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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: March 3, 2004

Subject: Occupational and Residential Risk Assessment for Mesosulfuron-methyl on Wheat

DP Barcode:	PC Code:	Trade Name:	EPA Reg#	MRID #	Class
298763	122009	Osprey™ Herbicide	264-INE	N/A	Herbicide
298763		Silverado™ Wild Oat Herbicide	264-INR	N/A	

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INTRODUCTION

The registrant, Aventis CropScience requests the establishment of tolerances for residues of the herbicide, mesosulfuron-methyl, on wheat. Mesosulfuron-methyl is the active ingredient (ai) in Osprey™ (a water dispersible granule [WDG] formulated for use in post-emergent control of annual grass and broadleaf weeds) and Silverado™ (a WDG formulated for use in post-emergent control of wild oat and wild mustard). This memorandum addresses risk from occupational

exposure to mesosulfuron-methyl. An aggregate human risk assessment will be included as a separate Health Effects Division (HED) document.

1.0 EXECUTIVE SUMMARY

Mesosulfuron-methyl is being considered as a new active ingredient (ai) in products to control weeds in wheat. The formulated end use products will be labeled under the trade name Osprey and Silverado. In this document, the name mesosulfuron-methyl will be used for the ingredient being assessed, and will be referred to as the "ai."

An occupational and/or residential exposure assessment is required for an ai if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete. For mesosulfuron-methyl both criteria have been met. Occupational exposure is expected for mesosulfuron-methyl, and therefore occupational exposure and risk are assessed in this document. However, there are no residential uses registered or proposed for mesosulfuron-methyl, and therefore residential exposure and risk are not assessed. The following occupational exposure scenarios are assessed in this document:

- mixer/loader: short- and intermediate-term inhalation (for aerial and groundboom application)
- applicator: short- and intermediate-term inhalation (for aerial and groundboom application)

Occupational handlers may be exposed during mixing, loading and application of mesosulfuron-methyl using aerial and groundboom equipment through the following routes:

- *Dermal*

Although dermal exposure is expected, short- and intermediate-term dermal endpoints were not identified due to the lack of acute dermal, systemic, neurological, and developmental toxicity concerns. A long-term dermal endpoint was not identified, nor would long-term dermal occupational exposure be expected. Therefore dermal exposure was not assessed.

- *Inhalation*

A short- and intermediate-term inhalation endpoint was identified based on the chronic oral toxicity study in dogs (NOAEL = 155 mg/kg/day). The observed effects were increased mucus secretion in the cardiac and fundic sections of the stomach, and chronic superficial gastritis. Absorption via inhalation was assumed to be equivalent to oral absorption (100% oral absorption factor). A long-term inhalation endpoint was also identified based on the chronic oral toxicity study in dogs, however long-term inhalation occupational exposure is not expected. Therefore, short- and intermediate-term inhalation exposure was assessed.

Margins of Exposure (MOEs) for inhalation exposure from all occupational handler scenarios were well above the target MOE of 100, and thus do not trigger HED concern. Inhalation exposure is considered negligible for postapplication activities, and dermal exposure was not considered because an endpoint for dermal exposure was not identified; thus an occupational postapplication assessment was not required.

Incident reports are not relevant for a new ai, such as mesosulfuron-methyl.

2.0 HAZARD PROFILE

On January 20, 2004 the HED Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology database on mesosulfuron-methyl, and selected toxicological endpoints for occupational risk assessments. The results from acute studies with the technical grade substance and the endpoints are shown in Tables 1 and 2, respectively.

Table 1. Acute Toxicity of Mesosulfuron-methyl - Technical

Guideline No.	Study Type	MRID No.	Results	Toxicity Category
870.1100	Acute oral toxicity	45386321	LD ₅₀ > 5000 mg/kg [M/F]	IV
870.1200	Acute dermal toxicity	45386322	LD ₅₀ > 5000 mg/kg [M/F]	IV
870.1300	Acute inhalation toxicity	45386323	LC ₅₀ > 1.33 mg/kg [M/F]	III
870.2400	Acute eye irritation	45386324	Conjunctival irritation at 24 hrs in 1/3 which cleared by 48 hrs.	III
870.2500	Acute dermal irritation	45386325	Non Irritant	IV
870.2600	Skin sensitization	45386326	Unacceptable	Negative ¹

¹ There was no indication that the material is a dermal sensitizer; however, the study is unacceptable because the submitted positive control study was not conducted within 6 months (i.e., they were approximately 9 months apart).

