Caswell 497E

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

FEB 16 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Imidacloprid (NTN) through the Use on Fruiting Vegetables and *Brassica* Leafy Vegetables Crop Groups, Lettuce, Grapes, Tomato Processed Commodities; Meat, Milk, Poultry and Eggs (PP#3F4231/3H5675).

FROM: 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: Elizabeth A. Doyle, 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 proposed uses on various raw agricultural commodities (RACs). The following tolerances are being assessed in this analysis:

· Fruiting Vegs Crop Group	1.00 ppm
· *Brassica* Vegs Crop Group	3.50 ppm
· Grapes	1.00 ppm
· Lettuce	3.50 ppm
· Tomato paste	6.00 ppm
· Tomato puree	3.00 ppm
· meat, fat and byproducts of cattle, horses, sheep, goats and hogs	0.30 ppm
· meat, fat and meat byproducts of poultry	0.05 ppm
· eggs	0.02 ppm
· milk	0.10 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 (M. Ottley and 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, and increased resorptions, abortion and increased skeletal abnormalities.

2.Residue Information: Food uses evaluated in this analysis were the published tolerances listed in 40 CFR §180.472 and the proposed new uses as recommended in a CBTS memo by F. Griffith dated 1/19/95. Hops is included in this analysis as a published commodity with an expiration date of 6/28/95.

Meat and milk tolerances, 0.3 and 0.1 ppm, respectively, for imidacloprid have recently been published. These published tolerances are equal to the proposed meat and milk tolerances in this petition.

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.

The following table provides exposure information for the U.S. population and the most highly exposed subgroup, children one to six years old. Exposure and percent of the Reference Dose for each proposed commodity is given in the table as well.

TMRC Exposure Estimates for Imidacloprid

Commodity Type	U.S. Population (TMRC) (µg/kg/day)	U.S. Population (%RfD)	Children (1-6 yrs) (TMRC) (µg/kg/day)	Children (1-6 yrs) (%RfD)
Published Uses				
- hops				
- meat				
- milk				
- cottonseed				
- potatoes				
- apples				
- sorghum				
- TOTAL	2.594130	5	6.577375	12
Proposed Uses				
- Fruiting Vegs	3.682286	6	7.797148	14
- *Brassica* Vegs	0.718137	1	0.887115	2
- Grapes	0.265345	0.5	0.772070	1
- Poultry	0.025334	0.04	0.051560	0.09
- Eggs	0.011607	0.02	0.025999	0.05
- Tomato paste/puree[1]	2.964333	5	6.619601	12
- Lettuce	0.790699	1	0.623376	1
Total	8.087994	14	16.734728	29

[1] Tomatoes are part of the Fruiting Vegetables Crop Group. The exposure due to tomato paste and puree listed here is also reflected in the exposure from this crop group. Total exposure was calculated with tomato commodities included only once.

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 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. Although the analysis considered only those individuals who consumed any of the commodities in the DRES data file for imidacloprid, the consuming population represents approximately 99% of the surveyed individuals. 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 = 0.048 mg/kg/day
NOEL/Exposure = 24 mg/kg/day ÷ 0.048 mg/kg/day = 500

Using the given endpoints, the MOE is not of concern for the subgroup females (13+ years) with an estimated MOE above 100. See attached Table 3 for a distribution of acute exposure.

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 considering the proposed tolerances.

There appears to be no dietary concern for the tolerances on the recommended commodities found on page 1 of this memo.

Attachments

cc: DRES, Caswell #497E, Tox I (M. Ottley), CBTS (Griffith)

Table 1.

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E DATE: 02/13/95 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 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
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
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	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
14013HA	POTATOES(WHITE)-PEEL ONLY	3F4169			0.300000
24006AA	SORGHUM (INCLUDING MILO)	4F4337			0.050000
27003OA	COTTONSEED-OIL	4F4169			6.000000
27003WA	COTTONSEED-MEAL	4F4169			9.000000
43058AA	WINE AND SHERRY	3F4231	1.000000		
50000DB	MILK-NON-FAT SOLIDS	4F4169			0.100000

Table 1.

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E DATE: 02/13/95 PAGE: 2

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FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
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
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		

Table 1.

CHEMICAL INFORMATION FOR CASWELL NUMBER 497E DATE: 02/13/95 PAGE: 3

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FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
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: Imidacloprid on Petition 3F4231/3H5675

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	0.002594	0.008088	14.189463	9.638358		
U.S. POPULATION - SPRING SEASON	0.002430	0.007688	13.487042	9.223460		
U.S. POPULATION - SUMMER SEASON	0.002499	0.007728	13.557321	9.173293		
U.S. POPULATION - FALL SEASON	0.002744	0.008459	14.840837	10.027309		
U.S. POPULATION - WINTER SEASON	0.002699	0.008457	14.836598	10.101014		
NORTHEAST REGION	0.002722	0.008410	14.754535	9.978268		
NORTH CENTRAL REGION	0.002667	0.008291	14.545756	9.867540		
SOUTHERN REGION	0.002332	0.007284	12.779346	8.688951		
WESTERN REGION	0.002764	0.008722	15.301900	10.452581		
HISPANICS	0.003044	0.008528	14.961621	9.621442		
NON-HISPANIC WHITES	0.002609	0.008210	14.403633	9.827302		
NON-HISPANIC BLACKS	0.002271	0.006994	12.270568	8.286121		
NON-HISPANIC OTHERS	0.002667	0.008576	15.046021	10.367528		
NURSING INFANTS (< 1 YEAR OLD)	0.004831	0.005485	9.623265	1.146958		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.011653	0.014746	25.870911	5.427146		
FEMALES (13+ YEARS, PREGNANT)	0.001790	0.006714	11.778432	8.637902		
FEMALES 13+ YEARS, NURSING	0.002142	0.007632	13.388868	9.630498		
CHILDREN (1-6 YEARS OLD)	0.006577	0.016735	29.359172	17.819918		
CHILDREN (7-12 YEARS OLD)	0.004040	0.012404	21.760947	14.673144		
MALES (13-19 YEARS OLD)	0.002675	0.008391	14.721891	10.028779		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.002151	0.007105	12.464561	8.691330		
MALES (20 YEARS AND OLDER)	0.001790	0.006156	10.800475	7.659696		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.001533	0.005993	10.514782	7.824637		

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

Table 3: Acute Exposure Distribution for Imidacloprid

NOEL = 24.0 mg/kg bwt/day

DETAILED ACUTE ANALYSIS INCLUDING AR'S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION 10:35 Friday, February 10, 1995 9

*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

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:	99.82	0.006277	261.53

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	96	89	81	73	66	60	54	49	45	41	27	19	14	4	1	0

Exposure = RDV x X = 0.0024 x 20 = 0.048 mg/kg/day

NOEL / Exposure = 24 mg/kg/day / 0.048 mg/kg/day = 500