497E

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

JAN 24 1996

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Imidacloprid in/on Leafy Vegetables. PP# 5F4522.

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

Through: Elizabeth Doyle, Section Head
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SAB/Health Effects Division
E. A. Doyle

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

Action Requested

Provide a dietary exposure analysis for the use of imidacloprid in/on leafy vegetables. The petition requests and CBTS recommends that a tolerance of 3.5 ppm be established on leafy vegetables.

Discussion

The petition requests a tolerance of 3.5 ppm on the leafy vegetables crop group, leafy greens subgroup. Representative commodities within DRES for the leafy greens subgroup include head and leaf lettuce, spinach, cress, dandelion, endive, and parsley. As there are presently established tolerances for leaf and head lettuce at the recommended tolerance levels, these commodities will appear as published in the enclosed analysis.

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, increased resorptions, abortions, and increased skeletal abnormalities.

Residue Information

Tolerances for imidacloprid are published in 40 CFR §180.472. For the purposes of this analysis, the new tolerance for canola (rape seed) was upgraded to pending status. There are no anticipated residues nor percent crop treated estimates. All uses assume 100 percent crop treated.

There are no livestock feed items associated with this petition; thus there is little likelihood of residues in meat, milk, poultry and eggs from the feeding of imidacloprid RACs and their processed commodities in this petition. The established secondary tolerances are adequate for this petition.

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.

Chronic Exposure Analysis

Exposure from Published Uses of imidacloprid:

Subgroup	Exposure (mg/kg/day)	%RfD
U.S. Population	0.008187	14.4
Non-Nursing Infants (< 1 year)	0.014818	26

Proposed new Tolerances on spinach, endive, cress, parsley & dandelion:

U.S. Population	0.000172	.300
Non-Nursing Infants (< 1 year)	0.000652	1.14

If the new tolerances on leafy green subgroup are approved:

U.S. Population	0.008358	14.7
Non-Nursing Infants (< 1 year)	0.015469	27.1

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 the leafy greens subgroup at 3.5 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 480 demonstrates no concern for females of child-bearing age considering the proposed tolerances.

Summaries of the acute dietary risk for the subgroup females(13+ years) are attached as Table 4.

There appears to be no acute dietary concern for the proposed tolerances on the leafy greens subgroup.

Attachments

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

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E   DATE: 11/28/95   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	TOLERANCE (PPM) NEW	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	5E4425			6.000000
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
13014AA	DANDELION	5F4522	3.500000		
13015AA	ENDIVE,CURLEY AND ESCAROLE	5F4522	3.500000		
13017AA	CRESS,GARDEN,FIELD	5F4522	3.500000		
13020AA	LETTUCE-UNSPECIFIED	3F4231			3.500000
13021AA	MUSTARD GREENS	3F4231			3.500000
13022AA	PARSLEY	5F4522	3.500000		
13024AA	SPINACH	5F4522	3.500000		
13039AA	CRESS,UPLAND	5F4522	3.500000		
13045AA	LETTUCE-HEAD VARIETIES	3F4231			3.500000
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

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FOOD CODE	FOOD NAME	PETITION NUMBER	NEW	TOLERANCE (PPM) PENDING	PUBLISHED
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
24007HA	WHEAT-BRAN	4F4337			0.050000
24007WA	WHEAT-FLOUR	4F4337			0.050000
25002SA	BEET SUGAR	4F4337			0.050000
27003OA	COTTONSEED-OIL	4F4169			6.000000
27003WA	COTTONSEED-MEAL	4F4169			9.000000
27017AA	RAPE SEED	5F4534		0.050000	
43058AA	WINE AND SHERRY	3F4231			1.000000
50000DB	MILK-NON-FAT SOLIDS	4F4169			0.100000
50000FA	MILK-FAT SOLIDS	4F4169			0.100000
50000SA	MILK SUGAR (LACTOSE)	4F4169			0.100000
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

