

US EPA ARCHIVE DOCUMENT



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 *James P. Kariya*, Section Head  
Dietary Risk Evaluation Section  
SAB/Health Effects Division *W. J. B...*

**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.

<u>Subgroup</u>	<u>Exposure(mg/kg/day)</u>	<u>%Reference Dose</u>
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:

$$\begin{aligned} \text{Females (13+ years) High End Exposure} &= 0.00288 \\ \text{NOEL/ Exposure} &= 24 \text{ mg/kg/day} \div 0.00288 = 8333 \end{aligned}$$

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	NEW	TOLERANCE (PPM)	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					
U.S. POPULATION : 48 STATES					
U.S. POPULATION - SPRING SEASON					
U.S. POPULATION - SUMMER SEASON					
U.S. POPULATION - FALL SEASON					
U.S. POPULATION - WINTER SEASON					
NORTHEAST REGION					
NORTH CENTRAL REGION					
SOUTHERN REGION					
WESTERN REGION					
HISPANICS					
NON-HISPANIC WHITES					
NON-HISPANIC BLACKS					
NON-HISPANIC OTHERS					
NURSING INFANTS (< 1 YEAR OLD)					
NON-NURSING INFANTS (< 1 YEAR OLD)					
FEMALES (13+ YEARS, PREGNANT)					
FEMALES (13+ YEARS, NURSING CHILDREN (1-6 YEARS OLD)					
CHILDREN (7-12 YEARS OLD)					
MALES (13-19 YEARS OLD)					
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)					
MALES (20 YEARS AND OLDER)					
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)					
TOTAL TMRC (MG/KG BODY WEIGHT/DAY)					
CURRENT TMRC*		NEW TMRC**		DIFFERENCE AS PERCENT OF RFD	
EFFECT OF ANTICIPATED RESIDUES		ARC		2RFD	
0.000984	0.000984	1.726795	0.000000		
0.000945	0.000945	1.658274	0.000000		
0.000985	0.000985	1.727451	0.000000		
0.001015	0.001015	1.779881	0.000000		
0.000993	0.000993	1.741823	0.000000		
0.001013	0.001013	1.776786	0.000000		
0.001028	0.001028	1.803079	0.000000		
0.000892	0.000892	1.564568	0.000000		
0.001043	0.001043	1.829235	0.000000		
0.001214	0.001214	2.130267	0.000000		
0.000979	0.000979	1.717233	0.000000		
0.000900	0.000900	1.579661	0.000000		
0.001077	0.001077	1.888679	0.000000		
0.000916	0.000916	1.607267	0.000000		
0.003693	0.003693	6.478568	0.000000		
0.000698	0.000698	1.225409	0.000000		
0.000818	0.000818	1.434898	0.000000		
0.002363	0.002363	4.146407	0.000000		
0.001563	0.001563	2.742896	0.000000		
0.001086	0.001086	1.905291	0.000000		
0.000834	0.000834	1.463316	0.000000		
0.000729	0.000729	1.279179	0.000000		
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.

DETAILED ACUTE ANALYSIS INCLUDING AR'S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION

\*\*\*\*\*  
 \*NAME: INIDACLOPRID  
 \*CASWELL NO: 497E      CFR NO: CFR  
 \*CAS NO: 12909-90-0 SHAUGHNESSY NO: 129099 B  
 \*STATUS CODES:  
 \*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.  
 \*\*\*\*\*  
 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  
 AR DATA: No User Modifications\*  
 : FOOD FORM CONTRIBUTION  
 : TO EXPOSURE  
 : (UG/KG BODY WT PER DAY)

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Table 3: Acute Dietary Risk Evaluation for Imidacloprid

1 DETAILED ACUTE ANALYSIS INCLUDING AR'S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION 16:27 Friday, August 12, 1994 5  
 \*\*\*\*\*  
 \*NAME: IMIDACLOPRID \*\*\*\*\*  
 \*CASWELL NO: 497E CFR NO: CFR NO: 129099 B \*\*\*\*\*  
 \*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\* \*\*\*\*\*

FEMALES(13+ YRS)

ESTIMATED % OF POTENTIAL	PERSON DAYS THAT ARE USER-DAYS	MG/KG BODY WEIGHT/DAY	AS PERCENT OF RDV
0	0	0.000000	0.00
0	58	0.000658	27.41
0	2	1.2	1.4
0	4	1.2	1.4
0	6	1.2	1.4
0	20	1.2	1.4
0	58	1.2	1.4
0	2	1.6	1.8
0	4	1.6	1.8
0	6	1.6	1.8
0	20	1.6	1.8
0	58	1.6	1.8
0	2	2	2
0	4	2	2
0	6	2	2
0	20	2	2
0	58	2	2
0	2	3	3
0	4	3	3
0	6	3	3
0	20	3	3
0	58	3	3
0	2	4	4
0	4	4	4
0	6	4	4
0	20	4	4
0	58	4	4
0	2	5	5
0	4	5	5
0	6	5	5
0	20	5	5
0	58	5	5
0	2	10	10
0	4	10	10
0	6	10	10
0	20	10	10
0	58	10	10
0	2	15	15
0	4	15	15
0	6	15	15
0	20	15	15
0	58	15	15
0	2	20	20
0	4	20	20
0	6	20	20
0	20	20	20
0	58	20	20