations up to 150 mg/L during the 96-hr exposure period. No sublethal effects were observed in the study. The LD_{50} for blue gill sunfish from acute exposure to metsulfuron methyl is >150 mg/L.

An additional study with rainbow trout is available (MRID 45791501) and is under review. Based on provisional results, LC_{50} is >9.2 mg ai/L and the NOAEC is 9.2 mg ai/L. Until the review is complete, EFED cannot determine if the data are sufficient for risk assessment.

Chronic

An early life stage (ELS) study (MRID 44122801) with rainbow trout (*Onchorhynchus mykiss* is available for metsulfuron. Two replicates of each with two chambers of 20 larvae per incubation cup (80 fish total per concentration) were exposed to mean-measured concentrations of 0 (control), 2.4, 4.7, 9.5, 19, 38, 75 and 160 mg ai/L for larval survival and growth. Each replicate was thinned to 15 fish per chamber (30 fish per concentration). Significant effects on wet weight were reported at 8.0 mg ai/L, therefore the NOAEC is 4.5 mg ai/L. The study is classified as Acceptable.

ii. Estuarine/marine

Acute

No data on the effect of acute exposure to estuarine/marine fish are available for metsulfuron.

Chronic

No data on the effect of chronic exposure to estuarine/marine fish are available for metsulfuron.

B. Invertebrates

i. Freshwater
Acute

A 48-hr acute exposure study (MRID 00125818; acceptable) was conducted with *Daphnia magna*. Two replicates of ten daphnids each were exposed to nominal concentrations of 0 (control and 0.5 ml DMF/L solvent control), 25, 50, 100 and 150 mg ai/L. No mortalities were observed at test concentrations up to 150 mg/L during the 96-hr exposure period. No sublethal effects were observed in the study. The LD_{50} for daphnids from acute exposure to metsulfuron methyl is >150 mg ai/L and the NOAEC is 150 mg ai/L. Based on these results, metsulfuron methyl is classified as practically non-toxic to daphnids. However, since no verification of the test concentrations was provided, there is uncertainty surrounding the derived endpoints.

An additional study with daphnids is available (MRID 45791502) and is under review. Based on provisional results, LC_{50} is >9.3 mg ai/L and the NOAEC is 9.3 mg ai/L. Until the review is complete, EFED cannot determine if the data are sufficient for risk assessment.

Chronic

A chronic exposure study with daphnids is available (MRID 44704901) and is under review. Based on provisional results, the NOAEC is 100 mg ai/L. Until the review is complete, EFED cannot determine if the data are sufficient for risk assessment.

ii. Estuarine/marine
Acute

No data on the effect of acute exposure to estuarine/marine invertebrates are available for metsulfuron.

Chronic

No data on the effect of chronic exposure to estuarine/marine invertebrates are available for metsulfuron.

C. Plants

i. Vascular

A 14-day study with *Lemna minor* (MRID 41773902; Supplemental) is available for metsulfuron. Three replicates were exposed to nominal concentrations of 0 (control and 0.1 ml acetone/L solvent control) 0.04, 0.08, 0.16, 0.32 and 0.64 µg ai/L. Each replicate started with

five plants with 2-3 fronds each. Based on this study, the EC_{50} is 0.36 µg ai/L; the NOAEC is 0.16 µg ai/L.

A seven day study with *Lemna minor* (MRID 45109112; Supplemental) is available. Three replicates were exposed to mean-measured concentrations of 0.128 (contaminated control), 0.190, 0.283, 0.346, 0.495 and 0.912 µg ai/L. Each replicate started with 3-5 plants (12 fronds per replicate). The contamination of the control is a major deviation and would generally invalidate the study. However, some information can be gleaned from the study. Based on this study, the EC_{50} for this study is 0.440 µg ai/L; the NOAEC is 0.190 µg ai/L. This indicates AT LEAST equivalent toxic to aquatic vascular plants as the found in the other study.

ii. Nonvascular

A study (MRID 40639302; Acceptable) with the green alga *Pseudokirchneriella subcapitata* (formerly *Selanastrum capricornutum*) was submitted for metsulfuron. Three replicates for each nominal concentration of 0 (negative control), 1.0, 5.0, 10.0 and 45.0 µg ai/L were utilized. Since no verification of the test concentrations was provided, there is uncertainty surrounding the derived endpoints. After 96 hours, significant inhibition was reported at the two highest concentrations. The NOAEC for the study is 5.0 µg ai/L and the IC_{50} is 30.9 µg ai/L.

An additional study with *Pseudokirchneriella subcapitata* (MRID 45109108; Acceptable) is also available. Mean-measured concentrations of 0 (control), 14.47, 28.23, 58.40, 92.89, 180.78, 317.77 and 605.85 µg ai/L were replicated three times each. After 96 hours, the IC_{50} (area under the growth curve) was 130 µg ai/L and the NOAEC was 14.5 µg ai/L.

