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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 28 May 2002

SUBJECT: **DIFLUFENZOPYR** - Exposure/Risk Assessment for the Proposed New Uses of Distinct® Herbicide on "Commercial, Industrial Turf and Non Crop Areas".

DP Code: 282985 PC Codes: 005107

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INTRODUCTION

The BASF Corporation, Agricultural Products, has submitted a request to register the herbicide diflufenzopyr (2-(-[([3,5-difluorophenylamino]carbonyl)-hydrazono]ethyl)-3-pyridinecarboxylic acid) as formulated in Distinct® herbicide for the post-emergence control of annual and perennial broad leaf weed species. According to the supplemental label, Distinct® "may be used on cool and warm-season turfgrasses on golf courses, athletic fields, recreational and non-residential areas, commercial and industrial turf sites, sod farms, cemeteries and other similar areas." This memorandum presents the Health Effects Division's (HED) estimate of pesticide handler exposures and risks that might result from the proposed new uses. Post-application exposure and risk are also discussed.

Distinct® is a wettable granule herbicide that is comprised of 0.20 lb acid equivalent diflufenzopyr per pound of product and 0.50 lb acid equivalent dicamba per pound of product. The proposed new uses comprise an amendment to the EPA Registered Product No. 7969-150. Table 1.0 contains a summary of the proposed new use patterns.

Table 1.0 Use Pattern Summary of Proposed New Uses of *Diflufenzopyr* in Distinct® Herbicide "For Use in Commercial, Industrial Turf and Non Crop Areas"	
Formulation	Wettable Granule; diflufenzopyr 0.20 lb acid equivalent/ lb product
Use Site	non-residential turf including golf courses & recreational sites
Application Method	ground
Maximum Application Rate* **pounds acid equivalent/A**	0.075 lb a.e./A 0.125 lb a.e./A/SEASON
Frequency/Timing	two if max rate "split"
PHI	30 day for sod
REI	label lists 12 hours
Manufacturer	BASF Corporation

* 0.20 lb a.e./lb product ÷ 16 oz/lb product = 0.0125 lb a.e./oz. 6.0 oz/A * 0.0125 lb a.e./oz = 0.075 lb a.e./A
0.20 lb a.e./lb product ÷ 16 oz/lb product = 0.125 lb a.e./oz. 10.0 oz/A/Season * 0.0125 lb a.e./oz = 0.125 lb a.e./A/Season

HANDLER EXPOSURE

On 24 September 1998, the HED Hazard Identification Assessment Review Committee (HIARC) met to discuss the adequacy of the toxicology database with respect to the compound **diflufenzopyr** (Memo, W. Dykstra et al., 6 October 1998, HED Doc. No. 012894). Diflufenzopyr is in toxicity category IV for acute oral, dermal and inhalation toxicity, category III for primary eye irritation, category IV for primary skin irritation and it is not a dermal sensitizer. Diflufenzopyr is classified as "Not Likely" to be a human carcinogen. Short, Intermediate and Long-term dermal toxicological endpoints were **not** identified as "no dermal or systemic toxicity was seen at 1000 mg/kg/day in the 21 day dermal toxicity study in rabbits." Short-term and Intermediate-term inhalation toxicity endpoints were established (58 mg/kg/day based on subchronic feeding studies in dogs where compensated hemolytic anemia was observed in both sexes). A long-term inhalation toxicity endpoint was not identified. A Margin of Exposure (MOE) of 100 is adequate to ensure the safety of pesticide handlers in this case. See Appendix for a summary of toxicological endpoint selection for diflufenzopyr. HED recently completed a Section 3 risk assessment for the use of diflufenzopyr on sweet corn, pop corn, pasture and rangeland (Memo, J. Tyler 20 DEC 2001, DP 271603). The toxicological endpoints are those identified by the HIARC (Memo, W. Dykstra et al., 6 OCT 1998) and used in the Section 3 assessment.

HED has revised the definitions used in its human health risk assessments to describe occupational and residential exposure durations (Memo, M. Stasikowski, June 4, 2001, "Changes in the Definition of Exposure Durations for Occupational/Residential Risk Assessments

Performed in the Health Effects Division"). The new exposure durations are as follows: 1) short-term, defined as lasting from 1 day to 1 month; 2) intermediate-term, defined as lasting from 1 to 6 months; 3) long-term, defined as lasting longer than 6 months. The RAB1 toxicologists determined that the toxicity endpoint (subchronic feeding study in the dog) originally selected for the short- (1-7 days) and intermediate-term (7 days-3 months) inhalation endpoints is also applicable for the new short- and intermediate exposure duration definitions.

Since the HIARC did not identify dermal toxicological endpoints of concern, citing no effects at the limit dose of 1000 mg/kg bw/day, assessment of risk to pesticide handlers via the dermal route is not necessary and therefore not presented here. An assessment of exposure and risk is presented for pesticide handlers via the inhalation route since the toxicological endpoints of concern that were identified, are for short and intermediate term inhalation exposure to diflufenzopyr.

Based on the preceding information, estimates of exposure and risk were conducted for a mixer/loader and an applicator. See Table 2.0 for summary of findings.

