

US EPA ARCHIVE DOCUMENT



497E

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

JUN 8 1995

JUN - 8 1995

MEMORANDUM

SUBJECT: PP#4F4337/4H5700. Imidacloprid on Barley, Wheat, and Sugarbeets. DRES Dietary Exposure and Risk Estimates.

FROM: Brian Steinwand *BS*
Dietary Risk Evaluation Section
Science Analysis Branch/HED (7509C)

Through: Elizabeth Doyle, Section Head *E.A. Doyle*
Dietary Risk Evaluation Section
SAB/Health Effects Division *W.B.M.*

TO: D. Edwards, PM Team 19
Registration Division (7505C)

Action Requested

Provide a dietary exposure analysis for the use of imidacloprid in/on barley, wheat, and sugarbeets. The petition requests that a tolerance of 0.05 ppm be established. CBTS recommends against these proposed permanent tolerances due to outstanding data deficiencies as listed in the memo of F. Griffith (5/16/95). CBTS however, has no objections to establishing these tolerances with expiration dates (See memo, F. Griffith, 4/13/95).

Discussion

Toxicological Endpoint:

The Reference Dose (RfD) used in the analysis is 0.057 mg/kg bwt/day, based on a NOEL of 100 ppm (5.70 mg/kg bwt/day) from a two year rat feeding study with an uncertainty factor of 100 that demonstrated increased thyroid lesions in males as an endpoint. 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 (M. Ottley & K. 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,



Recycled/Recyclable
Printed with Soy/Canola Ink on paper that
contains at least 50% recycled fiber

increased resorptions, abortions, and increased skeletal abnormalities.

Residue Information

Tolerances for imidacloprid are published in 40 CFR §180.472.

There are no anticipated residues.

Percent Use:

There are no percent crop treated estimates. All uses assume 100 percent crop treated.

Results

A summary of the residue information considered in this analysis is attached as Table 1. 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 Reference Dose (RfD) are included as Tables 2 & 3. Summaries of the acute dietary risk for the subgroup females(13+ years) are attached as Table 4.

Chronic Exposure Analysis

Exposure from Published Uses of imidacloprid:

<u>Subgroup</u>	<u>Exposure (mg/kg/day)</u>	<u>%RfD</u>
U.S. Population	0.008088	14.2
Children 1-6 years	0.016735	29.4

Proposed new Tolerances on wheat, barley & sugarbeets:

U.S. Population	0.000091	.158
Children 1-6 years	0.000200	.350

If the new tolerances on vegetables are approved:

U.S. Population	0.008179	14.3
Children 1-6 years	0.016934	29.7

The chronic analysis for imidacloprid is a worst case estimate of dietary exposure with all residues at tolerance level and 100 percent of the commodities assumed to be treated with imidacloprid. Even without refinements, the chronic dietary risk from exposure to imidacloprid appears to be minimal for this petition on barley, wheat and sugarbeets at 0.05 ppm.

Acute Exposure:

The endpoint for acute dietary risk assessment is the NOEL (24 mg/kg/day) from the rabbit developmental toxicity study. The LEL (72 mg/kg/day) was based upon decreased body weight, and increased resorptions, abortion and increased skeletal abnormalities. Because the effects of concern are developmental in nature, the only subgroup of concern is females (13+ years old).

Generally, acute dietary margins of exposure greater than 100 tend to cause no dietary concern. The MOE value of 500 demonstrates no concern for females of child-bearing age considering the proposed tolerances.

There appears to be no acute dietary concern for the proposed tolerances on wheat, barley and sugarbeets.

