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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: 4 MAY 2004

SUBJECT: **PENOXSULAM** - Exposure/Risk Assessment for the Proposed Use of Penoxsulam on Rice.

PC Code: 119031 DP Code: 301888

FROM: Mark I. Dow, Ph.D., Biologist *M. Dow*
Registration Action Branch 1 (RAB1)
Health Effects Division 7509C (HED)

THROUGH: P.V. Shah, Ph.D., Acting Branch Senior Scientist *P.V. Shah*
RAB1/HED 7509C

TO: William Cutchin, Chemist, Risk Assessor
Science Information Management Branch
Health Effects Division 7509C

INTRODUCTION

Under Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, the Dow AgroSciences company (Dow) has requested that the herbicide penoxsulam be registered for use on rice. This memorandum contains HED's estimates of exposure and risk to occupational pesticide handlers, (i.e., mixers, loaders, applicators) and to agricultural workers (from post-application exposures).

USE PATTERN SUMMARY

Dow has requested registration of three products, one liquid formulation and two granular formulations. The liquid formulation is known as GF-443 SC SF (EPA File Symbol 62719 - LNN) and is a 21.7 % (2.0 lb active ingredient per gallon) liquid. The proposed use is for selective postemergence weed control in rice. The proposed label indicates it may be used in Arkansas, Florida, Louisiana, Mississippi, Missouri, Tennessee and Texas.

It may be applied one time per year by aerial or ground equipment at a maximum rate of 0.044 lb a.i./A. It may not be applied through any type of irrigation equipment. It may be applied to water seeded rice or dry seeded rice. The application is to be made between the 1 leaf stage of

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crop growth and 60 days before harvest. The label states: "Use of an agriculturally approved crop oil concentrate at a rate of 1 quart per acre must be used for all applications of GF-443 SC SF." Depending upon cropping practices, the label includes specific water management directions relative to an application of penoxsulam.

The second product is GF-947 Granule SF (EPA File Symbol 62719 - LNG) for selective weed control in water-seeded rice. It is a 0.24 % granular formulation. The proposed product is designated for use in Arkansas, Florida, Louisiana, Mississippi, Missouri, Tennessee and Texas at a rate of 18.5 lb (0.044 lb a.i.) per acre. It may be applied one time per year in ground or aerial equipment. The application should occur between the 1 leaf stage of rice growth and 60 days prior to harvest. For optimum performance, fields should be flooded to a depth of 2 to 4 inches prior to application and water maintained at 2 to 4 inches in depth for 10 days following application.

The third proposed product is GF-947 Granule CA and is intended to be used for selective weed control in water-seeded rice in California. The product is a 0.24 % granule and may be applied by air or ground equipment to water seeded rice in California. Penoxsulam should be applied in California to rice and susceptible weeds from the 1 to 3 leaf stage of growth at a rate of 18.5 lb (0.044 lb a.i.) per acre. This usually occurs 7 - 12 days after seeding. After application, water should be maintained at 2 - 4 inches of depth. It may not be applied within 60 days of harvest. It may not be applied through any type of irrigation system.

All three products suggest a 12 hour restricted entry interval (REI). All proposed labels indicate pesticide handlers must wear long sleeved shirt, long pants and shoes plus socks. See Table 1.0 for a summary of the proposed new use pattern.

Table 1.0 Summary of Proposed New Use of Penoxsulam for Weed Control in Rice	
Formulation	GF-443 SC SF, 2.0 lb a.i./gallon liquid (EPA File Symbol 62719 - LNN); GF-947 Granule SF, 0.24 % granule (EPA File Symbol 62719 - LNG); GF-947 Granule CA, 0.24 % granule (EPA File Symbol 62719 - LNR).
Method of Application	aerial or ground; spray for liquid or granular broadcast
Use Site	rice
Pest	certain grass, broadleaf and sedge weeds
Rate of Application	0.044 lb a.i./A
Maximum Rate/Yr	0.044 lb a.i./A/year = one application
PreHarvest Interval	60 days
Restricted Entry Interval	12 hours
Manufacturer	Dow AgroSciences

OCCUPATIONAL PESTICIDE HANDLERS

Based upon the proposed new use pattern, HED believes the most highly exposed occupational pesticide handlers are:

- 1) mixer/loader using open pour loading of granules,
- 2) mixer/loader using open pour liquid,
- 3) applicator using open cab ground boom equipment,
- 4) applicator using open cab granular broadcast equipment.