Table 2. Summary of Toxicological Doses and Endpoints for Mesosulfuron-methyl

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary: All populations	An endpoint attributable to a single dose was not identified in the database.		
Chronic Dietary: All populations	NOAEL= 155 mg/kg/day UF = 100 Chronic RfD = 1.55 mg/kg/day	FQPA SF = 1X cPAD = <u>chronic RfD</u> FQPA SF = 1.55 mg/kg/day	Chronic oral toxicity study in dogs. LOAEL = 574 mg/kg/day [M] based on increased mucus secretion in the cardiac and fundic sections of the stomach, and chronic superficial gastritis (1/6) of male dogs.
Incidental Oral: Short and Intermediate-Term)	No Residential Uses are Proposed for Mesosulfuron-methyl.		
Dermal Exposure: Short, Intermediate and Long-Term	Quantification of dermal risk is not required for this route of exposure due to the lack of dermal, systemic, neurological, and developmental toxicity concerns.		
Inhalation Exposure: Short , Intermediate and Long-Term	Oral NOAEL= 155 mg/kg/day (100% Oral Absorption Factor)	Residential LOC for MOE = NA Occupational LOC for MOE = 100	Chronic oral toxicity study in dogs. LOAEL = 574 mg/kg/day [M] based on increased mucus secretion in the cardiac and fundic sections of the stomach, and chronic superficial gastritis (1/6) of male dogs.
Cancer (oral, dermal, inhalation)	"Not likely to be carcinogenic to humans" based on the lack of evidence of carcinogenicity in the rats and mice.		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

The HIARC concluded the FQPA Safety Factor could be removed (1X) based on the following:

- No evidence of increased quantitative/qualitative susceptibility in the available acceptable/guideline studies.
- Identification of clear NOAELS for the effects of concern.
- No adverse effects noted at the highest dose tested in acceptable/guideline developmental toxicity and reproduction studies in rats and in the developmental toxicity study in rabbits.

Furthermore the HIARC concluded mesosulfuron-methyl is "not likely to be a human carcinogen" based on the lack of evidence of carcinogenicity in both the rat and the mouse carcinogenicity studies.

3.0 USE PROFILE

The use profile for this Section 3 registration is summarized in Table 3:

Table 3: Use Profile for Mesosulfuron-methyl

Product Name (formulation)	Use Sites (diseases/pests controlled)	Max. Rate for Single Application (lb ai/A)	Max. Rate per Growing Season (lb ai/A/gr. sea.)	Interval Between Applications	Pre-Harvest Interval (days)	Application Method
Osprey™ Herbicide WDG (4.5% ai)	winter wheat (controls post-emergent annual grass and broadleaf weeds)	0.013	0.013	N/A*	30 (wheat forage) 55 (grain and straw)	Labeled as: foliar application: • aerial • groundboom
Silverado™ Wild Oat Herbicide WDG (2% ai)	wheat, including durum (controls post-emergent wild oat and wild mustard)	0.0022-0.0028 (suggested)	0.0056	not specified	30 (wheat forage) 55 (grain and straw)	Labeled as: foliar application: • aerial • groundboom

*not applicable, applied only once per growing season

4.0 OCCUPATIONAL EXPOSURES AND RISKS

4.1 Handler Exposure and Risk

There is potential for exposure to mesosulfuron-methyl during mixing, loading, and application activities. An exposure/risk assessment using applicable endpoints selected by the HIARC (1/20/04) was performed. Handler's exposure and risk were estimated for the following scenarios: (1) mixer/loader: open mixing and loading dry flowable for aerial; (2) aerial application of liquid: closed cockpit; (3) flagging for aerial applications; (4) mixer/loader: open mixing and loading dry flowable for groundboom; (5) groundboom application of liquid: open cab.