Attachments

cc: DRES; Caswell 497E; RCAB; CBTS (F. Griffith); Tox I

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E

DATE: 05/25/95

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 carcinogenicity 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)	PENDING	PUBLISHED
01013AA	GRAPES-FRESH	3F4231		1.000000		
01014DA	GRAPES-RAISINS	3F4231		1.000000		
01014JA	GRAPES-JUICE	3F4231		1.000000		
04001AA	APPLES-FRESH	3F4169		0.500000		
04001DA	APPLES-DRIED	3F4169		0.500000		
04001JA	APPLES-JUICE	3F4169		0.500000		
06007AA	MANGOES	4F4285		0.200000		
08020AA	HOPS	300343		3.000000		
08020AA	HOPS	5E4425		3.000000		
11001AA	EGGPLANT	3F4231		1.000000		
11003AA	PEPPERS, SWEET, GARDEN	3F4231		1.000000		
11003AB	CHILI PEPPERS	3F4231		1.000000		
11003AD	PEPPERS-OTHER	3F4231		1.000000		
11004AA	PIMIENTOS	3F4231		1.000000		
11005AA	TOMATOES-WHOLE	3F4231		1.000000		
11005JA	TOMATOES-JUICE	3F4231		1.000000		
11005RA	TOMATOES-PUREE	3F4231		3.000000		
11005TA	TOMATOES-PASTE	3F4231		6.000000		
11005UA	TOMATOES-CATSUP	3F4231		1.000000		
13005AA	BROCCOLI	3F4231		3.500000		
13006AA	BRUSSEL SPROUTS	3F4231		3.500000		
13007AA	CABBAGE-GREEN AND RED	3F4231		3.500000		
13008AA	CAULIFLOWER	3F4231		3.500000		
13009AA	COLLARDS	3F4231		3.500000		
13010AA	CABBAGE-CHINESE/CELERY, INC. BOK CHOY	3F4231		3.500000		
13011AA	KALE	3F4231		3.500000		
13012AA	KOHLRABI	3F4231		3.500000		
13013AA	LETTUCE-LEAFY VARIETIES	3F4231		3.500000		
13020AA	LETTUCE-UNSPECIFIED	3F4231		3.500000		
13021AA	MUSTARD GREENS	3F4231		3.500000		
13045AA	LETTUCE-HEAD VARIETIES	3F4231		0.300000		
14013AA	POTATOES(WHITE)-WHOLE	3F4169		0.300000		
14013AB	POTATOES(WHITE)-UNSPECIFIED	3F4169		0.300000		
14013AC	POTATOES(WHITE)-PEELED	3F4169		0.300000		
14013DA	POTATOES(WHITE)-DRY	3F4169		0.300000		
14013HA	POTATOES(WHITE)-PEEL ONLY	3F4169		0.300000		
24001AA	BARLEY	4F4337	0.050000			
24006AA	SORGHUM (INCLUDING MILO)	4F4337	0.050000			
24007AA	WHEAT-ROUGH	4F4337	0.050000			
24007GA	WHEAT-GERM	4F4337	0.050000			

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

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM)	
			NEW	PENDING PUBLISHED
24007HA	WHEAT-BRAN	4F4337	0.050000	
24007MA	WHEAT-FLOUR	4F4337	0.050000	
25002SA	BEET SUGAR	4F4337	0.050000	
270030A	COTTONSEED-OIL	4F4169	6.000000	
27003MA	COTTONSEED-NEAL	4F4169	1.000000	
43058AA	WINE AND SHERRY	3F4231	0.100000	
500000B	MILK-NON-FAT SOLIDS	4F4169	0.100000	
50000FA	MILK-FAT SOLIDS	4F4169	0.100000	
50000SA	MILK SUGAR (LACTOSE)	4F4169	0.300000	
53001BA	BEEF-MEAT BYPRODUCTS	4F4169	0.300000	
53001BB	BEEF(ORGAN MEATS)-OTHER	4F4169	0.300000	
53001DA	BEEF-DRIED	4F4169	0.300000	
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	4F4169	0.300000	
53001KA	BEEF(ORGAN MEATS)-KIDNEY	4F4169	0.300000	
53001LA	BEEF(ORGAN MEATS)-LIVER	4F4169	0.300000	
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	4F4169	0.300000	
53002BA	GOAT-MEAT BYPRODUCTS	4F4169	0.300000	
53002BB	GOAT(ORGAN MEATS)-OTHER	4F4169	0.300000	
53002FA	GOAT(BONELESS)-FAT	4F4169	0.300000	
53002KA	GOAT(ORGAN MEATS)-KIDNEY	4F4169	0.300000	
53002LA	GOAT(ORGAN MEATS)-LIVER	4F4169	0.300000	
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	4F4169	0.300000	
53003AA	HORSE	4F4169	0.300000	
53005BA	SHEEP-MEAT BYPRODUCTS	4F4169	0.300000	
53005BB	SHEEP(ORGAN MEATS)-OTHER	4F4169	0.300000	
53005FA	SHEEP(BONELESS)-FAT	4F4169	0.300000	
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	4F4169	0.300000	
53005LA	SHEEP(ORGAN MEATS)-LIVER	4F4169	0.300000	
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT)	4F4169	0.300000	
53006BA	PORK-MEAT BYPRODUCTS	4F4169	0.300000	
53006BB	PORK(ORGAN MEATS)-OTHER	4F4169	0.300000	
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	4F4169	0.300000	
53006KA	PORK(ORGAN MEATS)-KIDNEY	4F4169	0.300000	
53006LA	PORK(ORGAN MEATS)-LIVER	4F4169	0.300000	
53006MA	PORK-LEAN	4F4169	0.300000	
55008BA	TURKEY-BYPRODUCTS	3F4231	0.050000	
55008LA	TURKEY-GIBLETS (LIVER)	3F4231	0.050000	
55008MA	TURKEY-FLESH(W/O SKIN, W/O BONES)	3F4231	0.050000	
55008NB	TURKEY-FLESH(+SKIN, W/O BONES)	3F4231	0.050000	
55008NC	TURKEY-UNSPECIFIED	3F4231	0.050000	

