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

OPP OFFICIAL RECORD  
HEALTH EFFECTS DIVISION  
SCIENTIFIC DATA REVIEWS  
EPA SERIES 361

OFFICE OF  
PREVENTION, PESTICIDES, AND  
TOXIC SUBSTANCES

**MEMORANDUM**

DATE: 19-JUN-2001

SUBJECT: PP# 9F05092. Imazapic in/on Grass Pastures and Rangeland: **Chronic Dietary Exposure Analysis**. Chemical#s: 128943 and 129041. DP Barcode: D275580.

FROM: William H. Donovan, Ph.D., Chemist *William H. Donovan*  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

THROUGH: Douglas Dotson, Chemist *D. Dotson*  
Christina Swartz, Chemist *Christina Swartz*  
Dietary Exposure Science Advisory Council Reviewers

G. Jeffrey Herndon, Branch Senior Scientist *G. Jeffrey Herndon*  
RAB1/HED (7509C)

TO: William Dykstra, Ph.D., Toxicologist  
RAB1/HED (7509C)

**Executive Summary**

Dietary Exposure Evaluation Model (DEEM™) analysis indicates that the estimated dietary exposure and risk associated with the existing and proposed new uses of the herbicide imazapic are below the HED's level of concern for chronic exposure scenarios. The chronic analysis presented here is highly conservative, making use of tolerance level residues, 100% crop treated assumptions, and default concentration factors (Tier 1 analysis).

**Action Requested**

Provide an estimate of the chronic dietary exposure and associated risk for imazapic resulting from the proposed new uses from PP# 9F05092, submitted by American Cyanamid Company.

The recommended tolerance levels resulting from the petition 9F05092 are as follows (D269038, W. Donovan, 12-JUN-2001):

Grass, forage .....	30 ppm
Grass, hay .....	15 ppm
Milk .....	0.10 ppm
Meat* .....	0.10 ppm
Fat* .....	0.10 ppm
Meat byproducts (except kidney)* .....	0.10 ppm
Kidney* .....	1.0 ppm

\* Of cattle, sheep, goats, and horses

**Toxicological Information**

The HED Hazard Identification Assessment Review Committee (HIARC) met on 17-APR-2001 to select doses and endpoints for the human health risk assessment for imazapic (HED Doc. No. 014560, W. Dykstra, 03-MAY-2001). The FQPA safety factor required under the FQPA of 1996 was reduced to 1X (HED Doc. No. 014xxx, B. Tarplee, xx-JUN-2001). A summary of the imazapic doses and endpoints relevant to dietary exposure assessment are presented in Table 1.

Table 1. Summary of Toxicological Endpoints for Dietary Risk Assessment for Imazapic.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary		An acute dietary endpoint was not selected based on the absence of an appropriate endpoint attributable to a single dose	
		<b>Acute RfD = not established</b>	
Chronic Dietary	LOAEL = 137 mg/kg/day UF = 300 FQPA SF =1	Increased incidence of minimal degeneration and/or necrosis of skeletal muscle	One-year feeding toxicity study in dogs
		<b>Chronic RfD = 0.50 mg/kg/day Chronic PAD = 0.50 mg/kg/day</b>	
Chronic (cancer) Dietary	Carcinogenic classification: "Group E" (no evidence of carcinogenicity)		

**Residue Information**

Permanent and temporary tolerances have been established for imazapic, as listed in 40 CFR 180.490. Tolerances are currently established under §180.490(a) for residues of imazapic and its metabolites CL 263284 and CL 189215 in/on peanut, nutmeat at 0.1 ppm. Time-limited tolerances set to expire 12/31/01 are established under §180.490(b) in connection with Section 18 emergency exemptions (99NE0009) for residues of imazapic and its metabolites CL 263284 and CL 189215 for grass forage at 30 ppm, grass hay at 15 ppm, milk at 0.10 ppm, fat, meat, and meat byproducts (except kidney) of cattle, goats, hogs, horses, and sheep at 0.10 ppm, and kidney of cattle, goats, hogs, horses, and sheep at 1.0 ppm. The present analyses included the published peanut values together with re-evaluated tolerance levels for livestock-derived commodities, based on the new grass use proposed in the present Section 3 request.

