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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: March 13, 2008

Subject: Spirotetramat: Occupational and Residential Exposure/Risk Assessment for the New Use on Citrus, Grape and Small Fruit Vine Climbing, Pome Fruit, Stone Fruit, Tree Nuts, Hops, Christmas Trees, Cucurbits, Fruiting Vegetables, Leafy Vegetables (non-Brassica and Brassica), Potato and other Tuberous and Corm Vegetables, and Greenhouses/Nurseries

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INTRODUCTION

Under Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, the Bayer Environmental Science company has requested registration of the insecticide spirotetramat for use on citrus, grape and small fruit vine climbing, pome fruit, stone fruit, tree nuts, hops, Christmas trees, cucurbits, fruiting vegetables, leafy vegetables (non-Brassica and Brassica), potato and other tuberous and corm vegetables, and greenhouses/nurseries. This memorandum serves as HED's assessment of nondietary exposure and risk that might result from the proposed use.

USE PATTERN SUMMARY

Table 1 summarizes the proposed use patterns and formulations specified in the end-use products containing spirotetramat.

Table 1. Proposed Use Patterns and Formulations

Product	Formulation	Use Sites	Application Rates	Application Equipment	PHI	Application Interval	Max App Rate per crop season	REI
BYI 8330 150 OD Insecticide	Oil dispersion	Citrus	0.16 lb ai/A	Aerial, Airblast	1 day	21 days	0.32 lb ai/A	24 hours
		Grape and Small Fruit Vine Climbing	0.125 lb ai/A	Aerial, Groundboom	7 days	30 days	0.2 lb ai/A	
		Pome Fruit	0.14 lb ai/A	Aerial, Airblast	7 days	14 days	0.4 lb ai/A	
		Stone Fruit	0.14 lb ai/A	Aerial, Airblast	7 days	14 days	0.24 lb ai/A	
Ultor™	Liquid	Tree Nuts	0.14 lb ai/A	Aerial, Airblast	7 days	14 days	0.34 lb ai/A	12 hours
		Hops	0.098 lb ai/A	Aerial, Groundboom	7 days	14 days	0.2 lb ai/A	
		Christmas trees	0.16 lb ai/A	Aerial, Airblast	N/A	14 days	0.32 lb ai/A	
		Cucurbit vegetables	0.078 lb ai/A	Aerial, Groundboom, Chemigation	1 day	7 days	0.16 lb ai/A	
Movento™	Liquid	Fruiting vegetables	0.078 lb ai/A	Aerial, Groundboom, Chemigation	1 day	7 days	0.16 lb ai/A	12 hours
		Leafy vegetables (non-Brassica)	0.078 lb ai/A	Aerial, Groundboom, Chemigation	3 days	7 days	0.16 lb ai/A	
		Leafy vegetables (Brassica)	0.078 lb ai/A	Aerial, Groundboom, Chemigation	1 days	7 days	0.16 lb ai/A	
		Potato and other Tuberous and Corm Vegetables	0.078 lb ai/A	Aerial, Groundboom, Chemigation	7 days	7 days	0.16 lb ai/A	
Spirotetramat 240 SC Greenhouse and Nursery Insecticide/ Miticide	Liquid	Greenhouses, nurseries, interior plantscapes	0.16 lb ai/A (0.00125 lb ai/gallon)	Chemigation, Groundboom, Airblast, High Pressure Handwand	N/A	14-28 days	0.39 lb ai/A/year	24 hours

Bayer CropScience has submitted an occupational exposure assessment for spirotetramat, specifically for the Spirotetramat 240 SC Greenhouse and Nursery Insecticide/Miticide product (MRID 470593-02). This assessment utilizes PHED unit exposures and calculates risks for occupational handlers, including mixer/loaders and applicators, as well as reentry workers. All handler and postapplication risks reported by the Registrant were not of concern (i.e., MOEs>LOC = 100). Due to the Toxicity Category II for eye irritation, the Registrant noted that a 24-hour REI would be required.

HAZARD INFORMATION

RAB1 toxicologists met and determined appropriate toxicological endpoints of concern for spirotetramat. Adverse effects were identified at durations of exposure ranging from short-term (up to 30 days) to intermediate-term durations (1 to 6 months) to long-term (chronic) durations (more than 6 months).

