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

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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 *Jennifer Wintersteen*
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TO: Dennis Edwards, PM Team 19
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THROUGH: Elizabeth A. Doyle, Ph.D., Section Head *E.A. Doyle*
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



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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		Non-Nursing Infants	
	(TMRC) ($\mu\text{g}/\text{kg}/\text{day}$)	(%RfD)	(TMRC) ($\mu\text{g}/\text{kg}/\text{day}$)	(%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 ($\text{NOEL}/\text{exposure} = \text{MOE}$). 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 in/on Mango Petition

Table 1: Imidacloprid on Mango

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Imidacloprid #497E Caswell No. 105827-78-9 A.I. CODE: 129099	2Yr feeding- fat NOEL= 5.7000 mg/kg 100.00 ppm LEL= 16.9000 mg/kg 700.00 ppm (MRL: 16.9 mg/kg (Mango Committee))	Increased incidence of mineralized particles in thyroid colloid. No evidence of occurrence in lots of mice.	ADI UF -->100 OPP RfD= 0.057000 EPA RfD= 0.000000	No data gaps.	RfD/PR reviewed 04/22/93
066077AA MANGOCES					
08020AA HOPS		4F4285	0.200000		
500000B MILK-NON-FAT SOLIDS		300343		3.000000	
500001A MILK-FAT SOLIDS		3F4169		0.050000	
500005A MILK SUGAR (LACTOSE)		3F4169		0.050000	
530011A BEEF-MEAT BYPRODUCTS		3F4169		0.200000	
530018B BEEF(ORGAN MEATS)-OTHER		3F4169		0.200000	
530010A BEEF-DEBILD		3F4169		0.200000	
530011A BEEF(BONELESS)-FAT (BEEF TALLOW)		3F4169		0.200000	
530011A BEEF(ORGAN MEATS)-KIDNEY		3F4169		0.200000	
530011A BEEF(ORGAN MEATS)-LIVER		3F4169		0.200000	
530028A GOAT-MEAT BYPRODUCTS		3F4169		0.200000	
530028B GOAT(ORGAN MEATS)-OTHER		3F4169		0.200000	
530021A GOAT(BONELESS)-FAT		3F4169		0.200000	
530021A GOAT(ORGAN MEATS)-KIDNEY		3F4169		0.200000	
530021A GOAT(ORGAN MEATS)-LIVER		3F4169		0.200000	
530021A GOAT(BONELESS)-LEAN (w/O REMOVABLE FAT)		3F4169		0.200000	
530021A HORSE		3F4169		0.200000	
530058A SHEEP-MEAT BYPRODUCTS		3F4169		0.200000	
530058B SHEEP(ORGAN MEATS)-OTHER		3F4169		0.200000	
530051A SHEEP(BONELESS)-FAT		3F4169		0.200000	
530051A SHEEP(ORGAN MEATS)-KIDNEY		3F4169		0.200000	
530051A SHEEP(ORGAN MEATS)-LIVER		3F4169		0.200000	
530051A SHEEP(BONELESS)-LEAN (w/O REMOVABLE FAT)		3F4169		0.200000	
530051A SHEEP-MEAT BYPRODUCTS		3F4169		0.200000	
530061A PORK(ORGAN MEATS)-FAT (INCLUDING LARD)		3F4169		0.200000	
530061A PORK(ORGAN MEATS)-KIDNEY		3F4169		0.200000	
530061A PORK(ORGAN MEATS)-LIVER		3F4169		0.200000	
530061A PORK-LEAN		3F4169		0.200000	

NEW TOLERANCE (M) PUBLISHED
NEW REACTIVE

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 OPR RfD= 0.057000 EPA RfD= 0.000000	UF -->100	No data gaps.	RfD/PR reviewed 04/22/93
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	TOTAL THRC (MG/KG BODY WEIGHT/DAY)	CURRENT THRC*	NEW THRC AS PERCENT OF OLD	DIFFERENCE AS PERCENT OF RfD	EFFECT OF ANTICIPATED RESIDUES
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	
MISCELLANEOUS	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	
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000676	0.000676	1.608767	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	1.454898	0.000000	
CHILDREN (1-6 YEARS OLD)	0.002365	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 (19 YEARS AND OLDER)	0.000729	0.000729	1.279307	0.000128	
FEMALES (19 YEARS AND OLDER, NOT PREG. OR NURSING)	0.000584	0.000584	1.025078	0.000244	

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

Table 3: Imidacloprid on Mango

TOLERANCE ASSESSMENT PRIMARY FOR Imidacloprid DATE: 11/08/94
 JELL #497E

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: 0.000985 MG/KG/DAY
 1.727 % OF THE ADI.

NEW TOLERANCES (CURRENT PETITION ONLY)
 RESULT IN A TMRC OF:
 THE NEW TMRC WILL OCCUPY: 0.000001 MG/KG/DAY
 0.000 % OF THE ADI.

IF THE NEW TOLERANCES (CURRENT PETITION ONLY)
 ARE APPROVED THE RESULTANT TMRC WILL BE:
 THE NEW TMRC WILL OCCUPY: 0.000985 MG/KG/DAY
 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:
 THE EXISTING TMRC IS EQUIVALENT TO: 0.003693 MG/KG/DAY
 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:
 THE EXISTING TMRC IS EQUIVALENT TO: 0.002364 MG/KG/DAY
 4.146 % OF THE ADI.

PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)
 RESULT IN A TMRC OF:
 THESE NEW TOLERANCES WILL OCCUPY: <0.000001 MG/KG/DAY
 0.000 % OF THE ADI.

IF THE NEW TOLERANCES (CURRENT PETITION ONLY)
 ARE APPROVED THE RESULTANT TMRC WILL BE:
 THE NEW TMRC WILL OCCUPY: 0.002364 MG/KG/DAY
 4.147 % OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE