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

MAR 11 1988

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Avermectin - TAS Analysis of Proposed Section 18 Exemption for Use on Fresh Market Tomatoes (#88-FL-05).

FROM: Susan L. Stanton
Tolerance Assessment Program Susan L Stanton 03/10/88
HED/RCB (TS-769C)

THRU: Karl Arne, Ph.D. KArne
Branch Senior Scientist
HED/RCB (TS-769C)

TO: D. Stubbs/L. Pemberton, PM Team 41
Registration Support and Emergency Response Branch
Registration Division (TS-767C)

Action Requested

Provide an analysis of dietary exposure to avermectin in conjunction with the proposed new use on tomatoes. The Florida Department of Agriculture and Consumer Services has requested a Section 18 emergency exemption for the use of avermectin to control leaf miners on tomatoes grown for fresh market only. Tox consideration permitting, RCB has no objections to this Section 18 request (memo Cheng to Stubbs/Pemberton, 03/09/88).

Discussion

I. Analysis of Chronic Dietary Exposure:

1. The reference dose (PADI) used in the analysis was 0.00012 mg/kg body weight/day, derived from a NOEL of 0.12 mg/kg body weight/day from a 2-generation rat reproduction study with an uncertainty factor of 1000. The high uncertainty factor is due to the serious nature of the effects seen in the critical study and to existing data gaps. As new studies are submitted and reviewed in TOX Branch, the reference dose may change.

2. Currently, there are no permanent tolerances established for avermectin. The food uses evaluated in the analysis were the published temporary tolerances (citrus, cottonseed, milk, & cattle) and the proposed use on fresh market tomatoes. The residue value used for tomatoes was 0.005 ppm (memo Cheng to Stubbs/Pemberton, 03/09/88). A complete listing of residue information is provided in Table 1.

It should be noted that the TAS database does not contain consumption estimates for "fresh market tomatoes" per se, but rather for "whole tomatoes". Since "whole tomatoes" would include fresh market as well as canned whole tomatoes, the analysis may somewhat overestimate exposure resulting from the proposed use on fresh market tomatoes.

3. The TAS routine chronic analysis estimates the Theoretical Maximum Residue Contribution (TMRC) for the U.S. population and for each of 22 population subgroups and compares this exposure estimate to the acceptable daily intake (Provisional ADI in this case). The results are presented in Table 2 and may be summarized as follows for the U.S. population and the two most highly exposed subgroups, non-nursing infants and children, ages 1-6:

	Published Temporary Tolerances	Sec. 18 (88-FL-05) Tomatoes	Total
U.S. Population	0.000039[a] (32.1%)[b]	0.000002 (2.05%)	0.000041 (34.2%)
Non-Nursing Infants	0.000105 (87.8%)	0.000003 (1.9%)	0.000108 (89.7%)
Children, 1-6 yrs.	0.000093 (77.3%)	0.000004 (3.3%)	0.000097 (80.6%)

[a]Theoretical Maximum Residue Contribution (TMRC) in mg/kg/day.
[b]Exposure as percent of the PADI.

II. Analysis of Acute Dietary Exposure:

1. A menu screen analysis of acute exposure was conducted using a NOEL of 0.06 mg/kg body weight for developmental effects. A summary of the analysis by population subgroup is provided in Table 3. A summary by menu category is provided in Table 4.

2. In this case the population of interest was the subgroup of females 13 years of age and older. The theoretical average Margin of Safety (MOS) for developmental effects was calculated

by dividing the NOEL by the mean single-day exposure. The following results were obtained:

	Daily Exposure (mg/kg body wt)	MOS
Published Temp. Tolerances	0.00006	1000
Tomatoes (Pending Sec. 18)	0.00001	6000
All Uses (Published + Pending)	0.00007	860

3. The TAS menu screen analysis computes a conservative estimate of the mean acute exposure. It serves as a screen to determine if an acceptable margin of safety (MOS) exists for an acute effect. In the present case, since the calculated margins of safety are acceptable, a more detailed analysis of acute exposure was not deemed necessary.

Both the chronic and acute exposure analyses were conducted using tolerance level residues with an assumption of 100% of crop treated. This conservative approach no doubt overestimates exposure in both cases; however, since it yields acceptable exposure estimates and margins of safety, no further data are required at this time.

cc. TAS File
Reading File
circ.
Tox. Branch (Rathman)
W. Dykstra, TOX
PMSD
Avermectin SF

Table 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 063AB

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CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Avermectin Caswell #063AB CAS No. 65195-55-3 A I. CODE. 122804 CFR No. 180.	2gen reprod.- rat NOEL= 0 1200 mg/kg 0.00 ppm LEL= 0.4000 mg/kg 0.00 ppm ONCO: Undetermined	Decreased pup survival and body weight; increase in incidence of retinal abnormalities. Doses by gavage. No oncogenicity data available.	PADI 1000 OPP RfD= 0.000120 EPA RfD= 0.000000 WHO RfD 0.000000 Type	Chronic feeding- rat Chronic feeding- dog UF of 1000 due to serious effects in critical study and data gaps. Mouse teratogen.	TCX complete 7/11/86 TCX reassess 6/12/87 ORD not scheduled