Aerial applicators (pilots) are not assessed since many data available to HED indicate pilots are exposed to a much lesser extent than are applicators using open cab ground equipment.

HED expects occupational pesticide handler exposure will typically be short-term (1 - 30 days). One application per year is permitted. Since this is a new chemistry and use, it is not likely that even commercial applicators will experience intermediate-term (1 - 6 months) exposures applying this compound to rice.

It is expected that some private (i.e., grower) applicators may perform all tasks, that is, mix, load and apply the material. However, the HED Science Advisory Council for Exposure (ExpoSac) draft Standard Operating Procedure (SOP) (29 March 2000) directs that although the same individual may perform all tasks, in some cases they shall be assessed separately.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

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 Handler's Exposure Database (PHED) (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for 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 "baseline" **and plus the use of**

protective gloves or other Personal Protective Equipment (PPE) as might be necessary. The proposed product labels involved in this assessment directs applicators and other handlers to wear long-sleeved shirt, long pants and shoes and socks.

The HED Hazard Identification Assessment Review Committee (HIARC) met on 2 December 2003 to discuss the adequacy of the toxicological database relative to the compound penoxsulam (Memo, E. Budd, TXR NO. 0052273, 16 DEC 2003, "PENOXsulAM - 1st Report of the Hazard Identification Assessment Review Committee"). Relative to this assessment of handler exposure, the HIARC did **not** identify a short-term (1 - 30 days) dermal toxicological endpoint stating that there were no dermal, systemic, neuro or developmental toxicity concerns.

The HIARC did identify a short-term inhalation toxicological endpoint from a 13-week feeding study in the dog where histopathological changes were seen in the kidney. The No Observed Adverse Effect Level (NOAEL) is 17.8 mg a.i./kg bw/day.

The HIARC identified intermediate-term dermal and inhalation endpoints with the same NOAEL (17.8 mg a.i./kg bw/day) and from the same 13-week dog feeding study and noting the same toxicological effects. The estimated risks from short-term inhalation exposures would be the same as those estimated for intermediate-term inhalation exposures. HIARC also identified a 50 % dermal absorption factor to be used since dermal endpoints were not identified from dermal toxicity studies. See Appendix for a summary of acute toxicity and toxicological endpoint selection.

Although HED does not expect handlers to experience intermediate-term exposures, risks are estimated for short-term inhalation exposures and for intermediate-term combined risks (i.e., dermal plus inhalation exposures). See Table 2.0 for a summary of estimated exposures and risks.

The HED Cancer Assessment Review Committee (CARC) reviewed the carcinogenic potential of penoxsulam (Memo, J. Kidwell, TXR NO. 0050702, 24 March 2004, "Penoxsulam: Report of the Cancer Assessment Review Committee PC Code 119031"). The CARC determined that there was "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential therefore quantification of human cancer risk is not required."

