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

OFFICE OF CHEMICAL
SAFETY AND
POLLUTION
PREVENTION

PC Code: 121027
DP Barcode: 427543
Date: September 16, 2015

MEMORANDUM

SUBJECT: Registration Review: Preliminary Environmental Fate and Ecological Risk Assessment Endangered Species Effects Determination for Methoxyfenozide

TO: Bonnie Adler, Chemical Review Manager
Jill Bloom, Team Leader
Linda Arrington, Branch Chief
Risk Management and Implementation Branch V
Pesticide Re-evaluation Division (7508P)

FROM: Mary Clock-Rust, Biologist
Karen Milians, Ph.D., Chemist
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507P**)**

REVIEWED BY: Thomas Steeger, Ph.D., Senior Science Advisor
Jim Carleton, Ph.D., Senior Scientist
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507P**)**

APPROVED BY: Jean Holmes, DVM, MPH, Branch Chief
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507P**)**

The Environmental Fate and Effects Division (EFED) has completed a preliminary risk assessment for the insecticide methoxyfenozide. EFED's analysis has determined that the use of methoxyfenozide has the potential for direct effects on Federally listed threatened/endangered (hereafter referred to as "listed") and non-listed freshwater invertebrates following acute exposure, and on listed and non-listed freshwater and estuarine/marine invertebrates following chronic exposure. Acute risk to listed estuarine/marine invertebrates is also possible for the majority of methoxyfenozide uses evaluated. The likelihood of direct adverse effects on birds, terrestrial-phase amphibians, reptiles, mammals, fish, aquatic-phase amphibians, and terrestrial and aquatic plants

from exposure to methoxyfenozide as a result of the registered uses is expected to be low. However, the extent to which other taxa that depend on aquatic invertebrate species may be indirectly affected is uncertain. Finally, data are incomplete but available lines of evidence suggest that methoxyfenozide risk to terrestrial and aquatic plants is likely to be low.

The potential for direct adverse effects to adult honey bees (*Apis mellifera*) is considered low. A review of submitted field studies on honey bee brood development and colony survival (including overwintering) does not indicate that honey bee brood (larvae/pupae) are adversely affected by exposure to the compound, although uncertainties were noted in the submitted toxicity data. A recently submitted laboratory-based acute toxicity study on larval honey bees raises new concerns. Using the new toxicity data combined with default exposure and larval food consumption rates from the *Guidance for Assessing Pesticide Risks to Bees* (US EPA, 2014) results in risk estimates that exceed EFED's levels of concern (LOC) for honey bee larvae.

Uncertainties

Although methoxyfenozide is intended to act specifically on immature stages of insects within the order Lepidoptera (moths/butterflies), there is uncertainty about the extent to which larval stages of other insects (excluding honey bees) may be affected, since the compound acts as an ecdysone agonist and is intended to induce premature molts thereby resulting in death of the target organism. There are also concerns for beneficial lepidopterans that co-occur in areas where methoxyfenozide is used.

No data are available to assess the potential for adverse effects on terrestrial plants or to aquatic vascular plants from exposure to methoxyfenozide; however, toxicity data available for aquatic non-vascular plants did not indicate any adverse effects from exposure up to the solubility limit of the compound (3.3 mg/L). Also, terrestrial and vascular aquatic plant data on tebufenozide, another ecdysone agonist in the same chemical class as methoxyfenozide, suggest that methoxyfenozide toxicity to terrestrial and aquatic plants is likely to be low. Further, no reports of plant damage resulting from exposure to methoxyfenozide have been recorded in EFED's incident databases. Given the mode of action of these compounds, it is uncertain whether any analogous pathways (*i.e.*, ecdysone receptors) exist in plants.