The present analysis was made using tolerance-level residues and a 100% crop treated assumption (Tier 1 approach). DEEM™ default values were used for processing factors (adjustment factor 1 in DEEM™). A full listing of the residue information used in the chronic analysis is given in Attachment 1.

**Results**

*Chronic Analysis*

DEEM™ analysis (version 7.73) evaluated the individual food consumption as reported by respondents in the USDA 1989-92 nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. HED's level of concern is for exposures >100% cPAD. The chronic DEEM™ analysis used mean consumption (3 day average) data and gave the results listed in Table 2:

Table 2. Summary of Results from Chronic Dietary Exposure Analysis for Imazapic.

Subgroups	Exposure (mg/kg/day)	% cPAD
U.S. Population (48 states)	0.000269	0.1
All infants (< 1 year)	0.000505	0.1
Children 1-6 years old	0.000684	0.1
Children 7-12 years old	0.000425	0.1
Females 13-50 years old	0.000189	<0.1
Males 13-19 years old	0.000297	0.1
Males 20+ years old	0.000208	<0.1
Seniors 55+ years old	0.000165	<0.1

HED notes that there is a degree of uncertainty in extrapolating exposures for certain population

subgroups which may not be sufficiently represented in the consumption surveys, (e.g., nursing and non-nursing infants or Hispanic females). Therefore, risks estimated for these population subgroups were included in representative populations having sufficient numbers of survey respondents (e.g., all infants or females, 13-50 years). Thus, the population subgroups listed in Table 2 include those subgroups having sufficient numbers of survey respondents in the CSFII food consumption survey to be considered statistically reliable. The complete chronic analysis is attached (see Attachment 2).

### **Conclusion**

The results of this analysis indicates that the estimated chronic dietary exposure and risk associated with the existing and proposed uses of imazapic are below HED's level of concern.

### **Attachments**

Attachment 1: Imazapic Tier 1 residue file for chronic DEEM™ analyses.

Attachment 2: Imazapic chronic DEEM™ analysis.

cc: W. Donovan; J. Tompkins (RD)

RDI: D. Dotson (14-JUN-2001), C. Swartz (18-JUN-2001)

W. Donovan:CM#2: 806-R:(703)305-7330

Attachment 1. Imazapic residue file for chronic DEEM™ analysis.

Filename: C:\deemepa\128943\128943.rs7 Chemical: Imazapic  
 RfD(Chronic): .5 mg/kg bw/day NOEL(Chronic): 0 mg/kg bw/day  
 RfD(Acute): 0 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day  
 Date created/last modified: 06-13-2001/13:06:50/8 Program ver. 7.73  
 Comment: PP# 9F05092