Table 2.0 Estimated Handler Exposure and Risk from the Use of Penoxsulam on Rice						
Unit Exposure ¹ mg a.i./lb handled	Applic. Rate ²	Units Treated ³ Per Day	Average Daily Dose ⁴ mg a.i./kg bw/day	NOAEL ⁵ mg a.i./kg bw/day	Short-term Inhalation MOE Intermediate-term Combined MOE ⁶	
<i>Mixer/Loader - Granular - Open Pour Supporting Aerial Operations</i>						
Inhal. 0.0017 HC Dermal: No Glove 0.0084 LC With Glove 0.0069 MC	0.044 lb a.i./A	1200 A	Inhal 0.00128 Dermal: No Glove 0.003168 W Glove 0.0026	17.8	Short term inhalation 13,906 Intermed. Term No Glove 4001 W Glove 4587	
<i>Mixer/Loader - Liquid - Open Pour Supporting Aerial Operations</i>						
Inhal. 0.0012 HC Dermal: No Glove 2.9 HC With Glove 0.023 HC	0.044 lb a.i./A	1200 A	Inhal 0.000905 Dermal: No Glove 1.09 W Glove 0.00867	17.8	Short term inhalation 19,668 Intermed. Term No Glove 16 W Glove 1859	
<i>Applicator - Open Cab - Ground-boom</i>						
Inhal 0.00074 HC Dermal: No Glove 0.014 HC With Glove 0.014 MC	0.044 lb a.i./A	200 A	Inhal 0.000093 Dermal: No Glove 0.00088 W Glove 0.00088	17.8	Short term inhalation 191,397 Intermed. Term No Glove 18,293 W Glove 18,293	
<i>Applicator - Open Cab - Granule Broadcast</i>						
Inhal 0.0012 LC Dermal: No Glove 0.0099 LC With Glove 0.0069 LC	0.044 lb a.i./A	200 A	Inhal 0.000151 Dermal: No Glove 0.000622 W Glove 0.000434	17.8	Short term inhalation 117,880 Intermed. Term No Glove 23,027 W Glove 30,427	

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.

2. Applic. Rate. = Taken from proposed labels.

3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000.

4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * % absorption (50 % dermal absorption; 100 % inhalation absorption) ÷ Body Weight (70 kg).

5. No Observed Adverse Effect Level (NOAEL) short-term inhalation NOAEL = 17.8 mg a.i./kg bw/day; intermediate-term (1 - 60 months) dermal and inhalation NOAEL from 13 week dog feeding study NOAEL 17.8 mg a.i./kg bw/day.

6. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. For intermediate-term risk, dermal exposure and inhalation exposure are summed then divided into the NOAEL.

A MOE of 100 is adequate to protect occupational pesticide handlers. All estimated MOE's are > 100 **except for intermediate-term exposures to mixer/loaders not using gloves** with liquid, open-pour loading in support of aerial operations (at either 1200 acres per day or 350 acres per day). Loaders using liquid open-pour in support of aerial operations (and who may experience intermediate-term exposures) should wear protective gloves. Generally speaking, HED advises the use of protective gloves for mixer/loaders. Otherwise, the proposed uses do not exceed HED's level of concern.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

The HED HIARC **did not** identify a short-term (1 - 30 days) dermal toxicological endpoint. There is a 12 hour restricted entry interval. HED expects post-application inhalation exposure to be negligible. Therefore, post-application exposures of agricultural workers does not exceed HED's level of concern.

RESTRICTED ENTRY INTERVAL (REI)

Penoxsulam is classified in acute toxicity category IV for acute dermal toxicity, primary eye irritation, primary skin irritation and it is not a dermal sensitizer. Therefore, the interim Worker Protection Standard (WPS) REI of 12 hours is adequate to protect agricultural workers from post-application exposures to penoxsulam.

RESIDENTIAL

There are no residential uses of penoxsulam known or proposed to HED.

INCIDENTS

The Office of Pesticide Programs' Incident Data System (IDS) (7 April 2004) indicates there are no known incidents with regards to penoxsulam.

APPENDIX

Acute Toxicity of Penoxsulam (PC Code 119031)

Six acute studies conducted on Penoxsulam (XDE-638) Technical (EPA File Symbol 62719-U00); Lot No. NDO5167938; purity = 97.5%; off-white powder. All studies were classified as Acceptable/Guideline, except for the acute inhalation study which was classified as Unacceptable/guideline.