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FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
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
55008MB	TURKEY-FLESH(+SKIN,W/O BONES)	3F4231			0.050000
55008MC	TURKEY-UNSPECIFIED	3F4231			0.050000
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: 11/28/95 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
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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	0.008186	0.008360	14.667272	0.305228		
U.S. POPULATION - SPRING SEASON	0.007785	0.007966	13.975381	0.316619		
U.S. POPULATION - SUMMER SEASON	0.007825	0.007983	14.006019	0.277093		
U.S. POPULATION - FALL SEASON	0.008559	0.008733	15.320565	0.305086		
U.S. POPULATION - WINTER SEASON	0.008555	0.008739	15.330891	0.321946		
NORTHEAST REGION	0.008515	0.008743	15.337840	0.398749		
NORTH CENTRAL REGION	0.008392	0.008522	14.950840	0.227228		
SOUTHERN REGION	0.007376	0.007544	13.235349	0.295151		
WESTERN REGION	0.008818	0.008996	15.781589	0.310660		
HISPANICS	0.008620	0.008756	15.361326	0.237933		
NON-HISPANIC WHITES	0.008311	0.008470	14.859049	0.278272		
NON-HISPANIC BLACKS	0.007079	0.007362	12.915814	0.495751		
NON-HISPANIC OTHERS	0.008668	0.008918	15.646456	0.439196		
NURSING INFANTS (< 1 YEAR OLD)	0.005513	0.005544	9.726430	0.055330		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.014817	0.015476	27.150674	1.155404		
FEMALES (13+ YEARS, PREGNANT)	0.006778	0.006843	12.005825	0.114268		
FEMALES 13+ YEARS, NURSING	0.007715	0.008051	14.125070	0.590123		
CHILDREN (1-6 YEARS OLD)	0.016933	0.017157	30.099430	0.391642		
CHILDREN (7-12 YEARS OLD)	0.012548	0.012791	22.439763	0.425856		
MALES (13-19 YEARS OLD)	0.008499	0.008654	15.183200	0.272905		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.007187	0.007293	12.794525	0.186147		
MALES (20 YEARS AND OLDER)	0.006255	0.006410	11.244968	0.270486		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.006056	0.006215	10.903175	0.278440		

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

TABLE 3

TOLERANCE ASSESSMENT SUMMARY FOR Imidacloprid DATE: 11/28/95
CASWELL #497E

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

EXISTING TOLERANCES (PUBLISHED ONLY) RESULT IN A TMRC OF:	0.008187	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	14.362	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY) RESULT IN A TMRC OF:	0.000172	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	0.300	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY) ARE APPROVED THE RESULTANT TMRC WILL BE:	0.008358	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	14.662	% OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE CURRENT NEW PETITION HAVE A TMRC OF:	0.000003	MG/KG/DAY
THIS TMRC WILL OCCUPY	0.005	% OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE CURRENT NEW PETITION) ARE GRANTED THE RESULTANT TMRC WILL BE:	0.008361	MG/KG/DAY
THE TOTAL TMRC WILL OCCUPY	14.667	% OF THE ADI.

ANALYSIS FOR POPULATION SUB-GROUP: NON-NURSING INFANTS (< 1 YEAR OLD)

EXISTING TOLERANCES (PUBLISHED ONLY) RESULT IN A TMRC OF:	0.014818	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	25.995	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY) RESULT IN A TMRC OF:	0.000652	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	1.143	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY) ARE APPROVED THE RESULTANT TMRC WILL BE:	0.015469	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	27.138	% OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE CURRENT NEW PETITION HAVE A TMRC OF:	0.000007	MG/KG/DAY
THIS TMRC WILL OCCUPY	0.012	% OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE CURRENT NEW PETITION) ARE GRANTED THE RESULTANT TMRC WILL BE:	0.015476	MG/KG/DAY
THE TOTAL TMRC WILL OCCUPY	27.151	% OF THE ADI.

TABLE 4

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1DETAILED ACUTE ANALYSIS INCLUDING AR'S:  ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION      15:09 Tuesday, November 28, 1995  43
*************************************************************************************************************************************
*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  0.01      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
                                                                ------------------------------------------
   ESTIMATES BASED ON         PERSON DAYS THAT ARE USER-DAYS    MG/KG BODY WEIGHT/DAY       AS PERCENT OF RDV
            TOLERANCES:                 0.00                          0.000000                    0.00
    ANTICIPATED RESIDUES:               99.85                         0.006518                    65.18
0                             ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=
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	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	73	50	35	26	19	15	11	9	7	6	2	1	0	0	0	0

Exposure = RDV x X
= 0.01 x 5
High End Exposure = 0.05

MOE = Noel + Exposure
= 24 mg/kg/day + 0.05 mg/kg/day
MOE = 480