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

NOV 17 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Imidacloprid (NTN) through the Use on Mango (PP#4F4285).

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, Ph.D., 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 use on mango.

Discussion

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.

Residue Information:

Food uses evaluated in this analysis were the published interim tolerance on hops listed in the Tolerance Index System (TIS) and 40 CFR §180.472. Hops is included in this analysis as a published commodity with an expiration date of 6/28/95. Meat and

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

milk tolerances, 0.2 and 0.05 ppm, respectively, are also published as interim tolerances along with hops.

CBTS recommends for a tolerance on mango at 0.2 ppm in a F. Griffith memo dated 7/22/94. Mango is included in the analysis as a new tolerance.

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.

Results:

Chronic Exposure

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 1-6 years old. The 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)	(%RfD)	**Non-Nursing Infants** (TMRC) (μg/kg/day)	(%RfD)
Published Uses hops, meat & milk	0.000985	2	0.003693	6
Proposed New Use mango	<0.000001	0	0	0
Total	0.000985	2	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 for hops, meat, milk and mango 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 mg/kg/day
NOEL/Exposure = 24 mg/kg/day ÷ 0.00288 mg/kg/day = 8333

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 considering the proposed tolerances.

There appears to be no excessive dietary risk from the proposed new tolerance for imidacloprid on mango at 0.2 ppm.

Attachments

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

Table 1: Imidacloprid on Mango

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Imidacloprid Caswell #497E CAS No. 105827-78-9 A.I. CODE: 129099	2yr feeding- rat NOEL= 5.7000 mg/kg 100.00 ppm LEL= 16.9000 mg/kg 300.00 ppm (MRID [illegible], HED RfD 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 ID	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
06007AA	MANGOES	4F4285	0.200000		
08020AA	HOPS	300343			3.000000
50000DB	MILK-NON-FAT SOLIDS	3F4169			0.050000
50000FA	MILK-FAT SOLIDS	3F4169			0.050000
50000SA	MILK SUGAR (LACTOSE)	3F4169			0.050000
53001BA	BEEF-MEAT BYPRODUCTS	3F4169			0.200000
53001BB	BEEF(ORGAN MEATS)-OTHER	3F4169			0.200000
53001DA	BEEF-DRIED	3F4169			0.200000
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	3F4169			0.200000
53001KA	BEEF(ORGAN MEATS)-KIDNEY	3F4169			0.200000
53001LA	BEEF(ORGAN MEATS)-LIVER	3F4169			0.200000
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	3F4169			0.200000
53002BA	GOAT-MEAT BYPRODUCTS	3F4169			0.200000
53002BB	GOAT(ORGAN MEATS)-OTHER	3F4169			0.200000
53002FA	GOAT(BONELESS)-FAT	3F4169			0.200000
53002KA	GOAT(ORGAN MEATS)-KIDNEY	3F4169			0.200000
53002LA	GOAT(ORGAN MEATS)-LIVER	3F4169			0.200000
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	3F4169			0.200000
53004AA	HORSE	3F4169			0.200000
53005BA	SHEEP-MEAT BYPRODUCTS	3F4169			0.200000
53005BB	SHEEP(ORGAN MEATS)-OTHER	3F4169			0.200000
53005FA	SHEEP(BONELESS)-FAT	3F4169			0.200000
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	3F4169			0.200000
53005LA	SHEEP(ORGAN MEATS)-LIVER	3F4169			0.200000
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT	3F4169			0.200000
53006BA	PORK-MEAT BYPRODUCTS	3F4169			0.200000
53006BB	PORK(ORGAN MEATS)-OTHER	3F4169			0.200000
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	3F4169			0.200000
53006KA	PORK(ORGAN MEATS)-KIDNEY	3F4169			0.200000
53006LA	PORK(ORGAN MEATS)-LIVER	3F4169			0.200000
53006MA	PORK-LEAN	3F4169			0.200000

Table 2: Imidacloprid on Mango

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

	TOTAL TMRC (MG/KG BODY WEIGHT/DAY)		NEW TMRC AS PERCENT OF	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES %RFD
	CURRENT TMRC*	NEW TMRC**			
U.S. POPULATION - 48 STATES	0.000984	0.000984	1.726989	0.000195	
U.S. POPULATION - SPRING SEASON	0.000945	0.000945	1.658275	0.000002	
U.S. POPULATION - SUMMER SEASON	0.000985	0.000985	1.728151	0.000700	
U.S. POPULATION - FALL SEASON	0.001015	0.001015	1.779907	0.000026	
U.S. POPULATION - WINTER SEASON	0.000993	0.000993	1.741874	0.000051	
NORTHEAST REGION	0.001013	0.001013	1.777218	0.000432	
NORTH CENTRAL REGION	0.001028	0.001028	1.803089	0.000011	
SOUTHERN REGION	0.000892	0.000892	1.564798	0.000230	
WESTERN REGION	0.001043	0.001043	1.829319	0.000084	
HISPANICS	0.001214	0.001215	2.131086	0.000819	
NON-HISPANIC WHITES	0.000979	0.000979	1.717365	0.000132	
NON-HISPANIC BLACKS	0.000900	0.000900	1.579761	0.000100	
NON-HISPANIC OTHERS	0.001077	0.001078	1.890723	0.000044	
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	0.002364	4.146668	0.000261	
CHILDREN (7-12 YEARS OLD)	0.001563	0.001564	2.743291	0.000395	
MALES (13-19 YEARS OLD)	0.001086	0.001086	1.905321	0.000030	
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000834	0.000834	1.463335	0.000019	
MALES (20 YEARS AND OLDER)	0.000729	0.000729	1.279307	0.000128	
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000584	0.000584	1.025018	0.000244	

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

Table 3: Imidacloprid on Mango

TOLERANCE ASSESSMENT SUMMARY FOR Imidacloprid DATE: 11/08/94
WELL #497E

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

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.000985	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	1.727	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	<0.000001	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	0.000	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.000985	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	1.727	% OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

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

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.003693	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	6.479	% OF THE ADI.

NO NEW TOLERANCES ARE IN THE FILE.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

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

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.002364	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	4.146	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	<0.000001	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	0.000	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.002364	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	4.147	% OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE