UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

**OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES**

MEMORANDUM

DATE: 12/19/2007

SUBJECT: **Pyroxsulam** Chronic Aggregate Dietary (Food and Drinking Water) Exposure Analysis for the Section 3 Registration Action

Petition No.: 6F7101
PC Code: 108702
DP Number: 335502
Decision No.: 369826

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Executive Summary

Chronic aggregate dietary exposure analyses were performed for the new active ingredient pyroxsulam using both the Dietary Exposure Evaluation Model DEEM-FCID™, Version 2.03 and the Lifeline Version 4.2 Model. These Models use food consumption data from the U.S. Department of Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support a Section 3 request for use on wheat.

Acute Dietary Exposure Results and Characterization

An acute dietary exposure analysis was not performed because the HED risk assessment team did not select an endpoint for acute dietary exposure analysis.

Chronic Dietary (Food and Drinking Water) Exposure Results and Characterization

Unrefined chronic dietary exposure analyses were performed. In tolerance petition number 6F7101, the registrant requested a tolerance for only one crop: wheat. As a result, the analysis included wheat commodities and drinking water only. The recommended wheat tolerance (0.01 ppm) was used for wheat commodities. A conservative value was also used for drinking water. The SCI-GROW groundwater value of 0.465 ppb was greater than the surface water value of 0.102 ppb. As a result, the groundwater concentration was used. A percent crop treated value of 100% was used for all wheat commodities. By both models, the chronic dietary risk estimates for the general U.S. population and all population subgroups are below HED's level of concern. The general U.S. population and all subgroups utilize <1% of the cPAD. By the DEEM-FCID Model, the most highly exposed population subgroup is All Infants (<1 year), which utilizes 0.004% of the cPAD. The general U.S. population utilizes 0.003% of the cPAD. In the Lifeline Model, the most highly exposed population subgroup is Children 3-5, which utilizes 0.004% of the cPAD. The general U.S. population utilizes 0.002% of the cPAD.

Cancer Dietary Exposure Results and Characterization

Pyroxsulam is classified as "not likely to be carcinogenic to humans." A separate cancer dietary risk assessment was not performed.

I. Introduction

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the point of departure (e.g., NOAEL, LOAEL) divided by the required uncertainty or safety factors.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. HED is generally concerned when estimated cancer risk exceeds one in one million. References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides website: "Available Information on Assessing Exposure from Pesticides, A User's Guide," 6/21/2000, web link: http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf ; or see SOP 99.6 (8/20/1999).

Pyroxsulam is a new active ingredient. As a result, this dietary exposure analysis is the first analysis to be performed for the chemical.

II. Residue Information

As pyroxsulam is a new active ingredient, there are no tolerances listed for it in the 40CFR. The residue of concern for risk assessment is parent only. In the wheat field trials, the residue values for wheat grain were all below the limit of quantitation of 0.01 ppm. HED is recommending in favor of an LOQ tolerance. Therefore, a value of 0.01 ppm was entered for all wheat commodities. A processing study was not submitted for wheat. As a result, a value of 1.0 was used as the processing factor for flour, bran, and germ.

III. Drinking Water Data

The estimated drinking water concentration (EDWC) used in the dietary risk assessment was provided by the Environmental Fate and Effects Division (EFED, D332122, G. Orrick, 8/30/2007). The EDWC was incorporated directly into this dietary assessment in the food categories "water, direct, all sources" and "water, indirect, all sources." The EDWCs for pyroxsulam were generated with the coupled models PRZM and EXAMS for surface water and SCI-GROW for groundwater. Modeled application rates represent the maximum use pattern of two proposed labels for use on wheat. EDWCs reflect exposure to pyroxsulam and all potential degradates of concern. The SCI-GROW groundwater value of 0.465 ppb was greater than the PRZM-EXAMS 1-in-10 year annual mean exposure value of 0.164 ppb (surface water). As a result, the groundwater concentration was used. The SCI-GROW Model and its description are available at the EPA internet site: http://www.epa.gov/oppefed/models/water/.

IV. Program and Consumption Information

Several reasonable peer-reviewed software programs are available for modeling dietary exposure to pesticides. For a variety of technical, historical, and availability reasons, DEEM™ is the program that has generally been used by EPA's Office of Pesticide Programs for conducting its dietary risk assessments. With the advent and current availability of a number of other exposure software programs, OPP, registrants, and other interested parties have available to them the option of selecting other peer-reviewed exposure software in conducting risk assessments for pesticides. Lifeline™ is one such model and is being used along with the DEEM-FCID Model in this HED review. Dietary

Exposure assessments may also be performed with other, similar programs, and if submitted, such results will be reviewed by EPA for acceptability and comparability to existing peer-reviewed software being used by OPP.

