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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 26-MAR-2003

SUBJECT: **Imazapyr.** Chronic Dietary Exposure Assessment for the Section 3 Registration Action on Grasses and Aquatic Sites.

PC Code: 128821
DP Barcode: D288806

REVIEWER: William H. Donovan, Ph.D., Chemist
Reregistration Branch 3 (RRB3)/Health Effects Division (HED) (7509C)

THROUGH: Thurston Morton, Chemist
Sheila Piper, Chemist
Dietary Exposure Science Advisory Council (DESAC)
HED (7509C)

and

G. Jeffrey Herndon, Branch Senior Scientist
Registration Action Branch 1 (RAB1)/HED (7509C)

TO: Dana Vogel, Risk Assessor
RAB1/HED (7509C)

Executive Summary

The purpose of this memorandum is to report the results of a dietary exposure analysis for imazapyr. In this analysis the chronic dietary exposure and risk estimates resulting from food intake were determined for the general U.S. population and various population subgroups.

A chronic dietary exposure analysis was performed in order to determine the exposure and risk estimates which result from the addition of fish, shellfish, and livestock commodities to the commodity residue list for imazapyr. The proposed tolerances are associated with Section 3 requests.

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A chronic dietary exposure analysis was performed in order to determine the exposure and risk estimates which result from the addition of fish, shellfish, and livestock commodities to the commodity residue list for imazapyr. The proposed tolerances are associated with Section 3 requests.

The chronic dietary analysis for imazapyr shows that the exposure for all population subgroups is below HED's level of concern. All population subgroups are predicted to have exposures < 0.1% of the cPAD.

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. This is the population adjusted dose (PAD), which HED has concluded will result in no unreasonable adverse health effects. The PAD is the Reference Dose (RfD) divided by the special FQPA Safety Factor. Dietary risk is expressed as a percentage of the PAD. For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: "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 (8/20/99).

II. Residue Information

New Uses

For the proposed new uses, HED recommended tolerance levels were employed in the DEEM-FCID analysis together with 100% CT assumptions and DEEM default processing factors. These recommended levels were taken from the appropriate chemistry review (D275561, W. Donovan, 20-MAR-2003)] and are summarized as follows:

Grass, forage	100 ppm
Grass, hay	30 ppm
Fish	1.0 ppm
Shellfish	0.10 ppm
Fat of cattle, sheep, goats, and horses	0.05 ppm
Kidney of cattle, sheep, goats, and horses	0.20 ppm
Meat byproducts (except kidney) of cattle, sheep, goats, and horses	0.05 ppm
Meat of cattle, sheep, goats, and horses	0.05 ppm
Milk	0.01 ppm

Note that the above listed tolerance levels are expressed in terms of imazapyr *per se*, consistent with the HED Metabolism Assessment Review Committee (MARC) decision that the residue of concern for the tolerance expression and for risk assessment purposes is parent only in plants, livestock, fish, and water (TXR# 0051641, W. Donovan and E. Rinde, 13-MAR-2003).

Established Uses

A listing of established imazapyr tolerances (for residues of imazapyr *per se*) is given in 40 CFR §180.500. This listing consists of field corn raw agricultural commodities (RACs), all at 0.05 ppm.

III. DEEM-FCID™ Program and Consumption Information

An imazapyr chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-1996 and 1998 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. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk 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. The resulting residue consumption estimate for each food/food form is summed with the residue consumption 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.

IV. Toxicological Information

The Hazard Identification Assessment Review Committee (HIARC) discussed the toxicity of imazapyr in a meeting held on 06-FEB-2003 (TXR# 0051689, E. Rinde, 25-MAR-2003). The relevant dietary exposure toxicological doses and endpoints selected by the HIARC are summarized in Table 1. Based on the HIARC conclusions and the imazapyr risk assessment team's evaluation of the hazard and exposure data, the team recommended that the Special FQPA Safety Factor be reduced to 1x.

Table 1. Summary of Toxicological Doses and Endpoints for Imazapyr for Use in Dietary Exposure Assessment			
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 and general population	none	none	An appropriate endpoint attributable to a single oral dose was not available in the data base.
Chronic Dietary all populations	NOAEL= 250 mg/kg/day UF = 100 Chronic RfD = 2.5 mg/kg/day	FQPA SF = 1X cPAD = cRfD / FQPA SF = 2.5 mg/kg/day	1-year dog (feeding) study No LOAEL found as 250 mg/kg/day was highest dose tested (HDT). Endpoint of concern may be translated from that of imazapic where skeletal muscle effects were seen in dogs.
Cancer	Cancer classification "Group E" in 26-APR-1995 CPRC meeting	N/A	N/A

V. Results/Discussion

As stated above, for chronic assessments, HED is concerned when dietary risk exceeds 100% of the cPAD. The DEEM-FCID™ analysis estimates the dietary exposure of the U.S. population and 26 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, males 20-49, and adults 50+ years.