The acute toxicity categories for spirotetramat are summarized in Table 1. The doses selected for this risk assessment are summarized in Table 2. Short- and intermediate-term dermal and inhalation risks were assessed using a NOAEL of 10 mg/kg/day, based on a prenatal developmental toxicity study in the rabbit in which late abortion (≥GD 22), clinical signs, impaired food and water consumption and body weight loss were observed at a maternal LOAEL of 40 mg/kg/day. A dermal absorption factor of 10% is necessary. A 100% oral equivalent inhalation absorption factor is assumed. A body weight of 60 kg was used for the dermal and inhalation assessments.

Table 1. Acute Toxicity of Spirotetramat

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral (rat)	46904527	LD_{50} >2000 mg/kg (F)	III
870.1200	Acute dermal (rat)	46904529	LD_{50} >2000 mg/kg (M&F)	III
870.1300	Acute inhalation (rat)	46904530	LC_{50} >4.183 mg/L (M&F)	IV
870.2400	Primary eye irritation (rabbit)	46904531	Corneal opacity and iritis (grade 1); cleared by day 8	II
870.2500	Primary dermal irritation (rabbit)	46904532	Negative	IV
870.2600	Dermal sensitization (mouse)	46904565	Positive (LLNA)	N/A

Table 2. Summary of Toxicology Endpoint Selection for Spirotetramat.

Exposure Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL = 10 mg/kg/day Dermal absorption factor = 10%	UF_A = 10X UF_H = 10X	Occupational LOC for MOE < 100	**Prenatal developmental toxicity (rabbit)** Maternal LOAEL = 40 mg/kg/day based on late abortion (≥GD 22), clinical signs, impaired food and water consumption and body weight loss
Dermal Long-Term (>6 months)	NOAEL = 5 mg/kg/day Dermal absorption factor = 10%	UF_A = 10X UF_H = 10X	Occupational LOC for MOE < 100	**Chronic toxicity (dog; dietary)** LOAEL = 20 mg/kg/day (M) based on thymus involution and brain dilation
Inhalation Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL = 10 mg/kg/day 100% inhalation assumed	UF_A = 10X UF_H = 10X	Occupational LOC for MOE < 100	**Prenatal developmental toxicity (rabbit)** Maternal LOAEL = 40 mg/kg/day based on late abortion (≥GD 22), clinical signs, impaired food and water consumption and body weight loss

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Inhalation Long-Term (>6 months)	NOAEL = 5 mg/kg/day 100% inhalation assumed	UF_A = 10X UF_H = 10X	Occupational LOC for MOE < 100	**Chronic toxicity (dog; dietary)** LOAEL = 20 mg/kg/day (M) based on thymus involution and brain dilation
Cancer (oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans based on lack of evidence of carcinogenicity in two oral rodent carcinogenicity studies.			

Abbreviations: UF = uncertainty factor, UF_A = extrapolation from animal to human (interspecies), UF_H = potential variation in sensitivity among members of the human population (intraspecies), NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, MOE = margin of exposure, LOC = level of concern.

NON-OCCUPATIONAL/RESIDENTIAL EXPOSURE

The proposed use is on agricultural crops and commercial ornamentals; therefore, there is no potential for residential exposure. In addition, there are no proposed or existing spirotetramat products registered for residential use sites.

OCCUPATIONAL EXPOSURE

There is potential for occupational handler and postapplication exposure from the proposed uses on agricultural crops and commercial ornamentals. It is anticipated that the following scenarios could result in handler exposure: mixer/loaders of liquids for aerial, chemigation, airblast and groundboom applications, applicators using aerial, airblast and groundboom equipment, flaggers for aerial applications, and mixer/loader/applicators of liquid formulations using high pressure handwand. Based upon the use pattern, HED expects the most highly exposed occupational pesticide handlers are likely to be:

Mixer/Loaders:
(1) Mixing/Loading Liquids for Aerial Applications (PHED);

Applicators:
(2) Applying Sprays via Airblast Equipment (PHED); and

Mixer/Loader/Applicator
(3) Mixing/Loading/Applying Liquid Concentrates with a High Pressure Handwand (only study in PHED is for greenhouse use)

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the Pesticide Handlers Exposure Database (PHED, August, 1998). For pesticide handlers, HED presents estimates of dermal exposure for "baseline" (i.e., workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves), as well as for "baseline" and the use of protective gloves or other personal

protective equipment (PPE), as might be necessary. The spirotetramat product labels direct applicators and other handlers to wear a long-sleeve shirt, long pants, protective eyewear, chemical resistant gloves and shoes plus socks.

