129099

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

AUG 17 1994

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Dietary Exposure Analysis for Imidacloprid through the Use on Dried Hops.

FROM: Jennifer M. Wintersteen Jennifer M. Wintersteen
Dietary Risk Evaluation Section
Science Analysis Branch/HED (7509C)

TO: Dennis Edwards, PM Team 19
Insecticide-Rodenticide Branch
Registration Division (7505C)

THROUGH: James P. Kariya, Section Head
Dietary Risk Evaluation Section
SAB/Health Effects Division

Action Requested

Provide a Dietary Risk Evaluation System (DRES) analysis of the dietary exposure for imidacloprid through the published use on dried hops. The following interim tolerances (expire 6/28/95) are being assessed in this analysis:

- hops, dried . . . . . 3 ppm
- meat, fat and meat byproducts of cattle, horses, sheep, goats and hogs . . . 0.2 ppm
- milk . . . . . 0.05 ppm

Discussion

1. Toxicological Endpoint: The chronic analysis used a Reference Dose (RfD) of 0.057 mg/kg body weight/day, based on a no observed effect level (NOEL) of 5.7 mg/kg bwt/day and an uncertainty factor of 100. The NOEL is based on a chronic toxicity study in rats that demonstrated increased thyroid lesions in males as an endpoint effect. The HED RfD Peer Review Committee also classified imidacloprid as a Group E carcinogen (G. Ghali memo, 11/10/93).

An acute dietary assessment is required by the Toxicology Endpoint Selection Document for Imidacloprid (Karl Baetcke memo, 4/18/94). The endpoint for acute dietary risk assessment is 24 mg/kg/day from the rabbit developmental study. The LEL (72 mg/kg/day) was based upon decreased body weight, and increased resorptions, abortion and increased skeletal abnormalities.

2. Residue Information: Food uses evaluated in this analysis were the published interim tolerances listed in the Tolerance Index System (TIS) and 40 CFR §180.472. The commodities dried hops and meat and milk all have an

expiration date (6/28/95) and have been included in the DRES risk analysis as published commodities.

No information has been provided for refinement of percent of crop treated or anticipated residues for either chronic or acute analyses. A summary of the residue information used in the analysis is attached as Table 1.

3.Results: A DRES chronic exposure analysis was performed using tolerance level residues and 100 percent crop treated information to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups.

Summaries of the TMRCs and their representations as percentages of the RfD for imidacloprid are attached as Table 2.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.000984	2
Non-nursing Infants	0.003693	6

Acute Exposure

The DRES detailed acute exposure analysis evaluates individual food consumption as reported by respondents in the USDA 77-78 Nationwide Food Consumption Survey (NFCS) and estimates the distribution of single day exposures through the diet for the U.S. population and certain subgroups. The analysis assumes uniform distribution of imidacloprid in the commodity supply. Since the toxicological effect to which high end exposure is being compared to in this analysis is developmental toxicity, the DRES subgroup of concern is females (13+ years) which approximates women of child-bearing age.

The Margin of Exposure (MOE) is a measure of how closely the high end exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory study), and is calculated as the ratio of the NOEL to the exposure (NOEL/exposure = MOE). For substances whose acute NOEL is based on animal studies, the Agency is not generally concerned unless the MOE is below 100.

In the analysis, tolerance level residues were used to calculate the high-end exposure for the females (13+ years) subgroup. High end exposure was compared to the NOEL of 24 mg/kg bwt/day from the rabbit developmental study to get a high end Margin of Exposure. The MOE for females was calculated in the attached table and the results are as follows:

Females (13+ years) High End Exposure = 0.00288
NOEL/ Exposure = 24 mg/kg/day ÷ 0.00288 = 8333

This is the first time that acute exposure has been calculated for imidacloprid using the DRES system. Using the given endpoints, the MOE is not of concern for the subgroup females (13+ years) with an estimated MOE considerably above 100.

Discussion

To the extent that this analysis used tolerance level residues and 100 percent-crop-treated assumptions, it is considered a "worst-case" picture of the dietary risk from imidacloprid. The chronic dietary risk from exposure of imidacloprid appears to be of minimal concern, with all DRES subgroups having TMRC values well below the Reference Dose.

The acute dietary analysis of imidacloprid is not of concern for females of child-bearing age.