IVa. DEEM-FCID™ Program and Consumption Information

A chronic dietary exposure assessment for pyroxsulam was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™,Version 2.03 which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

IVb. Lifeline™ Program and Consumption Information

A chronic dietary exposure analysis was also conducted using the Lifeline™ Model (Version 4.41). The Lifeline™ Model used the same consumption data as did the DEEM-FCID™ Model (CSFII, 1994-1996 and 1998 consumption data with FCID). Lifeline™ uses the recipe file to relate RACs to foods "as-eaten." Lifeline™ converts the RAC residues into food residues by randomly selecting a RAC residue value from the "user defined" residue distribution (created from the residue, percent crop treated, and processing factors data), and calculating a net residue for that food based on the ingredients' mass contribution to that food item. For example, 'apple pie' will have a residue distribution based on the residues provided for apples (adjusted by the appropriate processing factors and percent crop treated), as well as the residues for each of the other ingredients in the apple pie recipe for which there may be tolerances. Lifeline™

calculates dietary exposure from 'apple pie' based on the amount eaten, and the residue drawn from the 'apple pie' residue distribution for that eating occasion.

Lifeline™ models the individual's dietary exposures over a season by selecting a new CSFII diary each day from a set of similar individuals based on age and season attributes. Lifeline™ groups CSFII diaries based on the respondents' age and the season during which the food diary was recorded. Further information regarding the Lifeline™ Model can be found on the following web site: www.theLifeline™group.org.

V. Toxicological Information

The HED risk assessment team selected endpoints for dietary exposure assessment. HED's Risk Assessment Review Committee met to review the endpoints. The endpoints that were selected are summarized in Table 1 below. The FQPA Safety Factor for pyroxsulam was reduced to 1x.

Table 1. Toxicological Doses and Endpoints for Pyroxsulam for Use in Dietary Exposure Assessment

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	N/A	N/A	N/A	**No appropriate endpoint identified;** no effects were attributable to a single dose, there are no developmental effects, neurotoxicity, or other hazard concerns
Acute Dietary (Females 13-49 years of age)	N/A	N/A	N/A	**No appropriate endpoint identified;** no effects were attributable to a single dose, there are no developmental effects, neurotoxicity, or other hazard concerns
Chronic Dietary (All Populations)	NOAEL = 100 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	Chronic RfD = 100 mg/kg/day cPAD = 1.0 mg/kg/day	Carcinogenicity study in mice LOAEL = 1000 mg/kg/day based on increased absolute and relative liver weights and increased incidence of hepatocellular clear cell foci of alteration in males
Cancer (oral, dermal, inhalation)	No treatment-related tumors were observed in carcinogenicity studies in rats and mice. Pyroxsulam was classified as "not likely to be carcinogenic to humans."			

NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. N/A = not applicable.

VI. Results/Discussion

As stated above, for acute and chronic assessments, HED is concerned when dietary risk exceeds 100% of the PAD. The DEEM-FCID™ and Lifeline analyses estimate the dietary exposure of the U.S. population and various population subgroups. The results reported in Table 2 are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years. Cancer risk is determined for the general U.S. population only.

Results of Chronic Dietary Exposure Analysis

The results of the chronic dietary exposure analysis are reported in Table 2. The chronic dietary risk estimates for the general U.S. population and all population subgroups are below HED's level of concern by both models. The general U.S. population and all subgroups utilize <1% of the cPAD. By the DEEM-FCID Model, the most highly exposed population subgroup is All Infants (<1 year), which utilizes 0.004% of the cPAD. The general U.S. population utilizes 0.003% of the cPAD. By the Lifeline Model, the most highly exposed population subgroup is Children 3-5, which utilizes 0.004% of the cPAD. The general U.S. population utilizes 0.002% of the cPAD.