HED believes most exposure durations will be short-term (1 - 30 days). However, HED's Science Advisory Council for Exposure (ExpoSAC) maintains it is possible for commercial applicators to be exposed to intermediate-term exposure durations (1 - 6 months). In addition, the short- and intermediate-term toxicological endpoints are the same; therefore, the estimates of risk for short-term duration exposures are protective of those for intermediate-term duration exposures. Long-term exposures are not expected, therefore, a long-term assessment was not conducted.

Daily dermal or inhalation handler exposures are estimated for each applicable handler task with the application rate, the area treated in a day, and the applicable dermal or inhalation unit exposure using the following formula:

Daily Exposure (mg ai/day) = Unit Exposure (mg ai/lb ai handled) x Application Rate (lbs ai/area) x Daily Area Treated (area/day)

Where:

Daily Exposure	=	Amount (mg ai/day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Unit Exposure	=	Unit exposure value (mg ai/lb ai) derived from August 1998 PHED data;
Application Rate	=	Normalized application rate based on a logical unit treatment, such as acres; and
Daily Area Treated	=	Normalized application area based on a logical unit treatment such as acres (A/day).

The daily dermal or inhalation dose is calculated by normalizing the daily exposure by body weight and adjusting, if necessary, with an appropriate dermal or inhalation absorption factor using the following formula:

Average Daily Dose (mg/kg/day) = Daily Exposure (mg ai/day) x (Absorption Factor (%/100)) / Body Weight (kg)

Where:

Average Daily Dose	=	Absorbed dose received from exposure to a pesticide in a given scenario (mg ai/kg body weight/day);
Daily Exposure	=	Amount (mg ai/day) deposited on the surface of the skin that is available for dermal absorption or amount inhaled that is available for inhalation absorption;
Absorption Factor	=	A measure of the amount of chemical that crosses a biological boundary such as the skin or lungs (% of the total available absorbed); and
Body Weight	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Non-cancer dermal and inhalation risks for each applicable handler scenario are calculated using a MOE, which is a ratio of the NOAEL to the daily dose. All MOE values were calculated using the formula below:

MOE= NOAEL or LOAEL (mg/kg/day) / Average Daily Dose (mg/kg/day)

Table 5 presents the estimated risks for workers based on the short and intermediate-term dermal and inhalation exposures at baseline. HED has determined that risks are not of concern (i.e., MOEs>100), **provided workers wear protective gloves as recommended on the label.**

Table 5. Occupational Handler Dermal and Inhalation Exposures and Risks.

Dermal and Inhalation Unit Exposures (mg/lb ai)	Application rate (lb ai/A)[a]	Area Treated Daily (A)[b]	Short- and Intermediate-term Doses (mg/kg/day)[c]	Short- and Intermediate-term MOEs[d]	Combined Short- and Intermediate-term MOEs[i]
Mixer/Loader – Aerial Application					
Dermal Baseline[e]: 2.9 (HC)[h] Single layer w/gloves[g]: 0.023 (HC) Inhalation Baseline[f]: 0.0012 (HC)	0.16	350	Dermal Baseline: 0.27 Single layer w/gloves: 0.0021 Inhalation Baseline: 0.0011	Dermal Baseline: 37 Single layer w/gloves: 4700 Inhalation Baseline: 8,900	Baseline: 37 Single layer w/gloves: 3100
Applicator –Airblast Application					
Dermal Baseline: 0.36 (HC) Single layer w/gloves[g]: 0.24 Inhalation Baseline: 0.0045 (HC)	0.16	40	Dermal Baseline: 0.0038 Single layer w/gloves: 0.0026 Inhalation Baseline: 0.00048	Dermal Baseline: 2,600 Single layer w/gloves: 3900 Inhalation Baseline: 21,000	Baseline: 2,300 Single layer w/gloves: 3,200
Mixer/Loader – High Pressure Handwand					
Dermal Baseline: No Data Single layer w/gloves[g]: 2.5 (LC) Inhalation Baseline: 0.12 (LC)	0.00125 lb ai/gallon	1000 gallons	Dermal Single layer w/gloves: 0.0052 Inhalation Baseline: 0.0025	Dermal Single layer w/gloves: 1,900 Inhalation Baseline: 4,000	Single layer w/gloves: 1300

a Application rates are the maximum recommended rates provided on the spirotetramat product labels.
b Area treated per day and amount handled values are HED estimates based on ExpoSAC Policy #9 "Standard Values for Daily Acres Treated in Agriculture," industry sources, and HED estimates.
c Dose (mg/kg/day) = Unit exposure(mg/lb ai) x App Rate (lb ai/acre or lb ai/gallon) x Area Treated/Amount Handled (acres/day or gallons/day) x %Absorption (10% dermal and 100% inhalation assumed) / Body weight (60 kg).
d MOE = NOAEL/Dose; where the short- and intermediate-term dermal and inhalation NOAEL = 10 mg/kg/day .
e Baseline Dermal: Long-sleeve shirt, long pants, and no gloves.
f Baseline Inhalation: no respirator.
g Single layer w/gloves: Single layer baseline attire plus chemical-resistant gloves.
h Data Confidence for PHED unit exposures: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
i. Combined MOE = NOAEL / (dermal + inhalation daily dose)