Results of Chronic Dietary Exposure Analysis

Table 2. Results of Chronic Dietary Exposure Analysis for Imazapyr.			
Population Subgroup	**cPAD (mg/kg/day)**	**Exposure (mg/kg/day)**	**% cPAD**
General U.S. Population	2.5	0.000340	<0.1
All Infants (< 1 year old)	2.5	0.000273	<0.1
Children 1-2 years old	2.5	0.000828	<0.1
Children 3-5 years old	2.5	0.000730	<0.1
Children 6-12 years old	2.5	0.000499	<0.1
Youth 13-19 years old	2.5	0.000309	<0.1
Adults 20-49 years old	2.5	0.000267	<0.1

Table 2. Results of Chronic Dietary Exposure Analysis for Imazapyr.

Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
Females 13-49 years old	2.5	0.000257	<0.1
Adults 50+ years old	2.5	0.000287	<0.1

VI. Discussion of Uncertainties

Adequate data are available for the determination of tolerance levels, as discussed in the applicable residue chemistry memos. For fish and shellfish, the tolerance levels are based on residue levels measured in magnitude of the residue studies, as opposed to being based on the method LOQ. For field corn, and all livestock commodities except kidney, the tolerance levels are set at the method LOQ. For kidney, use of maximum grass residue levels in conjunction with the results of a bovine feeding study, allowed projection of a maximum imazapyr residue level of 0.20 ppm (the recommended tolerance level).

The present dietary exposure analysis made use of tolerance-level residues, 100% crop treated assumptions, and DEEM default processing factors. All processing factors in the current analysis were 1.0 except for the "beef, meat, dried" factor where a value of 1.92 was used. Thus, the exposure estimates provided here overestimate the actual risk. With the current low-level of risk from imazapyr, refinement was determined to be unnecessary.

VII. Conclusions

The Tier 1 chronic dietary risk assessment for imazapyr shows that exposures for all population subgroups are below HED's level of concern. Total food exposure for all population subgroups was determined to occupy <0.1% cPAD.

VIII. List of Attachments

Attachment 1: Imazapyr Tier 1 residue file for chronic DEEM™ analysis.
Attachment 2: Imazapyr Chronic DEEM™ analysis.

cc (with Attachments): W. Donovan, W. Cutchin
RDI: G. Herndon (26-MAR-2003)
W.H. Donovan:821B:CM#2:(703)305-7330:7509C:RRB3

ATTACHMENT 1. RESULTS OF CHRONIC DEEM ANALYSIS.

U.S. Environmental Protection Agency Ver. 1.30
DEEM-FCID Chronic analysis for IMAZAPYR (1994-98 data)
Residue file name: C:\DEEMFCID\128821.r98 Adjustment factor #2 NOT used.
Analysis Date 03-20-2003/14:16:24 Residue file dated: 03-20-2003/14:11:01/8
Reference dose (RfD, Chronic) = 2.5 mg/kg bw/day
COMMENT 1: PP# 0F6166 (grass & aquatic uses)

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000340	0.0%
U.S. Population (spring season)	0.000360	0.0%
U.S. Population (summer season)	0.000344	0.0%
U.S. Population (autumn season)	0.000334	0.0%
U.S. Population (winter season)	0.000320	0.0%
Northeast region	0.000366	0.0%
Midwest region	0.000321	0.0%
Southern region	0.000324	0.0%
Western region	0.000360	0.0%
Hispanics	0.000349	0.0%
Non-hispanic whites	0.000312	0.0%
Non-hispanic blacks	0.000409	0.0%
Non-hisp/non-white/non-black	0.000566	0.0%
All infants (< 1 year)	0.000273	0.0%
Nursing infants	0.000075	0.0%
Non-nursing infants	0.000348	0.0%
Children 1-6 yrs	0.000739	0.0%
Children 7-12 yrs	0.000483	0.0%
Females 13-19 (not preg or nursing)	0.000276	0.0%
Females 20+ (not preg or nursing)	0.000266	0.0%
Females 13-50 yrs	0.000273	0.0%
Females 13+ (preg/not nursing)	0.000244	0.0%
Females 13+ (nursing)	0.000294	0.0%
Males 13-19 yrs	0.000343	0.0%
Males 20+ yrs	0.000283	0.0%
Seniors 55+	0.000287	0.0%
Children 1-2 yrs	0.000828	0.0%
Children 3-5 yrs	0.000730	0.0%
Children 6-12 yrs	0.000499	0.0%
Youth 13-19 yrs	0.000309	0.0%
Adults 20-49 yrs	0.000267	0.0%
Adults 50+ yrs	0.000287	0.0%
Females 13-49 yrs	0.000257	0.0%

ATTACHMENT 2. RESIDUE FILE LISTING FOR IMAZAPYR.