Table 2. Result of Chronic Dietary Exposure and Risk Estimates for Pyroxsulam

Population Subgroup	PAD, mg/kg/day	DEEM-FCID		Lifeline	
		Exposure, mg/kg/day	% PAD	Exposure, mg/kg/day	%PAD
Acute Dietary Estimates					
N/A					
Chronic Dietary Estimates					
U.S. Population	1.0	0.000027	<1	0.000017	<1
All infants (< 1 yr)	1.0	0.000040	<1	0.000007	<1
Children 1-2 yrs	1.0	0.000055	<1	0.000035	<1
Children 3-5 yrs	1.0	0.000055	<1	0.000041	<1
Children 6-12 yrs	1.0	0.000038	<1	0.000028	<1
Youth 13-19 yrs	1.0	0.000024	<1	0.000017	<1
Adults 20-49 yrs	1.0	0.000023	<1	0.000015	<1
Adults 50+ yrs	1.0	0.000021	<1	0.000014	<1
Females 13-49 yrs	1.0	0.000022	<1	0.000017	<1
Cancer Dietary Estimate					
U.S. Population	N/A				

VII. Characterization of Inputs/Outputs

Conservative estimates of the drinking water concentration and the food residue levels were used. Further refinements could be made to the analysis, but they are not necessary at the present time.

VIII. Conclusions

Based on conservative assumptions, the chronic dietary risk estimates for the general U.S. population and all population subgroups are below HED's level of concern regardless of which of the two models is used: DEEM-FCID or Lifeline. The chronic dietary risk estimates for the general U.S. population and all population subgroups are below HED's level of concern. The general U.S. population and all subgroups utilize <1% of the cPAD.

IX. List of Attachments:

Attachment 1: Residue Input File for Chronic Analysis
Attachment 2: Results of Chronic Dietary Exposure Analysis

Attachment 1: Residue Input File for Chronic Analysis

DEEM-FCID Program Version 2.03
NOAEL: 100 mg/kg bw/day
cPAD: 1.0 mg/kg bw/day

Filename: C:\Documents and Settings\ddotson\My Documents\DEEMFCID\Pyroxsulam\Pyroxsulam.R98
Date created/last modified: 11-01-2007/14:04:14/8

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
15004010	15	Wheat, grain	0.010000	1.000	1.000	
15004011	15	Wheat, grain-babyfood	0.010000	1.000	1.000	
15004020	15	Wheat, flour	0.010000	1.000	1.000	
15004021	15	Wheat, flour-babyfood	0.010000	1.000	1.000	
15004030	15	Wheat, germ	0.010000	1.000	1.000	
15004040	15	Wheat, bran	0.010000	1.000	1.000	
86010000	O	Water, direct, all sources	0.000465	1.000	1.000	
86020000	O	Water, indirect, all sources	0.000465	1.000	1.000	

Attachment 2: Results of Chronic Dietary Exposure Analysis

DEEM-FCID Version 2.03 Chronic Analysis for Pyroxsulam (1994-98 Data)

Residue file name: C:\Documents and Settings\ddotson\My Documents\DEEMFCID\Pyroxsulam\Pyroxsulam.R98
Adjustment factor #2 NOT used.
Analysis Date 11-02-2007/10:02:35 Residue file dated: 11-02-2007/10:01:15/8
Reference dose (RfD, Chronic) = 1 mg/kg bw/day

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000027	0.0%
U.S. Population (spring season)	0.000027	0.0%
U.S. Population (summer season)	0.000027	0.0%
U.S. Population (autumn season)	0.000027	0.0%
U.S. Population (winter season)	0.000027	0.0%
Northeast region	0.000027	0.0%
Midwest region	0.000028	0.0%
Southern region	0.000025	0.0%
Western region	0.000028	0.0%
Hispanics	0.000026	0.0%
Non-hispanic whites	0.000027	0.0%
Non-hispanic blacks	0.000025	0.0%
Non-hisp/non-white/non-black	0.000028	0.0%
All infants (< 1 year)	0.000040	0.0%
Nursing infants	0.000016	0.0%
Non-nursing infants	0.000049	0.0%
Children 1-6 yrs	0.000054	0.0%
Children 7-12 yrs	0.000036	0.0%
Females 13-19 (not preg or nursing)	0.000022	0.0%
Females 20+ (not preg or nursing)	0.000022	0.0%
Females 13-50 yrs	0.000023	0.0%
Females 13+ (preg/not nursing)	0.000024	0.0%
Females 13+ (nursing)	0.000030	0.0%
Males 13-19 yrs	0.000026	0.0%
Males 20+ yrs	0.000022	0.0%
Seniors 55+	0.000021	0.0%
Children 1-2 yrs	0.000055	0.0%
Children 3-5 yrs	0.000055	0.0%
Children 6-12 yrs	0.000038	0.0%
Youth 13-19 yrs	0.000024	0.0%
Adults 20-49 yrs	0.000023	0.0%
Adults 50+ yrs	0.000021	0.0%
Females 13-49 yrs	0.000022	0.0%