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 carcinog- enicity 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	PUBLISHED
55013BA	POULTRY, OTHER-BYPRODUCTS	3F4231		0.050000
55013LA	POULTRY, OTHER-GIBLETS(LIVER)	3F4231		0.050000
55013MA	POULTRY, OTHER-FLESH (+SKIN, W/O BONES)	3F4231		0.050000
55014AA	EGGS-WHOLE	3F4231		0.020000
55014AB	EGGS-WHITE ONLY	3F4231		0.020000
55014AC	EGGS-YOLK ONLY	3F4231		0.020000
55015BA	CHICKEN-BYPRODUCTS	3F4231		0.050000
55015LA	CHICKEN-GIBLETS(LIVER)	3F4231		0.050000
55015MA	CHICKEN-FLESH(W/O SKIN, W/O BONES)	3F4231		0.050000
55015MB	CHICKEN-FLESH(+SKIN, W/O BONES)	3F4231		0.050000

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 05/25/95

PAGE: 1

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 carcinogenicity in rats or mice.	ADI UF -->100 OPP Rfd= 0.057000 EPA Rfd= 0.000000	No data gaps.	Rfd/PR reviewed 04/22/93

TOTAL TMRC (MG/KG BODY WEIGHT/DAY)

POPULATION SUBGROUP	CURRENT TMRC*		NEW TMRC**		DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES
	TMRC	ADJ	TMRC	ADJ		
U.S. POPULATION - 48 STATES	0.008088	0.008189	14.367070	0.177607		
U.S. POPULATION - SPRING SEASON	0.007688	0.007789	13.664221	0.177179		
U.S. POPULATION - SUMMER SEASON	0.007728	0.007829	13.734228	0.176907		
U.S. POPULATION - FALL SEASON	0.008459	0.008562	15.020235	0.179398		
U.S. POPULATION - WINTER SEASON	0.008457	0.008558	15.013535	0.176937		
NORTHEAST REGION	0.008410	0.008519	14.946070	0.191535		
NORTH CENTRAL REGION	0.008291	0.008395	14.728440	0.182684		
SOUTHERN REGION	0.007284	0.007378	12.943367	0.164021		
WESTERN REGION	0.008722	0.008822	15.476839	0.174939		
HISPANICS	0.008528	0.008623	15.127811	0.166189		
NON-HISPANIC WHITES	0.008210	0.008314	14.586258	0.182625		
NON-HISPANIC BLACKS	0.006994	0.007081	12.422395	0.151826		
NON-HISPANIC OTHERS	0.008576	0.008671	15.212726	0.166705		
NURSING INFANTS (< 1 YEAR OLD)	0.005485	0.005516	9.677642	0.054377		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.014746	0.014824	26.007509	0.136598		
FEMALES (13+ YEARS, PREGNANT)	0.006714	0.006779	11.892400	0.113968		
FEMALES 13+ YEARS, NURSING	0.007632	0.007717	13.538268	0.149400		
CHILDREN (1-6 YEARS OLD)	0.016735	0.016934	29.708784	0.349612		
CHILDREN (7-12 YEARS OLD)	0.012404	0.012548	22.014528	0.253581		
MALES (13-19 YEARS OLD)	0.008391	0.008501	14.913200	0.191309		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.007105	0.007187	12.609547	0.144986		
MALES (20 YEARS AND OLDER)	0.006156	0.006263	10.987288	0.186812		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.005993	0.006058	10.627451	0.112668		