FOOD CODE	FOOD NAME		PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
02001AA	CITRUS CITRON	EXP. 05/88	7G3468			0.005000
02002AA	GRAPEFRUIT-UNSPECIFIED	EXP 05/88	7G3468			0.005000
02002AB	GRAPEFRUIT-PULP	EXP 05/88	7G3468			0.005000
02002JA	GRAPEFRUIT-JUICE	EXP 05/88	7G3468			0.005000
02003AA	KUMQUATS	EXP. 05/88	7G3468			0.005000
02004AA	LEMONS-UNSPECIFIED	EXP. 05/88	7G3468			0.005000
02004AB	LEMONS-PULP	EXP. 05/88	7G3468			0.005000
02004HA	LEMONS-PEEL	EXP. 05/88	7G3468			0.005000
02004JA	LEMONS-JUICE	EXP. 05/88	7G3468			0.005000
02005AA	LIMES-UNSPECIFIED	EXP 05/88	7G3468			0.005000
02005AB	LIMES-PULP	EXP. 05/88	7G3468			0.005000
02005HA	LIMES-PEEL	EXP. 05/88	7G3468			0.005000
02005JA	LIMES-JUICE	EXP. 05/88	7G3468			0.005000
02006AA	ORANGES-UNSPECIFIED	EXP. 05/88	7G3468			0.005000
02006AB	ORANGES-PULP	EXP. 05/88	7G3468			0.005000
02006HA	ORANGES-PEEL	EXP. 05/88	7G3468			0.005000
02006JA	ORANGES-JUICE	EXP. 05/88	7G3468			0.005000
02007AA	TANGELOS	EXP. 05/88	7G3468			0.005000
02008AA	TANGERINES	EXP. 05/88	7G3468			0.005000
02008JA	TANGERINE-JUICE	EXP. 05/88	7G3468			0.005000
11005AA	TOMATOES-WHOLE		88FL05	0.005000		
27003OA	COTTONSEED-OIL	EXP. 06/89	6G3320			0.005000
27003WA	COTTONSEED-MEAL	EXP. 06/89	6G3320			0.005000
50000DB	MILK-NON-FAT SOLIDS	EXP. 05/88	7G3468			0.001000
50000FA	MILK-FAT SOLIDS	EXP. 05/88	7G3468			0.001000
50000SA	MILK SUGAR (LACTOSE)	EXP. 05/88	7G3468			0.001000
53001BA	BEEF-MEAT BYPRODUCTS	EXP 05/88	7G3468			0.010000
53001BB	BEEF(ORGAN MEATS)-OTHER	EXP 05/88	7G3468			0.010000
53001DA	BEEF-DRIED	EXP. 05/88	7G3468			0.010000
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	05/88	7G3468			0.010000
53001KA	BEEF(ORGAN MEATS)-KIDNEY	EXP. 05/88	7G3468			0.010000
53001LA	BEEF(ORGAN MEATS)-LIVER	EXP. 05/88	7G3468			0.010000
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)		7G3468			0.010000

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Table 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

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CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Avermectin Caswell #063AB CAS No. 65195-55-3 A.I. CODE: 122804 CFR No. 180.	2gen reprod. - rat NOEL= 0.1200 mg/kg 0.00 ppm LEL= 0.4000 mg/kg 0.00 ppm ONCO: Undetermined	Decreased pup survival and body weight; increase in incidence of retinal abnormalities. Doses by gavage. No oncogenicity data available.	PADI 1000 OPP RfD= 0.000120 EPA RfD= 0.000000 WHO RfD 0.000000 Type:	Chronic feeding- rat Chronic feeding- dog UF of 1000 due to serious effects in critical study and data gaps. Mouse teratogen	TOX complete 7/11/86 TOX reassess 6/12/87 ORD not scheduled.

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	0.000039	0.000041	34.166667	2.050000		
U.S. POPULATION - SPRING SEASON	0.000038	0.000040	33.433333	1.958333		
U.S. POPULATION - SUMMER SEASON	0.000038	0.000041	34.284167	2.727500		
U.S. POPULATION - FALL SEASON	0.000039	0.000041	34.555000	1.691667		
U.S. POPULATION - WINTER SEASON	0.000039	0.000041	34.404167	1.825833		
NORTHEAST REGION	0.000042	0.000045	37.502500	2.222500		
NORTH CENTRAL REGION	0.000039	0.000042	34.661667	1.883333		
SOUTHERN REGION	0.000034	0.000036	30.055000	1.910833		
WESTERN REGION	0.000041	0.000043	36.080000	2.304167		
HISPANICS	0.000049	0.000053	43.824167	2.765833		
NON-HISPANIC WHITES	0.000038	0.000041	33.829167	2.090833		
NON-HISPANIC BLACKS	0.000036	0.000037	31.153333	1.465000		
NON-HISPANICS OTHER	0.000046	0.000048	39.824167	1.886667		
NURSING INFANTS (<1 YEAR OLD)	0.000033	0.000034	28.321667	0.636667		
NON-NURSING INFANTS (<1 YEAR OLD)	0.000105	0.000108	89.672500	1.888333		
FEMALES (13+ YEARS, PREGNANT)	0.000029	0.000031	25.654167	1.772500		
FEMALES 13+ YEARS, NURSING	0.000031	0.000033	27.855000	2.152500		
CHILDREN (1-6 YEARS OLD)	0.000093	0.000097	80.612500	3.334167		
CHILDREN (7-12 YEARS OLD)	0.000059	0.000062	51.859167	2.607500		
MALES (13-19 YEARS OLD)	0.000040	0.000042	34.928333	2.010833		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000033	0.000035	28.980833	1.791667		
MALES (20 YEARS AND OLDER)	0.000027	0.000029	24.516667	1.715833		
FEMALES (20 YEARS AND OLDER)	0.000026	0.000028	23.620000	1.880833		