Food Crop		Def Res (ppm)	Adj. Factors		Comment
Code	Grp Food Name		#1	#2	
323	M	Beef-dried	0.100000	1.920 1.000	9F5092
324	M	Beef-fat w/o bones	0.100000	1.000 1.000	9F5092
325	M	Beef-kidney	1.000000	1.000 1.000	9F5092
327	M	Beef-lean (fat/free) w/o bones	0.100000	1.000 1.000	9F5092
326	M	Beef-liver	0.100000	1.000 1.000	9F5092
321	M	Beef-meat byproducts	0.100000	1.000 1.000	9F5092
322	M	Beef-other organ meats	0.100000	1.000 1.000	9F5092
330	M	Goat-fat w/o bone	0.100000	1.000 1.000	9F5092
331	M	Goat-kidney	1.000000	1.000 1.000	9F5092
333	M	Goat-lean (fat/free) w/o bone	0.100000	1.000 1.000	9F5092
332	M	Goat-liver	0.100000	1.000 1.000	9F5092
328	M	Goat-meat byproducts	0.100000	1.000 1.000	9F5092
329	M	Goat-other organ meats	0.100000	1.000 1.000	9F5092
334	M	Horsemeat	0.100000	1.000 1.000	9F5092
319	D	Milk-fat solids	0.100000	1.000 1.000	9F5092
318	D	Milk-nonfat solids	0.100000	1.000 1.000	9F5092
320	D	Milk sugar (Lactose)	0.100000	1.000 1.000	9F5092
403	O	Peanuts-butter	0.100000	1.890 1.000	4F4390
940	O	Peanuts-hulled	0.100000	1.000 1.000	4F4390
293	O	Peanuts-oil	0.100000	1.000 1.000	4F4390
344	M	Pork-fat w/o bone	0.100000	1.000 1.000	9F5092
345	M	Pork-kidney	1.000000	1.000 1.000	9F5092
347	M	Pork-lean (fat free) w/o bone	0.100000	1.000 1.000	9F5092
346	M	Pork-liver	0.100000	1.000 1.000	9F5092
342	M	Pork-meat byproducts	0.100000	1.000 1.000	9F5092
343	M	Pork-other organ meats	0.100000	1.000 1.000	9F5092
338	M	Sheep-fat w/o bone	0.100000	1.000 1.000	9F5092
339	M	Sheep-kidney	1.000000	1.000 1.000	9F5092
341	M	Sheep-lean (fat free) w/o bone	0.100000	1.000 1.000	9F5092
340	M	Sheep-liver	0.100000	1.000 1.000	9F5092
336	M	Sheep-meat byproducts	0.100000	1.000 1.000	9F5092
337	M	Sheep-other organ meats	0.100000	1.000 1.000	9F5092
429	M	Veal-dried	0.100000	1.920 1.000	9F5092
424	M	Veal-fat w/o bones	0.100000	1.000 1.000	9F5092
426	M	Veal-kidney	1.000000	1.000 1.000	9F5092
425	M	Veal-lean (fat free) w/o bones	0.100000	1.000 1.000	9F5092
427	M	Veal-liver	0.100000	1.000 1.000	9F5092
430	M	Veal-meat byproducts	0.100000	1.000 1.000	9F5092
428	M	Veal-other organ meats	0.100000	1.000 1.000	9F5092

Attachment 2: Imazapic chronic DEEM™ analysis.

U.S. Environmental Protection Agency  
 DEEM Chronic analysis for IMAZAPIC  
 Residue file name: C:\deemepa\128943\128943.rs7 Adjustment factor #2 NOT used.  
 Analysis Date 06-13-2001/13:19:40 Residue file dated: 06-13-2001/13:06:50/8  
 Reference dose (Rfd, Chronic) = .5 mg/kg bw/day  
 COMMENT 1: 9F5092

Ver. 7.73

(1989-92 data)

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 Total exposure by population subgroup  
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Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.000269	0.1%
U.S. Population (spring season)	0.000268	0.1%
U.S. Population (summer season)	0.000269	0.1%
U.S. Population (autumn season)	0.000274	0.1%
U.S. Population (winter season)	0.000266	0.1%
Northeast region	0.000263	0.1%
Midwest region	0.000297	0.1%
Southern region	0.000266	0.1%
Western region	0.000249	0.0%
Hispanics	0.000288	0.1%
Non-hispanic whites	0.000267	0.1%
Non-hispanic blacks	0.000269	0.1%
Non-hisp/non-white/non-black	0.000269	0.1%
All infants (< 1 year)	0.000505	0.1%
Nursing infants	0.000147	0.0%
Non-nursing infants	0.000655	0.1%
Children 1-6 yrs	0.000684	0.1%
Children 7-12 yrs	0.000425	0.1%
Females 13-19 (not preg or nursing)	0.000237	0.0%
Females 20+ (not preg or nursing)	0.000168	0.0%
Females 13-50 yrs	0.000189	0.0%
Females 13+ (preg/not nursing)	0.000218	0.0%
Females 13+ (nursing)	0.000223	0.0%
Males 13-19 yrs	0.000297	0.1%
Males 20+ yrs	0.000208	0.0%
Seniors 55+	0.000165	0.0%
Pacific Region	0.000245	0.0%