A study (MRID 45109109; Acceptable) with the diatom *Navicula pellicosa* was submitted for metsulfuron. Three replicates for each mean-measured concentration of 0 (negative control), 8.40, 14.19, 27.77, 50.49 and 92.83 mg ai/L were utilized. After 96 hours, maximum inhibition was 4.8 and 9.6 the two highest concentrations, respectively. The NOAEC for the study is 29.50 mg ai/L and the IC_{50} is >92.83mg ai/L. However, an additional study (MRID 44420901; under review) indicates *Navicula pellicosa* may be considerably more sensitive to formulated metsulfuron products.

A limit test with the cyanobacteria *Anabaena flos-aquae* (MRID 44244001; Acceptable) is available. Four replicates were exposed to 0 (control) and 95.4 µg ai/L (mean-measured) metsulfuron. There was a 2.2 percent inhibition reported in the treatment, likely due to natural variation in the test organism. Therefore, the NOAEC is 95.4 µg ai/L and the IC_{50} is >95.4 µg ai/L.

A limit test with the diatom *Skeletonema costatum* (MRID 44244002; Acceptable) is available. Four replicates were exposed to 0 (control) and 93.6 µg ai/L (mean-measured) metsulfuron. There was no inhibition reported in the treatment. Therefore, the NOAEC is 93.6 µg ai/L and the IC_{50} is >93.6 µg ai/L.

II. Terrestrial

A. Birds

Acute and Subacute Dietary

An acute oral toxicity study with mallard duck (*Anas platyrhynchos*) is available and under review (MRID 00125819). Provisionally, the LD50 is >2510 mg ai/kg-bw, although w

An eight-day subacute dietary study (MRID 00125820; Acceptable) was conducted with mallard duck. Ten birds in five pens each were exposed to basal diet (control), 562, 1000, 1780, 3160 and 5620 mg ai/ kg-diet. Equal numbers of birds were also exposed to a laboratory standard (dieldrin) at 72, 100, 139, 193 and 269 mg/kg-diet. There were no mortalities in the metsulfuron treatments. Lower limb weakness was observed on day five in some (number undefined) birds the 1000 through 5620 mg ai/kg-diet concentration levels. No effect on body weight gain or feed consumption was observed in any metsulfuron treatment groups. The LC_{50} for mallard duck is greater than 5620 mg ai/kg-diet.

An eight-day subacute dietary study (MRID 00125821; Acceptable) was conducted with bobwhite quail (*Colinus virginianus*). Ten birds in five pens each were exposed to basal diet (control), 562, 1000, 1780, 3160 and 5620 mg ai/ kg-diet. Equal numbers of birds were also exposed to a laboratory standard (dieldrin) at 72, 100, 139, 193 and 269 mg/kg-diet. There were no mortalities in the metsulfuron treatments. An increase in feed consumption was noted in the 5620 mg ai/kg-diet concentration level. The LC_{50} for mallard duck is greater than 5620 mg ai/kg-diet.

Chronic

A one generation avian reproduction toxicity study (MRID 44115701; Acceptable) was conducted with metsulfuron methyl. Effects were assessed over 23 weeks on 64 pairs of 19-week old northern bobwhite quail. Metsulfuron methyl was administered to the birds in the diet at mean measured concentrations of 0 (control), 40.1, 209, and 1020 mg ai/kg- diet. No adverse effects were reported on the adult quail. Although there were four adult mortalities, these were not considered dose-related. No dose-related effects were observed on reproductive parameters. The NOAEC was determined to be 1020 mg ai/kg-diet based on the absence of effects at the highest concentration tested.

A one generation avian reproduction toxicity study (MRID 44115702; Acceptable) was conducted with metsulfuron methyl. Effects were assessed over 24 weeks on 16 pairs of 27-week old mallard ducks. Metsulfuron methyl was administered to the birds in the diet at mean measured concentrations of 0 (control), 40.1, 209, and 1020 mg ai/kg- diet. No adverse effects were reported on the adult mallards. Although there were four adult mortalities, these were not considered dose-related. Statistically significant effects at 1020 mg ai/kg-diet on mallard reproduction included a 7.3 percent reduction in the percent of hatchling survival per number of hatched and a 6.2 percent reduction in hatchling body weight. Based on these effects, the LOAEC is 1020 mg ai/kg-diet and the NOAEC is 209 mg ai/kg-diet.

B. Mammals

Acute

According to a study reviewed by Health Effect Division (HED; MRID 47018706), single oral doses of technical metsulfuron were administered to Sprague-Dawley rats (*Rattus norvegicus*) at a rate of 5000 mg ai/kg-bw using the Up-Down test. No mortalities or clinical signs were reported. The LD_{50}>5000 mg ai/kg-bw. Metsulfuron is classified as practically nontoxic to rats on an acute exposure basis.