Postapplication

HED expects that postapplication exposure will occur since spirotetramat is applied as a foliar spray. Since no postapplication data were submitted in support of this registration action, exposures during postapplication activities were estimated using dermal transfer coefficients from HED's ExpoSAC Policy Number 3.1 "Agricultural Transfer Coefficients" (August, 2000). Two representative scenarios were assessed: grapes (with an application rate of 0.125 lb ai/A and a high transfer coefficient of 10,000 cm^2/hr) and Christmas trees (with an application rate of 0.16 lb ai/A and a high transfer coefficient of 8,000 cm^2/hr). Table 6 summarizes the scenarios assessed. In addition, the following assumptions were used in the calculations:

Assumptions:

- Exposure Duration = 8 hours per day
- Body Weight = 60 kg
- Dermal Absorption = 10%
- Fraction of a.i. retained on foliage = assumed to be 20% on day zero (= % dislodgeable foliar residue, DFR, after initial treatment). This fraction is assumed to further dissipate at the rate of 10% per day on following days. These are default values established by ExpoSAC.

Table 6: Anticipated Postapplication Activities and Dermal Transfer Coefficients

Proposed Crops	Policy Crop Group Category	Application Rate (lb ai/acre)	Transfer Coefficients (cm^2/hr)	Activities
Grape	Vine / trellis	0.125	10,000	Tying (Cane turning); Turning (Cane turning); Girdling
Christmas trees	Tree, "fruit", evergreen	0.16	8,000	Hand-harvest; Staking; Topping; Training

The information in the table is based on proprietary and non-proprietary data.

Daily dermal exposures were calculated on each postapplication day after application using the following equation:

$$DE_{(t)}\ (mg/day) = (TR_{(t)}\ (\mu g/cm^2) \times TC\ (cm^2/hr) \times Hr/Day)/1000\ (\mu g/mg)$$

Where:

DE(t)	=	Daily exposure or amount deposited on the surface of the skin at time (t) attributable for activity in a previously treated area, also referred to as potential dose (mg ai/day);
TR(t)	=	Transferable residues that can be dislodgeable foliar residue at time "t" ($\mu g/cm^2$);
TC	=	Transfer Coefficient (cm^2/hour); and
Hr/day	=	Exposure duration meant to represent a typical workday (8 hours).

Note that the ($TR_{(t)}$) input may represent levels on the day of application in the case of short-term risk calculations. Once daily exposures are calculated, the calculation of daily absorbed dose and the resulting Margin of Exposures use the same algorithms that are described above for the handler exposures. These calculations are completed for each day or appropriate block of time after application.

HED has determined that risks are not of concern (i.e., MOEs>100) on the day of treatment (i.e., Day 0) for all postapplication exposure activities. Table 7 presents a summary of occupational postapplication risks associated with use of spirotetramat.

Table 7. Summary of Occupational Postapplication Risks for Spirotetramat

Crop Grouping	Application rate (lb ai/acre)	Transfer Coefficient ($\mu g/cm^2$)	Day after Treatment	Short- and Intermediate-term MOE at Day 0 (Level of Concern = 100)
Vine / trellis	0.125	10,000 (Tying (Cane turning); Turning (Cane turning); Girdling)	0 (12 hours)	270
Tree, "fruit", evergreen	0.16	8,000 (Hand-harvest; Staking; Topping; Training)		260

RESTRICTED-ENTRY INTERVAL (REI)

Spirotetramat is classified as Toxicity Category III for acute oral and acute dermal; Toxicity Category II for primary eye irritation; and as Toxicity Category IV for acute inhalation and primary dermal irritation. It is a positive dermal sensitizer. Therefore, while an assessment of systemic toxicity from postapplication exposure would indicate acceptable MOEs on the day of treatment, the acute toxicity categories for this chemical require a 24 hour REI for this product under the Worker Protection Standard. **HED recommends that the REI for all spirotetramat labels have an REI of 24 hours.**