Attachments
cc: DRES, Caswell #497E, Tox I, CBTS

Table 1: Chronic Dietary Risk Evaluation for Imidacloprid

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E DATE: 08/16/94 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Imidacloprid Caswell #497E CAS No. 105827-78-9 A.I. CODE: 129099 CFR No.	2yr feeding- rat NOEL= 5.7000 mg/kg 100.00 ppm LEL= 16.9000 mg/kg 300.00 ppm ONCO: E (RfD/PR Committee)	Increased incidence of mineralized particles in thyroid colloid. No evidence of oncogenicity in rats or mice.	ADI UF -->100 OPP RfD= 0.057000 EPA RfD= 0.000000	No data gaps.	RfD/PR reviewed 04/22/93

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
08020AA	HOPS	300343			3.000000
50000DB	MILK-NON-FAT SOLIDS	300343			0.050000
50000FA	MILK-FAT SOLIDS	300343			0.050000
50000SA	MILK SUGAR (LACTOSE)	300343			0.050000
53001BA	BEEF-MEAT BYPRODUCTS	300343			0.200000
53001BB	BEEF(ORGAN MEATS)-OTHER	300343			0.200000
53001DA	BEEF-DRIED	300343			0.200000
53001FA	BEEF(BONELESS)-FAT.(BEEF TALLOW)	300343			0.200000
53001KA	BEEF(ORGAN MEATS)-KIDNEY	300343			0.200000
53001LA	BEEF(ORGAN MEATS)-LIVER	300343			0.200000
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	300343			0.200000
53002BA	GOAT-MEAT BYPRODUCTS	300343			0.200000
53002BB	GOAT(ORGAN MEATS)-OTHER	300343			0.200000
53002FA	GOAT(BONELESS)-FAT	300343			0.200000
53002KA	GOAT(ORGAN MEATS)-KIDNEY	300343			0.200000
53002LA	GOAT(ORGAN MEATS)-LIVER	300343			0.200000
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	300343			0.200000
53003AA	HORSE	300343			0.200000
53005BA	SHEEP-MEAT BYPRODUCTS	300343			0.200000
53005BB	SHEEP(ORGAN MEATS)-OTHER	300343			0.200000
53005FA	SHEEP(BONELESS)-FAT	300343			0.200000
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	300343			0.200000
53005LA	SHEEP(ORGAN MEATS)-LIVER	300343			0.200000
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT	300343			0.200000
53006BA	PORK-MEAT BYPRODUCTS	300343			0.200000
53006BB	PORK(ORGAN MEATS)-OTHER	300343			0.200000
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	300343			0.200000
53006KA	PORK(ORGAN MEATS)-KIDNEY	300343			0.200000
53006LA	PORK(ORGAN MEATS)-LIVER	300343			0.200000
53006MA	PORK-LEAN	300343			0.200000

Table 2: Chronic Dietary Risk Evaluation for Imidacloprid

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Imidacloprid Caswell #497E CAS No. 105827-78-9 A.I. CODE: 129099 CFR No.	2yr feeding- rat NOEL= 5.7000 mg/kg 100.00 ppm LEL= 16.9000 mg/kg 300.00 ppm ONCO: E (RfD/PR Committee)	Increased incidence of mineralized particles in thyroid colloid. No evidence of oncogenicity in rats or mice.	ADI UF -->100 OPP RfD= 0.057000 EPA RfD= 0.000000	No data gaps.	RfD/PR reviewed 04/22/93

POPULATION SUBGROUP	TOTAL TMRC (MG/KG BODY WEIGHT/DAY) CURRENT TMRC*	NEW TMRC**	NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	%RFD
U.S. POPULATION - 48 STATES	0.000984	0.000984	1.726795	0.000000		
U.S. POPULATION - SPRING SEASON	0.000945	0.000945	1.658274	0.000000		
U.S. POPULATION - SUMMER SEASON	0.000985	0.000985	1.727451	0.000000		
U.S. POPULATION - FALL SEASON	0.001015	0.001015	1.779881	0.000000		
U.S. POPULATION - WINTER SEASON	0.000993	0.000993	1.741823	0.000000		
NORTHEAST REGION	0.001013	0.001013	1.776786	0.000000		
NORTH CENTRAL REGION	0.001028	0.001028	1.803079	0.000000		
SOUTHERN REGION	0.000892	0.000892	1.564568	0.000000		
WESTERN REGION	0.001043	0.001043	1.829235	0.000000		
HISPANICS	0.001214	0.001214	2.130267	0.000000		
NON-HISPANIC WHITES	0.000979	0.000979	1.717233	0.000000		
NON-HISPANIC BLACKS	0.000900	0.000900	1.579661	0.000000		
NON-HISPANIC OTHERS	0.001077	0.001077	1.888679	0.000000		
NURSING INFANTS (< 1 YEAR OLD)	0.000916	0.000916	1.607267	0.000000		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.003693	0.003693	6.478568	0.000000		
FEMALES (13+ YEARS, PREGNANT)	0.000698	0.000698	1.225409	0.000000		
FEMALES 13+ YEARS, NURSING	0.000818	0.000818	1.434898	0.000000		
CHILDREN (1-6 YEARS OLD)	0.002363	0.002363	4.146407	0.000000		
CHILDREN (7-12 YEARS OLD)	0.001563	0.001563	2.742896	0.000000		
MALES (13-19 YEARS OLD)	0.001086	0.001086	1.905291	0.000000		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000834	0.000834	1.463316	0.000000		
MALES (20 YEARS AND OLDER)	0.000729	0.000729	1.279179	0.000000		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000584	0.000584	1.024774	0.000000		

*Current TMRC does not include new or pending tolerances.
**New TMRC includes new, pending, and published tolerances.