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

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Table 3


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*NAME  AVERMECTIN                          STUDY     RDV      NOEL      SF    STUDY TYPE   SPECIES   EFF LEV   CORE GRADE   DOC NO *
*CASWELL NO  063AB    CFR NO: CFR           A  00000.0012             000100 Reprodctn      Rat     Systemic                      *
*CAS NO  65195 55-3 SHAUGHNESSY NO  122804 B                                                                                      *
*STATUS CODES                              C                                                                                      *
*RDV INFO   The LD  value used in this analysis is  .0006      MG/KG  of BODY WEIGHT/DAY                                         *
*FILE INFO:   NEW ACTION: User Modifications        APPROVED:Data NOT Used     PUBLISHED: Data Used                                 *
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SUBGROUP TOTALS OVER MENU CATEGORIES
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED (WATER:OIL)

NOTE. THIS ANALYSIS SHOULD BE USED FOR SCREENING PURPOSES ONLY, SINCE RESIDUE CONTRIBUTIONS ARE BIASED HIGH (BOTH WITHIN AND ACROSS MENU CATEGORIES).

POPULATION SUBGROUP	MENU PATTERN	ACCUMULATED ACUTE(DAILY) EXPOSURE BASED ON MAXIMUM TOLERANCE WITHIN MENU CATEGORY (MG/KG BODY WT/DAY)			ACCUMULATED ACUTE EXPOSURE AS PERCENT OF RDV	
		PRIOR	NEW	DIFFERENCE	PRIOR	NEW
U S POP --48 STATES	I	0.00008	0.00010	0.00001	14.09	16.30
INFANTS(<1 YEAR)	II	0.00027	0.00029	0.00001	45.22	47.60
CHILDREN(1-6 YRS)	III	0.00020	0.00022	0.00003	32.63	37.26
FEMALES(13+ YRS)	I	0.00006	0.00007	0.00001	10.03	11.79
MALES(13+ YRS)	I	0.00007	0.00008	0.00001	10.86	12.69

Table 4


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*NAME. AVERMECTIN                          STUDY    RDV       NOEL      SF    STUDY TYPE   SPECIES   EFF. LEV.  CORE GRADE   DOC  NO *
*CASWELL NO  063AB    CFR NO: CFR            A  00000.0012              000100 Reprodctn      Rat      Systemic                        *
*CAS NO. 65195-55-3 SHAUGHNESSY NO:  122804 B                                                                                        *
*STATUS CODES:                             C                                                                                        *
*RDV INFO   The LD  value used in this analysis is  .0006      MG/KG  of BODY WEIGHT/DAY                                            *
*FILE INFO:   NEW ACTION. User Modifications        APPROVED:Data NOT Used     PUBLISHED: Data Used                                   *
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SUMMARY BY MENU CATEGORY
FEMALES(13+ YRS)
MENU PATTERN I : CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED (WATER:OIL)

MENU CATEGORY	NO. OF CONSUMER DAYS, AS % OF POTENTIAL PERSON DAYS	MEAN CONSUMPTION PER CONSUMER DAY (G/KG BODY WT/DAY)	MAXIMUM TOLERANCE PRIOR	MAXIMUM TOLERANCE NEW	MAXIMUM RESIDUE CONTRIBUTION AS PERCENT OF RDV PRIOR	MAXIMUM RESIDUE CONTRIBUTION AS PERCENT OF RDV NEW
1 MEATS	99.17	2.368287	0.0100	0.0100	3.95	3.95
4 MILK: NON-FAT SOLIDS	96.54	3.819864	0.0010	0.0010	0.64	0.64
5 MILK. FAT SOLIDS	96.79	2.084150	0.0010	0.0010	0.35	0.35
6 GRAINS(EXCL RICE),SOYBEANS,VEG. OILS	98.87	1.563421	0.0050	0.0050	1.30	1.30
8 TOMATOES	54.97	2.117000	.	0.0050		1.76
10 FRUITS	70.83	4.555970	0.0050	0.0050	3.80	3.80

NOTE. THIS ANALYSIS SHOULD BE USED FOR SCREENING PURPOSES ONLY, SINCE RESIDUE CONTRIBUTIONS ARE BIASED HIGH (BOTH WITHIN AND ACROSS MENU CATEGORIES).