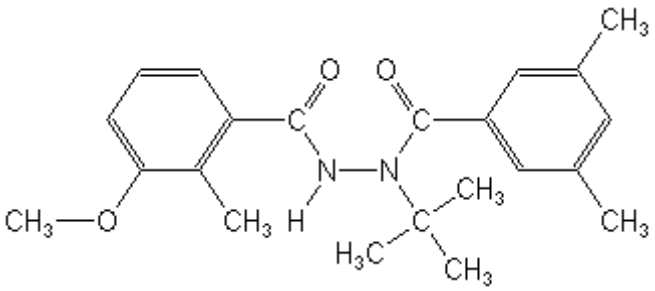
For uses where the retreatment interval (RTI) was not specified, a three-day interval was assumed. The RTI was not specified on two labels, EPA Reg, # 62719-442 (corn) and EPA Reg. # 62719-666 (peanuts).

Although whole colony studies are available for methoxyfenozide and did not demonstate any consistent long-term adverse effects on brood development, a laboratory-based chronic toxicity study with larval honey bees, in which exposure conditions can be more readily controlled, would increase the confidence in risk conclusions and help to address uncertainties regarding repeated direct exposure of larvae to methoxyfenozide. Specifically, a 21-day larval honey bee toxicity study extending through adult emergence would be informative.

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

OFFICE OF CHEMICAL
SAFETY AND POLLUTION
PREVENTION

Environmental Fate and Ecological Risk Assessment for Registration Review of Methoxyfenozide.



Methoxyfenozide

CAS Registry No: 161050-58-4 PC Code: 121027

Prepared by: Mary Clock-Rust, Biologist Karen Milians, Ph.D., Chemist	U.S. Environmental Protection Agency Office of Pesticide Programs Environmental Fate and Effects Division Environmental Risk Branch IV 1200 Pennsylvania Ave., NW Mail Code 7507P Washington, DC 20460
Reviewed by: Jean Holmes D.V.M, Branch Chief Thomas Steeger, Ph.D., Senior Science Advisor Jim Carleton, Ph.D., Senior Scientist	

September 16, 2015

Executive Summary

The preliminary risk assessment (PRA) in support of Registration Review for methoxyfenozide, examines the risks to wildlife associated with the compound's labeled uses. The risk assessment is based on the best available scientific and commercial information on the use, environmental fate and transport, and ecological effects of methoxyfenozide on non-target organisms.

Methoxyfenozide is a dibenzoyl hydrazine insecticide which acts as an insect growth regulator (IGR) and registered for use on a variety of agricultural as well as non-agricultural sites across the US. The chemical is an agonist for the invertebrate molting hormone, ecdysone, and induces a precocious incomplete molt in invertebrates, particularly lepidopterans (butterflies/moths).

Methoxyfenozide may be applied using ground, aerial, conventional spray or chemigation application methods. Single application rates range from 0.16 lb a.i./A (for cotton and peanuts) to a maximum of 0.40 lb a.i./A (for cotton). Use sites include citrus, cotton, fruiting vegetables (Crop Group 1B), globe artichokes, bushberries (Crop Group 13-07B), corn, peanuts, grapes, stone fruits (Crop Group 12-12) and tree nuts (Crop Group 14-12; including almonds, walnuts, and other nuts). Annual maximum application rates across all methoxyfenozide use sites do not exceed 1.0 lb a.i./acre/year. The technical registrant for this pesticide is Dow AgroSciences (DAS).

The compound is considered very persistent and moderately mobile based on a soil aerobic metabolism half-lives range from 336 to 1100 days; organic carbon partition coefficient (K_{oc}) range from 219 to 922 mL/g_{oc}; and, a log octanol-water partition coefficient (K_{ow}) of 3.72. Once applied, methoxyfenozide has the potential to move off the site of application by leaching, erosion and runoff where it can accumulate in aquatic systems.