Table 2.0
Estimated Exposures and Risk to Pesticide Handlers Applying *DIFLUFENZOPYR* In Distinct® Herbicide "For Use in Commercial, Industrial Turf and Non Crop Areas"

Unit Exposure[1] mg a.i./lb handled	Application Rate[2] lb a.i. handled/A	Units Treated[3]	Avg. Daily Dose[4] mg a.i./kg bw/day	NOAEL[5] mg a.i./kg bw/day	MOE[6]
Mixer/Loader - Dry Flowable - Open Pour					
INHALAT. 0.00077 HC	0.075	200 A/day	1.65×10^{-4}	58	351,000
Applicator - Ground Boom - Open Cab					
INHALAT 0.00074 HC	0.075	200 A/day	1.59×10^{-4}	58	365,000

1. Unit Exposure = mg a.i./lb a.i. handled; taken from the Pesticide Handler's Exposure Database PHED Surrogate Exposure Guide version 1.1; August 1998; Inhalat. = Inhalation. HC = high confidence data;
2. Application Rate from proposed amendments to EPA Reg No. 7969-150. 0.20 lb a.e./lb product ÷ 16 oz/lb = 0.0125 lb a.e./oz product * 6 oz product/A = 0.075 lb a.e./A
3. Acres Treated are derived from EXPO Sci.Adv.Coun Pol. No. 9.
4. Average Daily Dose (ADD) = Unit Exposure * Application Rate * Units Treated ÷ 70 kg body weight. Inhalation exposure assumes 100% inhalation absorption.
5. NOAEL = No Observed Adverse Effect Level (mg a.i./kg bw/day). For diflufenzopyr, the short- and intermediate- term inhalation endpoint is 58 mg a.i./kg bw/day.
6. Margin of Exposure (MOE) = NOAEL ÷ ADD

MOEs ≥ 100 are acceptable to protect pesticide handlers and do not exceed HEDs level of concern. Since the estimated MOEs for the proposed new use patterns are > 100, they do not exceed HEDs level of concern.

POST-APPLICATION EXPOSURE

After treatment, there is a possibility for post-application exposure to "workers" or other persons entering treated turf/sod areas. However, since the HIARC did not identify dermal toxicological endpoints of concern, estimates of post-application exposure and risk are not necessary.

APPENDIX[1]

Summary of Toxicological Endpoints for Use in Human Risk Assessment[2].

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary Females 13-50 years old	NOAEL = 100 mg/kg/day UF = 100 **Acute RfD = 1.0** mg/kg/day	FQPA SF = **1x** **aPAD** = acute RfD / FQPA SF = **1.0** mg/kg/day	Rabbit Developmental Study. LOAEL = 300 mg/kg/day based on extra ribs and other skeletal variations in the rabbit developmental study. These effects can occur from a single dose and females 13-50 are the population subgroup of concern. The developmental findings occurred at a level of severe maternal toxicity.
Acute Dietary general population	NOAEL = None UF = None Acute RfD = None	An appropriate endpoint attributable to a single exposure for this population subgroup was not identified in the oral toxicity studies including the maternal effects in rat and rabbit developmental studies.	
Chronic Dietary all populations	NOAEL= 26 mg/kg/day UF =100 Chronic RfD = 0.26 mg/kg/day	FQPA SF = **1x** **cPAD** = chronic RfD / FQPA SF = **0.26** mg/kg/day	52-week Dog Feeding Study. LOAEL = 299 mg/kg/day based on compensated hemolytic anemia in both sexes of dogs
Short-Term Dermal (1 to 30 days) (Occupational)	NOAEL= None	No dermal or systemic toxicity was seen at 1000 mg/kg/day in the 21-day dermal toxicity study in rabbits. Therefore, this risk assessment is not required.	
Intermediate-Term Dermal (1 to 6 months) (Occupational)	NOAEL= None	No dermal or systemic toxicity was seen at 1000 mg/kg/day in the 21-day dermal toxicity study in rabbits. Therefore, this risk assessment is not required.	
Long-Term Dermal (6 months to lifetime) (Occupational)	NOAEL= None	The use pattern does not indicate a concern for potential dermal exposure. Therefore, this risk assessment is not required.	

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Endpoint for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1 to 30 days) (Occupational)	oral study NOAEL = 58 mg/kg/day (inhalation absorption factor = 100%)	LOC for MOE = 100 (Occupational)	Subchronic feeding- dog. LOAEL = 403 mg/kg/day based on the occurrence of erythroid hyperplasia in the bone marrow, extramedullary hemopoiesis in the liver, and hemosiderin deposits in Kupffer cells.
Intermediate-Term Inhalation (1 to 6 months) (Occupational)	oral study NOAEL =58 mg/kg/day (inhalation absorption factor = 100%)	LOC for MOE = 100 (Occupational)	Subchronic feeding- dog. LOAEL = 403 mg/kg/day based on the occurrence of erythroid hyperplasia in the bone marrow, extramedullary hemopoiesis in the liver, and hemosiderin deposits in Kupffer cells.
Long-Term Inhalation (6 months to lifetime) (Occupational)	inhalation (or oral) study NOAEL= None (inhalation absorption factor = 100%)	The use pattern does not indicate a concern for potential exposure via this route. Therefore, this risk assessment is not required.	
Cancer (oral, dermal, inhalation)	None	Q* = None	In accordance with the *1996 Proposed Guidelines for Carcinogenicity Risk Assessments*, diflufenzopyr was classified as **"Not Likely"** to be a human carcinogen. This classification is based on the lack of evidence of carcinogenicity in mice and rats when tested at doses that were judged to be adequate to assess carcinogenicity.

1. Taken from Memo, J. Tyler, 20 DEC 2001, DP Code 271603
2. UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, cPAD = chronic population adjusted dose, RfD = reference dose, MOE = margin of exposure, LOC = level of concern.

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