



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. *K. Arne*
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:

	<u>Published Temporary Tolerances</u>	<u>Sec. 18 (88-FL-05) Tomatoes</u>	<u>Total</u>
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%)

^aTheoretical Maximum Residue Contribution (TMRC) in mg/kg/day.

^bExposure 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:

	<u>Daily Exposure</u> <u>(mg/kg body wt)</u>	<u>MOS</u>
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

DATE: 03/10/98

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

FOOD CODE	FOOD NAME	PETITION NUMBER	NEW	TOLERANCE (PPM)	
				PENDING	PUBLISHED
02001AA	CITRUS CITRON	763468			0.005000
02002AA	GRAPEFRUIT-UNSPECIFIED	763468			0.005000
02002AB	GRAPEFRUIT-PULP	763468			0.005000
02002JA	GRAPEFRUIT-JUICE	763468			0.005000
02003AA	KUMQUATS	763468			0.005000
02004AA	LEMONS-UNSPECIFIED	763468			0.005000
02004AB	LEMONS-PULP	763468			0.005000
02004HA	LEMONS-PEEL	763468			0.005000
02004JA	LEMONS-JUICE	763468			0.005000
02005AA	LINES-UNSPECIFIED	763468			0.005000
02005AB	LINES-PULP	763468			0.005000
02005HA	LINES-PEEL	763468			0.005000
02005JA	LINES-JUICE	763468			0.005000
02006AA	ORANGES-UNSPECIFIED	763468			0.005000
02006AB	ORANGES-PULP	763468			0.005000
02006HA	ORANGES-PEEL	763468			0.005000
02006JA	ORANGES-JUICE	763468			0.005000
02007AA	TANGELOS	763468			0.005000
02008AA	TANGERINES	763468			0.005000
02008JA	TANGERINE-JUICE	763468			0.005000
11005AA	TOMATOES-WHOLE	88FL05	0.005000		0.005000
270030A	COTTONSEED-OIL	663320			0.005000
27003AA	COTTONSEED-NEAL	663320			0.005000
50000DB	MILK-NON-FAT SOLIDS	763468			0.001000
50000FA	MILK-FAT SOLIDS	763468			0.001000
50000FA	MILK SUGAR (LACTOSE)	763468			0.001000
53001BA	BEEF-HEAT BYPRODUCTS	763468			0.010000
53001BB	BEEF (ORGAN MEATS)-OTHER	763468			0.010000
53001DA	BEEF-DRIED	763468			0.010000
53001FA	BEEF (BONELESS)-FAT (BEEF TALLOW)	763468			0.010000
53001KA	BEEF (BONELESS)-KIDNEY	763468			0.010000
53001LA	BEEF (ORGAN MEATS)-LIVER	763468			0.010000
53001WA	BEEF (BONELESS)-LEAN (W/O REMOVABLE FAT)	763468			0.010000

Table 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 03/10/98

PAGE: 1

CHEMICAL INFORMATION			STUDY TYPE		EFFECTS		REFERENCE DOSES		DATA GAPS/COMMENTS		STATUS	
Averectin	2gen reprod. - rat	Decreased pup survival	PADI	1000	Chronic feeding- rat	TOX complete 7/11/86						
Caswell #063AB	NOEL= 0.1200 mg/kg	and body weight; increase	OPP RfD=	0.000120	Chronic feeding- dog	TOX reassess 6/12/87						
CAS No. 65195-55-3	0.00 ppm	in incidence of retinal	EPA RfD=	0.000000	UF of 1000 due to serious	ORD not scheduled.						
A.I. CODE: 122804	LEL= 0.4000 mg/kg	abnormalities. Doses by			effects in critical study							
CFR No. 180	0.00 ppm	gavage. No oncogenicity	WHO RfD	0.000000	and data gaps.							
	ONCO: Undetermined	data available.	Type:		Mouse teratogen							
POPULATION SUBGROUP												
TOTAL TMRC (MG/KG BODY WEIGHT/DAY)					NEW TMRC**		NEW TMRC AS PERCENT OF RFD		DIFFERENCE AS PERCENT OF RFD		EFFECT OF ANTICIPATED RESIDUES	
CURRENT TMRC*											ARC	

Table 3

MENU REPORT
 12 TO WEDNESDAY, MAR 11, 1948 17
 NAME AVERMECTIN
 CASWELL NO 063AB CFR NO: CFR A 00000.0012 SF STUDY TYPE SPECIFS EFF LEV CODE USELE DAY NO
 CAS NO 65195 55-3 SHAUGHNESSY NO 122804 B 000100 Reproductn Rat Systemc
 STATUS CODES
 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

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	

12 29 WEDNESDAY, MARCH 9, 1993 10

Table 4

MENU SCREEN

NAME: AVERNETHIN STUDY RDV NOEL SF STUDY TYPE SPECIES EFF. LEV. CORE GRADE DOC NO
CASHILL NO 061AB CFR NO: CFR A 00000.0012 000100 Reproductn 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 MC/KG of BODY WEIGHT/DAY
FILE INFO: NEW ACTION: User Modifications APPROVED: Data NOT Used PUBLISHED: Data Used

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		MAXIMUM RESIDUE CONTRIBUTION AS PERCENT OF RDV	
			PRIOR	NEW	PRIOR	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).