While methoxyfenozide is expected to persist in the environment and move to surface water via runoff and erosion based on laboratory studies, a monitoring study was recently completed which showed no apparent accumulation of methoxyfenozide in sediment and water at any of the monitoring sites under the conditions tested. Furthermore, bioconcentration data with both fish and invertebrates indicate that the compound does not bioconcentrate appreciably (BCF range: 1.1 – 22.1X) and it depurates relatively quickly once organisms are no longer exposed. Available data indicate that for both freshwater and estuarine/marine fish, the toxicity of methoxyfenozide appears limited by its solubility in water (3.3 mg a.i./L) and at this concentration, no adverse effects (*i.e.*, mortality or sublethal effects) were observed on fish following acute exposure.

EFED's analysis has determined that all of the registered uses of methoxyfenozide have the potential to result in direct adverse effects to freshwater and estuarine/marine invertebrates. Specifically, federally listed threatened/endangered (hereafter referred to as "listed") and non-listed freshwater invertebrates are at risk following acute exposure to methoxyfenozide, and listed and non-listed aquatic freshwater and estuarine/marine invertebrates following chronic exposure. Acute risk to listed estuarine/marine invertebrates is also possible for the majority of registered methoxyfenozide use sites that are in close proximity to these environments. A low likelihood of direct adverse effects to birds, terrestrial-phase amphibians, reptiles, mammals, fish, aquatic-phase amphibians, and terrestrial and aquatic plants is expected from exposure to methoxyfenozide as a

result of the registered uses. However, there is the potential for indirect effects on taxa that depend on aquatic invertebrate species for prey and/or habitat, although the magnitude and likelihood of indirect effects are uncertain.

There are data to indicate that lepidopteran species of terrestrial invertebrates are sensitive to methoxyfenozide, consistent methoxyfenozide's use in controlling lepidopteran pests (such as the corn root worm, cabbage moth, diamond back moth). While available acute toxicity data do not indicate potential risk to adult honey bees, a laboratory-based study indicates that larval honey bees may be sensitive to methoxyfenozide following a single (acute) exposure. Screening-level risk quotient (RQ) values exceed the acute risk level of concern (LOC) for honey bee larvae, although refined RQ values based on measured residue levels in pollen/nectar are below the acute risk LOC. Field-based studies of whole colonies fed methoxyfenozide-spiked diets did not exhibit any consistent, long-term adverse effect on brood development and/or colony overwintering capacity. Laboratory-based chronic toxicity data for larval honey bees would increase the confidence in risk conclusions and address uncertainties about methoxyfenozide risk to terrestrial invertebrates and lead to more robust risk conclusions. Specifically, a 21-day larval bee toxicity study extending through adult emergence would help to address uncertainties.

1.0 Problem Formulation

The problem formulation sets the objectives for the risk assessment and provides a plan for analyzing the data and characterizing the risk (USEPA 1998a). EFED completed the preliminary problem formulation for the environmental fate, ecological risk, endangered species, and drinking water exposure assessments to be conducted as part of the Registration Review of methoxyfenozide (USEPA, 2013b).

The following section summarizes the key points of that document and discusses any differences between the analysis outlined in the preliminary problem formulation and the analysis conducted in this risk assessment.

1.1 Nature of Regulatory Action

The risk assessment is conducted as part of the Agency's Registration Review process for pesticide active ingredients. The Registration Review process was established under the Food Quality Protection Act (FQPA 1996).

2. Nature of Chemical Stressor

Methoxyfenozide, 3-methoxy-2-methylbenzoic acid 2-(3,5-dimethylbenzoyl)-2-(1,1-dimethylethyl)hydrazide (CAS No. 161050-58-4), belongs to the diacylhydrazine class of insecticides that interfere with the binding of the endogenous steroidal molting hormone 20-hydroxyecdysone with its nuclear receptor protein complex. As such, methoxyfenozide is referred to as an ecdysteroid (ecdysone) agonist[1]. Exposure of sensitive organisms (pests including fruit worm, diamond back moth, corn root worm, leaf roller, armyworm, grapevine moth and other

[1] Shimizu *et al.*, 1997.