*Current TMRC does not include new or pending tolerances.

**New TMRC includes new, pending, and published tolerances.

TABLE 3

TOLERANCE ASSESSMENT SUMMARY FOR Imidacloprid
CASWELL #497E

DATE: 05/25/95

ANALYSIS FOR POPULATION SUB-GROUP: U.S. POPULATION - 48 STATES

EXISTING TOLERANCES (PUBLISHED ONLY) RESULT IN A TMRC OF: THE EXISTING TMRC IS EQUIVALENT TO:	0.008088 14.189	MG/KG/DAY % OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY) RESULT IN A TMRC OF: THESE NEW TOLERANCES WILL OCCUPY:	0.000091 0.158	MG/KG/DAY % OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY) ARE APPROVED THE RESULTANT TMRC WILL BE: THE NEW TMRC WILL OCCUPY	0.008179 14.347	MG/KG/DAY % OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE CURRENT NEW PETITION HAVE A TMRC OF: THIS TMRC WILL OCCUPY	0.000012 0.020	MG/KG/DAY % OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE CURRENT NEW PETITION) ARE GRANTED THE RESULTANT TMRC WILL BE: THE TOTAL TMRC WILL OCCUPY	0.008190 14.367	MG/KG/DAY % OF THE ADI.

ANALYSIS FOR POPULATION SUB-GROUP: CHILDREN (1-6 YEARS OLD)

EXISTING TOLERANCES (PUBLISHED ONLY) RESULT IN A TMRC OF: THE EXISTING TMRC IS EQUIVALENT TO:	0.016735 29.359	MG/KG/DAY % OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY) RESULT IN A TMRC OF: THESE NEW TOLERANCES WILL OCCUPY:	0.000200 0.350	MG/KG/DAY % OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY) ARE APPROVED THE RESULTANT TMRC WILL BE: THE NEW TMRC WILL OCCUPY	0.016934 29.709	MG/KG/DAY % OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE CURRENT NEW PETITION HAVE A TMRC OF: THIS TMRC WILL OCCUPY	0.000001 0.000	MG/KG/DAY % OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE CURRENT NEW PETITION) ARE GRANTED THE RESULTANT TMRC WILL BE: THE TOTAL TMRC WILL OCCUPY	0.016935 29.709	MG/KG/DAY % OF THE ADI.

TABLE 4

DETAILED ACUTE ANALYSIS INCLUDING AR'S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION 11:18 Wednesday, May 31, 1995 43

 *NAME: IMIDACLOPRID *****
 *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* *****
 -FEMALES(13+ YRS) *****

ESTIMATED % OF POTENTIAL		MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY	
PERSON DAYS THAT ARE USER-DAYS	MG/KG BODY WEIGHT/DAY	AS PERCENT OF RDV	
0.00	0.000000	0.00	
99.85	0.006337	264.04	
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		
100	97	90	82
	74	67	60
	55	50	46
	42	28	19
	14	4	1
	0	0	0

ESTIMATES BASED ON TOLERANCES:
 ANTICIPATED RESIDUES:
 TOLERANCES:
 ANTICIPATED RESIDUES:
 Exposure = RDV x X
 = 0.0024 x 20
 High End Exposure = 0.048
 MOE = NOEL + Exposure
 = 24 mg/kg/day + 0.048 mg/kg/day
 MOE = 500
 Mean MOE = NOEL + Mean
 = 24 + 0.006337
 = >3,700