NAME: IMIDACLOPRID STUDY RDV NOEL SF STUDY TYPE SPECIES EFF. LEV. CORE GRADE DOC. NO.
*CASWELL NO: 497E CFR NO: CFR . A *
*CAS NO: 12909-90-0 SHAUGHNESSY NO: 129099 B *
*STATUS CODES: C *
*RDV INFO: The LD value used in this analysis is 0.0024 MG/KG of BODY WEIGHT/DAY *
FILE INFO: No Tolerance Data Are Used--Without User Modifications. AR DATA: No User Modifications

LISTING OF RELEVANT FOODS & FOOD FORMS, ORDERED BY MENU CATEGORY. MENU PATTERN = I
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED (WATER:OIL)

POPULATION = U.S. POP.--48 STATES

FOOD CODE	FOOD AND FOOD FORM DESCRIPTION	NUMBER OF CONSUMER DAYS AS PERCENT OF POTENTIAL PERSON DAYS	TOLERANCE DATA VALUE (PPM)	TOLERANCE DATA TYPE	AR DATA VALUE (PPM)	AR DATA REF.	FOOD FORM CONTRIBUTION TO EXPOSURE (UG/KG BODY WT PER DAY) DAILY MAXIMUM RESIDUE (EXCL. AR)	DAILY ANTICIPATED RESIDUE (INCL. AR)
	MENU CATEGORY 1: MEATS							
53001BA	BEEF-MEAT BYPRODUCTS							
21	COOKED-NFS	7.68			0.2000			0.042789
26	COOKED-FRESH-PICKLED,CORNED,OR CURED	0.88			0.2000			0.029024
53001BB	BEEF(ORGAN MEATS)-OTHER							
21	COOKED-NFS	7.72			0.2000			0.013324
51	COOKED-CANNED	0.22			0.2000			0.081669
53001DA	BEEF-DRIED							
21	COOKED-NFS	0.25			0.2000			0.193489
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)							
10	RAW-FRESH OR NFS	27.74			0.2000			0.001051
21	COOKED-NFS	86.58			0.2000			0.034395
22	COOKED-FRESH-BAKED	52.96			0.2000			0.009596
23	COOKED-FRESH-BOILED	11.38			0.2000			0.058397
24	COOKED-FRESH-BROILED	18.46			0.2000			0.154271
25	COOKED-FRESH-FRIED	40.70			0.2000			0.010718
53001KA	BEEF(ORGAN MEATS)-KIDNEY							
21	COOKED-NFS	0.02			0.2000			0.542542
53001LA	BEEF(ORGAN MEATS)-LIVER							
25	COOKED-FRESH-FRIED	1.00			0.2000			0.408616
31	COOKED-FRESH OR CANNED	0.00			0.2000			1.249926
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)							
10	RAW-FRESH OR NFS	0.00			0.2000			0.236680
21	COOKED-NFS	55.27			0.2000			0.251875
22	COOKED-FRESH-BAKED	4.67			0.2000			0.208010
23	COOKED-FRESH-BOILED	9.15			0.2000			0.158910
24	COOKED-FRESH-BROILED	18.46			0.2000			0.377698
53002BA	GOAT-MEAT BYPRODUCTS							
00	NOT SPECIFIED (NO CONSUMPTION)	0.00			0.2000			0.000000
53002BB	GOAT(ORGAN MEATS)-OTHER							
00	NOT SPECIFIED (NO CONSUMPTION)	0.00			0.2000			0.000000
53002FA	GOAT(BONELESS)-FAT							
23	COOKED-FRESH-BOILED	0.01			0.2000			0.062767
25	COOKED-FRESH-FRIED	0.00			0.2000			0.031364
53002KA	GOAT(ORGAN MEATS)-KIDNEY							
00	NOT SPECIFIED (NO CONSUMPTION)	0.00			0.2000			0.000000
53002LA	GOAT(ORGAN MEATS)-LIVER							
00	NOT SPECIFIED (NO CONSUMPTION)	0.00			0.2000			0.000000
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)							
23	COOKED-FRESH-BOILED	0.01			0.2000			0.300050