USE SCENARIO (PRZM scenario used; rate modeled in kg/ha)		Estimated Environmental Concentrations (EECs, ppb)				
		Application Method	Peak	96-hour	21-day	60-day
Globe Artichoke	CA lettuce, 0.28 x 4 applic @ 7-d interval	aerial	144	144	143	142
Grass, forage fodder hay	OR Grass seed x 8 applic @ 3-d interval	aerial	37.4	37.3	37.1	36.7
	FL turf, 0.07 x 8 applic @ 3-d interval	aerial	20.5	20.4	20.2	19.9
Bushberries	OR berries, 0.07 x 3 applic @ 7-d interval	aerial	13.2	13.1	13.0	12.9
	OR berries, 0.28 x 3 applic @ 7-d interval	aerial	52.7	52.6	52.2	51.6
Peanuts	NC peanuts, 0.09 x 3 applic @ 3-d interval	aerial	27.6	27.6	27.4	27.0
	NC peanuts, 0.18 x 3 applic @ 7-d interval	aerial	54.5	54.4	54.0	53.4
Corn	MS corn, 0.07 x 17 applic @ 3-d interval	aerial	144	144	143	141
	MS corn, 0.28 x 4 applic @ 3-d interval	aerial	130	130	127	127
Grapes[2]	NY grapes, 0.13 x 5 applic @ 3-d interval	aerial	63.9	63.8	63.5	63.1
	NY grapes, 0.26 x 5 applic @ 4-d interval	aerial	141	141	140	139
Tree nuts (almond, pistachio)	CA almond, 0.25 x 4 applic @ 3-d interval	aerial	66.0	65.8	65.3	64.3
	CA almond, 0.43 x 4 applic @ 10-d interval	aerial	101	101	100	99
	GA pecans, 0.13 x 8 applic @ 8-d interval	aerial	72.3	72.1	71.7	70.7

[1]Refer to the modeling results for NC cotton scenario in Appendix F
[2] Although methoxyfenozide is not registered for use on grapes in NY, this scenario was used for modeling purposes.
Bolded value represents the highest EDWC for methoxyfenozide

3.2.2.4 Aquatic Exposure Monitoring

Methoxyfenozide was not included in monitoring conducted by the U. S. Geological Survey (USGS) National Water Quality Assessment (NAWQA) program nor in the California Department of Pesticide Regulation (CDPR) Surface Water Database (CDPR 2003).

Because methoxyfenozide is very persistent, moderately mobile and may accumulate in the aquatic environment following repeated applications, the Agency recommended surface water and sediment studies using a representative sample of water bodies in high use areas (based on DAS record sales, growers and state and county government records). These studies were intended to determine whether multiple years of use would result in evidence of accumulation of methoxyfenozide residues in water and/or sediment in areas that represent vulnerable fields (prone to runoff). Samples for determining methoxyfenozide residues were collected over a two-year period (2012 and 2013) in two lotic (flowing) water bodies and five lentic (standing) water bodies in each of the following states: California, Mississippi, and Michigan.

The maximum concentration of methoxyfenozide detected in lotic surface water samples was 1.31 µg/L, found in Mississippi. The maximum concentration detected in lentic waters was 0.845 µg/L, in a pond in Michigan. The maximum concentration of methoxyfenozide in benthic sediments (31 µg/kg) was detected in Michigan. No apparent accumulation of methoxyfenozide was observed in sediment at any monitoring sites after years of use. There are deficiencies of the monitoring study such as analytical methods slightly modified (ECMs reported in the study differed from the one submitted to the Agency) and one sampling site was changed with an alternate sampling point.