Chronic

In a two generation study with rats is available from HED (MRID 00151028). The Levels tested in CRL:CD(SD)BR rats were 0 (control), 25, 500 and 5000 mg ai/kg-diet Based in the results of that study, the reproductive NOAEL = 5000 mg ai/kg-diet and the maternal NOEL = 500 mg ai/kg-diet based on decreased weight gain.

C. Invertebrates

Acute

Two 48-hr acute contact tests with honeybees (*Apis mellifera*) were conducted in the same study (MRID 00122010; Acceptable). One test (Test A) used 200 bees and the other (Test B) used 240 bees. The bees were tested at 0 (control), 6.25, 12.5 and 25 ug ai/bee in Test A and at 0 (control), 3.125, 6.25, 12.5 and 25 ug ai/bee in Test B. Carbaryl was used as a reference chemical. There were no mortalities in Test A. Mortality in Test B was 15%, 20% and 10% in 6.25, 12.5 and 25 ug ai/bee, respectively. Based on this study, the LD_{50}>25 ug ai/bee; therefore, metsulfuron is classified as practically non-toxic to honeybees on an acute exposure basis.

An acute exposure study (MRID 45109122) with earthworms (*Eisenia fetida*) is available. Earthworms were exposed to nominal metsulfuron concentrations of 0 (control), 100, 180, 320, 560 and 1000 mg ai/kg-soil. The LC50 for the study is > 1000 mg ai/kg-soil since no mortality was observed during the study, but based on body weight reductions at 14 days the NOAEC is 320 mg ai/kg-soil. The study is classified as Supplemental.

A reproduction study (MRID 45109124)with earthworms is also available. Worms were exposed to concentrations of 0 (control), 10 and 50 g ai/ha. No effects were observed in the study, therefore the NOAEC is 50 g ai/ha.

D. Plants

Seedling emergence and vegetative vigor studies (MRID 44050301) have been submitted for metsulfuron and are currently under review. Until the review is complete, EFED cannot determine whether these studies are suitable for use in risk assessment.

Additional data on a limited number of species are available under MRID 45213701, which is also under review.

Appendix D.

EIIS Pesticide Summary Report: General Information
Metsulfuron-methyl (122010)

Incident #	Date	County	State	Certainty	Legal.	Formul.	Appl. Method	Total Magnitude
AQUATIC								
Agricultural Area								
I005925-008	7/1/1996	CECIL	MD	1	UN			3000
PLANTS								
Agricultural area								
I020627-006		Douglas	WA	2	MA			1400 acres
I000903-001	9/1/1991	ANDERSON	TX	3	RU	F	Spray	N/R
I000903-004	8/25/1993	ANDERSON	TX	3	RU	F	Spray	N/R
I012366-047	4/25/2000	LONOKE	AR	3	UN		Unknown	42 acres
I016328-036	5/17/2005	Nez Perce	ID	2	RU	WDG	Broadcast	135 acres
Barley								
I020340-001	5/16/2008	Walla Walla	WA	4	RU	DF		80% of 235 acres
Conservation Reserve								
I014415-001	8/12/2003	Deaf Smith	TX	2	UN	EC	Spray	75% of 120 acres
Home								
I005192-001			TX	3	MA		Broadcast	Several
Right-of-way								

Certainty Code: 0=Unrelated, 1=Unlikely, 2=Possible, 3=Probable, 4=Highly Probable.
Legality Code: RU=Registered Use, M=Misuse, MA=Misuse (Accidental), MI=Misuse (Intentional), U=Unknown.

Incident #	Date	County	State	Certainty	Legal.	Formul.	Appl. Method	Total Magnitude
I015218-001	7/15/2004	Massac	IL	2	RU	DF	Spray	50-75 trees
Right-of-way, rail								
I007371-024	9/9/1997		PA	3	RU		N/R	N/R
Right-of-way, road								
I014290-001	7/3/2003	Lemhi	ID	4	MA	DF	Spray	900 square feet
Right-of-way, utility								
I015280-001	6/4/2004		AR	2	RU	DF	Spray	About 5 acres total
Turf, residential area								
I015266-001	6/7/2004	Madison	IL	2	UN	WDG	Unknown	Unknown
WHEAT								
I003386-001	4/11/1994	WASCO	OR	2	MI	N/R	Broadcast	665
I020627-007	4/18/2001	Adams	WA	2	UN		Spray	
I020998-007	4/29/2002	Douglas	WA	2	UN			
TERRESTRIAL/AQUATIC								
Fence row								
I000022-001	5/26/1992	AIKEN	SC	2	UN	N/R	Spray	72

Certainty Code: 0=Unrelated, 1=Unlikely, 2=Possible, 3=Probable, 4=Highly Probable.
Legality Code: RU=Registered Use, M=Misuse, MA=Misuse (Accidental), MI=Misuse (Intentional), U=Unknown.