Filename: C:\DEEMFCID\128821.r98 Chemical: Imazapyr
RfD(Chronic): 2.5 mg/kg bw/day NOEL(Chronic): 250 mg/kg bw/day
RfD(Acute): 0 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day
Date created/last modified: 03-20-2003/14:11:01/8 Program ver. 1.30
Comment: PP# 0F6166 (grass & aquatic uses)

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
21000440	M	Beef, meat	0.050000	1.000	1.000	N PP# 0F6166
21000441	M	Beef, meat-babyfood	0.050000	1.000	1.000	N PP# 0F6166
21000450	M	Beef, meat, dried	0.050000	1.920	1.000	N PP# 0F6166
21000460	M	Beef, meat byproducts	0.050000	1.000	1.000	N PP# 0F6166
21000461	M	Beef, meat byproducts-babyfood	0.050000	1.000	1.000	N PP# 0F6166
21000470	M	Beef, fat	0.050000	1.000	1.000	N PP# 0F6166
21000471	M	Beef,fat-babyfood	0.050000	1.000	1.000	N PP# 0F6166
21000480	M	Beef, kidney	0.200000	1.000	1.000	N PP# 0F6166
21000490	M	Beef, liver	0.050000	1.000	1.000	N PP# 0F6166
21000491	M	Beef, liver-babyfood	0.050000	1.000	1.000	N PP# 0F6166
15001200	15	Corn, field, flour	0.050000	1.000	1.000	PP# 6F4641
15001201	15	Corn, field, flour-babyfood	0.050000	1.000	1.000	PP# 6F4641
15001210	15	Corn, field, meal	0.050000	1.000	1.000	PP# 6F4641
15001211	15	Corn, field, meal-babyfood	0.050000	1.000	1.000	PP# 6F4641
15001220	15	Corn, field, bran	0.050000	1.000	1.000	PP# 6F4641
15001230	15	Corn, field, starch	0.050000	1.000	1.000	PP# 6F4641
15001231	15	Corn, field, starch-babyfood	0.050000	1.000	1.000	PP# 6F4641
15001240	15	Corn, field, syrup	0.050000	1.000	1.000	PP# 6F4641
15001241	15	Corn, field, syrup-babyfood	0.050000	1.000	1.000	PP# 6F4641
15001250	15	Corn, field, oil	0.050000	1.000	1.000	PP# 6F4641
15001251	15	Corn, field, oil-babyfood	0.050000	1.000	1.000	PP# 6F4641
80001570	F	Fish-freshwater finfish	1.000000	1.000	1.000	N PP# 0F6166
80001580	F	Fish-freshwater finfish, farm ra	1.000000	1.000	1.000	N PP# 0F6166
80001590	F	Fish-saltwater finfish, tuna	1.000000	1.000	1.000	N PP# 0F6166
80001600	F	Fish-saltwater finfish, other	1.000000	1.000	1.000	N PP# 0F6166
80001610	F	Fish-shellfish, crustacean	0.100000	1.000	1.000	N PP# 0F6166
80001620	F	Fish-shellfish, mollusc	0.100000	1.000	1.000	N PP# 0F6166
23001690	M	Goat, meat	0.050000	1.000	1.000	N PP# 0F6166
23001700	M	Goat, meat byproducts	0.050000	1.000	1.000	N PP# 0F6166
23001710	M	Goat, fat	0.050000	1.000	1.000	N PP# 0F6166
23001720	M	Goat, kidney	0.200000	1.000	1.000	N PP# 0F6166
23001730	M	Goat, liver	0.050000	1.000	1.000	N PP# 0F6166
24001890	M	Horse, meat	0.050000	1.000	1.000	N PP# 0F6166
28002210	M	Meat, game	0.050000	1.000	1.000	N PP# 0F6166
27002220	D	Milk, fat	0.010000	1.000	1.000	N PP# 0F6166
27002221	D	Milk, fat - baby food/infant for	0.010000	1.000	1.000	N PP# 0F6166
27012230	D	Milk, nonfat solids	0.010000	1.000	1.000	N PP# 0F6166
27012231	D	Milk, nonfat solids-baby food/in	0.010000	1.000	1.000	N PP# 0F6166
27022240	D	Milk, water	0.010000	1.000	1.000	N PP# 0F6166
27022241	D	Milk, water-babyfood/infant form	0.010000	1.000	1.000	N PP# 0F6166
27032251	D	Milk, sugar (lactose)-baby food/	0.010000	1.000	1.000	N PP# 0F6166
26003390	M	Sheep, meat	0.050000	1.000	1.000	N PP# 0F6166
26003391	M	Sheep, meat-babyfood	0.050000	1.000	1.000	N PP# 0F6166
26003400	M	Sheep, meat byproducts	0.050000	1.000	1.000	N PP# 0F6166
26003410	M	Sheep, fat	0.050000	1.000	1.000	N PP# 0F6166
26003411	M	Sheep, fat-babyfood	0.050000	1.000	1.000	N PP# 0F6166
26003420	M	Sheep, kidney	0.200000	1.000	1.000	N PP# 0F6166
26003430	M	Sheep, liver	0.050000	1.000	1.000	N PP# 0F6166