GDLN	Study Type	MRID	Results	Tox Category
870.1100	Acute Oral Rats	45830812	M: LD50 > 5000 mg/kg F: LD50 > 5000 mg/kg	IV
870.1200	Acute Dermal Rabbits	45830815	M: LD50 > 5000 mg/kg F: LD50 > 5000 mg/kg	IV
870.1300	Acute Inhalation Rats <u>UNACCEPTABLE/</u> guideline	45830818	-----	-----
870.2400	Primary Eye Irritation Rabbits	45830820	Minimal irritation	IV
870.2500	Primary Skin Irritation Rabbits	45830823	Minimal irritation	IV
870.2600	Dermal Sensitization Guinea Pigs (Maximization)	45830826	Negative for dermal sensitization	N/A

SUMMARY OF TOXICOLOGY ENDPOINT SELECTION**For Penoxsulam (PC Code 119031)**

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (all populations)	None UF = N/A	Not applicable	No toxicological endpoint attributable to a single exposure was identified in the available toxicology studies on penoxsulam.
Chronic Dietary (all populations)	NOAEL= 14.7 mg/kg/day UF = 100 Chronic RfD = 0.147 mg/kg/day	FQPA SF = 1X cPAD = chronic RfD FQPA SF = 0.147 mg/kg/day	1-Year Chronic Feeding Study in Dogs. LOAEL = 46.2 mg/kg/day based on multifocal hyperplasia of the pelvic epithelium of the kidney.
Incidental Oral Short-Term (1 - 30 days)	NOAEL = 17.8 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	13-Week Feeding Study in Dogs. LOAEL = 49.4 mg/kg/day based on histopathologic changes in kidneys.
Incidental Oral Intermediate-Term (1 - 6 months)	NOAEL = 17.8 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	13-Week Feeding Study in Dogs. LOAEL = 49.4 mg/kg/day based on histopathologic changes in kidneys.
Dermal Short-Term (1 - 30 days)	None	Not applicable	No dermal, systemic, neuro or developmental toxicity concerns.
Dermal Intermediate-Term (1 - 6 months)	Oral study NOAEL= 17.8 mg/kg/day (dermal absorption rate = 50%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	13-Week Feeding Study in Dogs. LOAEL = 49.4 mg/kg/day based on histopathologic changes in kidneys.
Dermal Long-Term (> 6 months)	Oral study NOAEL= 14.7 mg/kg/day (dermal absorption rate = 50%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	1-Year Chronic Feeding Study in Dogs. LOAEL = 46.2 mg/kg/day based on multifocal hyperplasia of the pelvic epithelium of the kidney.

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Inhalation Short-Term (1 - 30 days)	Oral study NOAEL= 17.8 mg/kg/day (inhalation absorption rate = 100%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	13-Week Feeding Study in Dogs. LOAEL = 49.4 mg/kg/day based on histopathologic changes in kidneys.
Inhalation Intermediate-Term (1 - 6 months)	Oral study NOAEL= 17.8 mg/kg/day (inhalation absorption rate = 100%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	13-Week Feeding Study in Dogs. LOAEL = 49.4 mg/kg/day based on histopathologic changes in kidneys.
Inhalation Long-Term (> 6 months)	Oral study NOAEL= 14.7 mg/kg/day (inhalation absorption rate = 100%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	1-Year Chronic Feeding Study in Dogs. LOAEL = 46.2 mg/kg/day based on multifocal hyperplasia of the pelvic epithelium of the kidney.
Cancer (oral, dermal, inhalation)	The results from the carcinogenicity studies in rats and mice together with other relevant data and information will be presented to the HED Cancer Assessment Review Committee (CARC) for further discussion and assessment of the carcinogenic potential of penoxsulam.		

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, N/A = Not Applicable.

NOTE: The Special FQPA Safety Factor recommended by the HIARC **assumes** that the exposure databases (dietary food, drinking water, and residential) are complete and that the risk assessment for each potential exposure scenario includes all metabolites and/or degradates of concern and does not underestimate the potential risk for infants and children.



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Chemical: Benzenesulfonamide, 2-(2,2-difluoroethox

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