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25	COOKED-FRESH-FRIED	0.00				0.2000			0.144310
53003AA	HORSE								
00	NOT SPECIFIED (NO CONSUMPTION)	0.00				0.2000			0.000000
53005BA	SHEEP-MEAT BYPRODUCTS								
21	COOKED-NFS	0.00				0.2000			0.252366
53005BB	SHEEP(ORGAN MEATS)-OTHER								
21	COOKED-NFS	0.00				0.2000			0.316277
53005FA	SHEEP(BONELESS)-FAT								
21	COOKED-NFS	0.61				0.2000			0.138588
53005KA	SHEEP(ORGAN MEATS)-KIDNEY								
21	COOKED-NFS	0.00				0.2000			0.114742
53005LA	SHEEP(ORGAN MEATS)-LIVER								
00	NOT SPECIFIED (NO CONSUMPTION)	0.00				0.2000			0.000000
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT)								
21	COOKED-NFS	0.62				0.2000			0.355060
31	COOKED-FRESH OR CANNED	0.04				0.2000			0.540673
53006BA	PORK-MEAT BYPRODUCTS								
21	COOKED-NFS	8.60				0.2000			0.058874
53006BB	PORK(ORGAN MEATS)-OTHER								
21	COOKED-NFS	6.68				0.2000			0.010607
26	COOKED-FRESH-PICKLED,CORNED,OR CURED	0.88				0.2000			0.005618
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)								
10	RAW-FRESH OR NFS	27.80				0.2000			0.001247
21	COOKED-NFS	92.99				0.2000			0.020915
23	COOKED-FRESH-BOILED	11.36				0.2000			0.040619
25	COOKED-FRESH-FRIED	40.60				0.2000			0.011957
26	COOKED-FRESH-PICKLED,CORNED,OR CURED	24.16				0.2000			0.051000
53006KA	PORK(ORGAN MEATS)-KIDNEY								
21	COOKED-NFS	0.00				0.2000			0.293686
53006LA	PORK(ORGAN MEATS)-LIVER								
21	COOKED-NFS	0.91				0.2000			0.096380
25	COOKED-FRESH-FRIED	0.03				0.2000			0.313470
53006MA	PORK(BONELESS)-LEAN (W/O REMOVEABLE FAT)								
21	COOKED-NFS	33.75				0.2000			0.107551
25	COOKED-FRESH-FRIED	3.16				0.2000			0.302427
26	COOKED-FRESH-PICKLED,CORNED,OR CURED	24.22				0.2000			0.133609
	MENU CATEGORY 4: MILK: NON-FAT SOLIDS								
50000DB	MILK-NON-FAT SOLIDS								
10	RAW-FRESH OR NFS	78.77				0.0500			0.366137
21	COOKED-NFS	90.38				0.0500			0.064633

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51	COOKED-CANNED	3.51				0.0500			0.368717
50000SA	MILK SUGAR (LACTOSE)								
21	COOKED-NFS	0.01				0.0500			0.005203
51	COOKED-CANNED	0.56				0.0500			0.345702
	MENU CATEGORY 5: MILK: FAT SOLIDS								
50000FA	MILK-FAT SOLIDS								
10	RAW-FRESH OR NFS	81.63				0.0500			0.164598
21	COOKED-NFS	90.30				0.0500			0.039787
51	COOKED-CANNED	3.51				0.0500			0.014677
	MENU CATEGORY 13: MISCELLANEOUS FOODS								
08020AA	HOPS								
21	COOKED-NFS	4.72				3.0000			1.380369

Table 3: Acute Dietary Risk Evaluation for Imidacloprid

1DETAILED ACUTE ANALYSIS INCLUDING AR'S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION 16:27 Friday, August 12, 1994 5

	STUDY	RDV	NOEL	SF	STUDY TYPE	SPECIES	EFF. LEV.	CORE GRADE	DOC. NO.
*NAME: IMIDACLOPRID	A								*
*CASWELL NO: 497E CFR NO: CFR .	B								*
*CAS NO: 12909-90-0 SHAUGHNESSY NO: 129099	C								*
*STATUS CODES:									*

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FEMALES(13+ YRS)

ESTIMATES BASED ON	ESTIMATED % OF POTENTIAL PERSON DAYS THAT ARE USER-DAYS	MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY MG/KG BODY WEIGHT/DAY	AS PERCENT OF RDV
TOLERANCES:	0.00	0.000000	0.00
ANTICIPATED RESIDUES:	99.55	0.000658	27.41

0 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

	0	.2	.4	.6	.8	1	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20
TOLERANCES:	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANTICIPATED RESIDUES:	100	58	20	6	2	1	0	0	0	0	0	0	0	0	0	0	0