No chemical-specific handler exposure data were submitted in support of this Section 3 registration. In accordance with HED's Exposure Science Advisory Council (SAC) policy, exposure data from the Pesticide Handlers Exposure Database (PHED) Version 1.1, as presented in PHED Surrogate Exposure Guide (8/98), were used with other HED standard values for areas treated per day, body weight, and the level of personal protective equipment, to assess handler exposures. The water dispersible granule formulation is also known as a dry flowable

formulation. Dry flowable data from the PHED Surrogate Exposure Guide was used in the exposure assessment. The Osprey™ application rate was used in exposure calculations. The maximum Osprey™ application rate (0.013 lb ai/A/growing season) is higher than the maximum Silverado™ application rate (0.0056 lb ai/A/growing season), and is therefore a conservative measure.

Short- and intermediate-term dermal toxicity endpoints were not identified by the HED HIARC. Although a long-term dermal endpoint was identified, long-term exposure (≥ 180 days) is not expected. Therefore, a dermal risk assessment was not conducted. Inhalation toxicity endpoints of concern were identified for all durations of exposure. Because long-term exposures are not anticipated, only short- and intermediate-term inhalation risks were assessed.

The HED HIARC identified the same toxicity endpoint for short- and intermediate-term inhalation. Therefore, daily inhalation exposures over the short- and intermediate-term were compared to the same NOAEL (155 mg/kg/day from the chronic oral toxicity study in male dogs), and result in the same MOE. The MOEs range from 900,000 (mixer/loader: open mixing dry flowable for aerial) to 10,000,000 (aerial application of liquid: closed cockpit). **These risks do not exceed HED's level of concern.** Exposure assumptions and estimates for occupational handlers are summarized in Table 4.

Table 4: Inhalation Exposure and Risk for Occupational Handlers

PHED Exposure Scenario	Maximum Application Rate (lb ai/A)	PHED Unit Exposure (mg/lb ai)	PHED Data Confidence	Area Treated per Day (acres)	Body Weight (kg)	Daily Inhalation Dose ² (mg/kg/day)	Short- and intermediate-term MOE ³
1. mixer/loader: open mixing and loading dry flowable for aerial	0.013	0.00077	High	1200	70	0.00017	900,000
2. aerial application of liquid: closed cockpit	0.013	0.000068	Medium	1200	70	0.000015	10,000,000
3. flagging for aerial applications	0.013	0.00035	High	350	70	0.000023	6,800,000
4. mixer/loader: open mixing and loading dry flowable for groundboom	0.013	0.00077	High	200	70	0.000029	5,400,000
5. groundboom application of liquid: open cab	0.013	0.00074	High	200	70	0.000027	5,600,000

¹ PHED unit exposure values are for baseline protection (i.e., no respirator)

² Daily Dose = [Application Rate (lb ai/A) x Area Treated (A/day) x Unit Exposure (mg/lb ai) x Absorption Factor (100%) / Body Weight: 70 kg male BW

³ MOE = NOAEL / Daily Dose. Short- and intermediate-term inhalation NOAEL = 155 mg/kg/day

4.2 Postapplication Exposure and Risk

Occupational exposure can occur via the dermal and/or inhalation route. Inhalation exposure during postapplication activities is considered negligible for all mesosulfuron-methyl use scenarios. Dermal exposure during postapplication activities is not considered because applicable dermal endpoints were not identified. Therefore a risk assessment for postapplication activities with mesosulfuron-methyl treated crops is not necessary. However because acute toxicity tests with technical grade mesosulfuron-methyl resulted in a toxicity category III for primary eye irritation, an interim 12-hour restricted entry interval (REI) is required under the Worker Protection Standard (WPS). Tests for acute dermal and primary skin irritation both resulted in toxicity category IV designations.

5.0 NON-OCCUPATIONAL/RESIDENTIAL EXPOSURE

There are no existing or proposed residential uses for this product. However, spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the groundboom application. The EPA has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The EPA is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The EPA has completed its evaluation of the new database submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the EPA may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

CC: RF

RDI: ORE Team Reviewers: J. Arthur & K. O'Rourke 02/17/04; S. Dapson 03/03/04