It may not be appropriate to make a direct comparison from the results of the monitoring study with the values obtained in modeling (using SWCC) because the frequency of sampling in the monitoring study may not have captured the peak concentration. Additionally, SWCC model simulates the impact of daily weather on the treated agricultural field, and resulting concentrations in an adjacent farm pond over a defined period (here, thirty years). During this time, pesticide is washed-off of the field into the water-body by twenty to forty rainfall/runoff events per year. Each new addition of pesticide mass from each runoff event adds to the existing pesticide mass in the pond from previous runoff and/or spray-drift events. Since methoxyfenozide is known to be persistent in aquatic environments, the mass of the pesticide accumulates in the pond from one year to the next. In the SWCC model, the yearly simulated peaks are not independent of each other but are temporally auto-correlated, meaning that the "1-in-10 year EECs" obtained from model post-processing are in part functions of the simulation duration. As a result, SWCC results likely overestimate concentrations in streams and various other kinds of water bodies, as over the course of thirty years, some loss of methoxyfenozide is expected due to washout, dispersion, burial of sediment and other dissipative processes that aren't simulated. In particular, methoxyfenozide concentrations in lotic (flowing) water bodies are not expected to accumulate at such a high concentrations from year to year because of downstream advective removal. **Table 8** below details the results of the monitoring study conducted by DAS.

Table 8: Summary of the Methoxyfenozide Sediment and Surface Water Monitoring Study

Site	Concentration of methoxyfenozide in surface water (µg/L), (Number of samples analyzed)		Concentration of methoxyfenozide in sediment (µg/kg), (Number of samples analyzed)	
	Lotic	Lentic	Lotic	Lentic
California	ND-1.01 (88)[1]	ND-0.0502 (20)	ND (8)	ND (20)
Mississippi	ND-1.31 (55)[2]	ND-0.233 (20)	ND (8)	ND (20)

Michigan	ND (36)[3]	ND-0.845 (23)	ND (4)	ND-31.0 (23)

LOQ=0.050 µg/L and LOD= 0.015µg/L in surface water and LOD= 3 µg/kg in sediment.
ND =below detection limit
[1]87, 7- day composite samples and 1, 28-day composite sample
[2]47, 7- day composite samples and 8, 28-day composite samples
[3]22, 7- day composite samples and 14, 28-day composite samples

OPP is not aware of any other monitoring programs in which methoxyfenozide is an analyte.

3.2.3 Measures of Terrestrial Exposure

Exposure to terrestrial organisms was assessed based on the registered uses of methoxyfenozide. Dietary exposure to birds and mammals was assessed using the T-REX model[2]. Terrestrial plant exposure was estimated using the TerrPlant model[13].

3.2.3.1. Ingestion of Foliar Residues by Birds and Mammals

Terrestrial wildlife exposure estimates are typically calculated for the dietary exposure of birds and mammals. Avian exposures are considered surrogates for exposures to terrestrial-phase amphibians and reptiles. For exposure to terrestrial organisms, such as birds and mammals, pesticide residues on food items are estimated, based on the assumption that organisms are exposed to pesticide residues in a given exposure use pattern. For methoxyfenozide, application methods for the registered uses include aerial, broadcast, banded, and directed spray of liquid formulations for all crops.

T-REX[14] (Version 1.5.2) is used to calculate upper-bound dietary EECs for estimating exposure to birds and mammals resulting from the registered uses of methoxyfenozide. A one year time period is simulated, and the default foliar dissipation half-life of 35 days was used for modeling the registered uses. An example printout from the T-REX model is provided in **Appendix D**.

Table 9: Input Parameters for Deriving Terrestrial EECs for Methoxyfenozide Labeled Uses (T-REX).

Use Site	Application Rate (lbs a.i./A)	Minimum Reapplication Interval (days)[1]	Number of Applications
Citrus	0.25	14	4
Cotton[3]	0.4	10	4
Fruiting Vegetables	0.25	7	4
Globe Artichokes	0.25	7	4
Bushberries	0.25	7	3
Corn	0.25	NS[2]	4
Peanuts	0.16	7	3

[13] http://www.epa.gov/oppefed1/models/terrestrial/index.htm
[14] USEPA. 2014. T-REX Version 1.5.2 (Terrestrial Residue Exposure). http://www.epa.gov/oppefed1/models/terrestrial/#trex (last accessed 02.24/15)