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

JAN 19 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Revised Chronic Exposure Analysis for the Use of Avermectin on Citrus

FROM: Richard Griffin
Dietary Risk Evaluation System (DRES) Staff
HED/SACB (H7509C)

THROUGH: Reto Engler, Ph.D.
Chief, Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: George LaRocca/Adam Heyward, PM 15
Insecticide-Herbicide Branch
Registration Division (H7505C)

Action Requested

Provide an estimate of dietary exposure for published uses of avermectin, including citrus (PP#8F3592), using anticipated residues for all citrus juice.

Discussion

1. Toxicology Endpoint: The routine chronic DRES analysis used a reference dose (ADI) of 0.004 mg/kg body weight/day, based upon a NOEL of 0.12 mg/kg body weight/day and an uncertainty factor of 300 from a 2 generation rat reproduction study. This value has been approved by HED (3/30/89) and Agency (4/20/89) reference dose committees.

2. Residue Information: Food uses evaluated were published tolerances from 40 CFR 180.449 and the recently published tolerance on citrus. Anticipated residues were developed from processing studies using field trial data for citrus, citrus juice, cottonseed, and extrapolated from animal feeding studies for milk (V. F. Boyd memo, 6/29/89). A previous DRES analysis (J. R. Tomerlin memo, 7/6/89) did not use appropriate anticipated residue data for all citrus juices. The present analysis is a revision of the 7/6/89 analysis using anticipated residues of 0.006 ppm for all citrus juices. A summary of the residue information used in the analysis is attached as Table 1.

3. Exposure Analysis: The DRES chronic exposure analysis uses tolerance level residues and 100 per cent crop treated to estimate

the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 population subgroups. The Anticipated Residue Contribution (ARC) is an estimate of exposure which more closely approximates actual exposure. The TMRC and ARC for all DRES population subgroups is shown in Table 2. The ARC exposure summaries for the overall U.S. population, non-nursing infants, and children aged 1 to 6 are shown in the following table.

Avermectin ARC Exposure Summary

Commodity Group	Overall U.S. Population	Non-Nurs. Infants	Children Aged 1 - 6
Meat	0.000032[a] 7.9[b]	0.000029 7.3	0.000057 14.3
Milk	0.000010 2.6	0.000065 16.3	0.000031 7.7
Citrus	0.000010 2.5	0.000017 4.2	0.000026 6.4
Cottonseed	< 0.000001 < 0.1	< 0.000001 < 0.1	< 0.000001 < 0.1
TOTAL	0.000052 13.1	0.000112 27.9	0.000114 28.5

[a]Estimated exposure in mg/kg body weight/day.
[b]Exposure estimate expressed as a percentage of the reference dose.

4. Dietary Risk Assessment: Using AR data for all citrus juices results in exposure estimates representing from 9 to 29 percent of the reference dose. Exposure from citrus represents 2.6, 4.2, and 6.4 percent of the reference dose for the overall U.S. population, non-nursing infants, and children aged 1 to 6, respectively. Therefore, currently published uses of avermectin, including the use on citrus, do not appear to pose a hazard to human health from chronic exposure.

The previous acute exposure analysis using tolerances (J. R. Tomerlin memo 7/6/89) demonstrated that the minimum Margin of Exposure for women is 250. Therefore, it is unnecessary to conduct an additional acute analysis at this time.

Attachments

cc: DRES, DEB (Loranger), Caswell #063AB, Dykstra (TOX)

Table 1

ANTICIPATED RESIDUE INFORMATION FOR CASWELL NUMBER 063AB DATE: 01/18/90 PAGE: 1

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: Negative- 2 species.	Incr retinal folds in weanlings, decr viability & lactation indices; decr pup body wt; incr of dead pups at birth. No evidence of oncogenicity.	ADI UF -->300 OPP RfD= 0.000400 EPA RfD= 0.000400	No data gaps. UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen.	HED complete 07/11/86. HED reassess 06/12/87. HED reassess 03/30/89. EPA verified 04/20/89. On IRIS.

FOOD CODE	FOOD	FOOD FORM	PET.#	TOLERANCE (ppm)	ANTICIPATED RESIDUE (ppm)	AR STATISTIC TYPE	% CROP TREATED	RES. VALUE USED IN TAS RUN (ppm)
02001AA	CITRUS CITRON	22 COOKED-FRESH-BAKED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02002AA	GRAPEFRUIT-UNSP	00 NOT SPECIFIED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02002AB	GRAPEFRUIT-PULP	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02002AB	GRAPEFRUIT-PULP	21 COOKED-NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02002JA	GRAPEFRUIT-JUICE	15 RAW-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02002JA	GRAPEFRUIT-JUICE	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02003AA	KUMQUATS	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004AA	LEMONS-UNSPEC	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004AA	LEMONS-UNSPEC	22 COOKED-FRESH-BAKED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004AB	LEMONS-PULP	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004AB	LEMONS-PULP	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004HA	LEMONS-PEEL	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004HA	LEMONS-PEEL	21 COOKED-NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02004JA	LEMONS-JUICE	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02004JA	LEMONS-JUICE	15 RAW-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02004JA	LEMONS-JUICE	21 COOKED-NFS	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02004JA	LEMONS-JUICE	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02005AA	LIMES-UNSPEC	00 NOT SPECIFIED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02005AB	LIMES-PULP	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02005HA	LIMES-PEEL	21 COOKED-NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02005JA	LIMES-JUICE	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02005JA	LIMES-JUICE	15 RAW-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02005JA	LIMES-JUICE	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02006AA	ORANGES-UNSPEC	00 NOT SPECIFIED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006AB	ORANGES-PULP	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006AB	ORANGES-PULP	21 COOKED-NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006HA	ORANGES-PEEL	21 COOKED-NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006HA	ORANGES-PEEL	22 COOKED-FRESH-BAKED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006HA	ORANGES-PEEL	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02006JA	ORANGES-JUICE	15 RAW-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02006JA	ORANGES-JUICE	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
02007AA	TANGELOS	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02008AA	TANGERINES	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.012000	PROCESSING	100.00	0.012000
02008JA	TANGERINE-JUICE	15 RAW-FRESH OR CANNED	8F3592	P 0.020000	0.006000C	PROCESSING	100.00	0.006000
27003OA	COTTONSEED-OIL	18 PROCESSED OIL	6G3320	P 0.005000	0.001000	FLD TRIALS	100.00	0.001000
27003WA	COTTONSEED-MEAL	18 PROCESSED OIL	6G3320	P 0.005000	0.001000	FLD TRIALS	100.00	0.001000
50000DB	MILK-NON-FAT SOL	10 RAW-FRESH OR NFS	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000DB	MILK-NON-FAT SOL	21 COOKED-NFS	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000DB	MILK-NON-FAT SOL	51 COOKED-CANNED	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000FA	MILK-FAT SOLIDS	10 RAW-FRESH OR NFS	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000

Table 1, continued

ANTICIPATED RESIDUE INFORMATION FOR CASWELL NUMBER 063AB DATE: 01/18/90 PAGE: 2

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: Negative- 2 species.	Incr retinal folds in weanlings, decr viability & lactation indices; decr pup body wt; incr of dead pups at birth. No evidence of oncogenicity.	ADI UF -->300 OPP RfD= 0.000400 EPA RfD= 0.000400	No data gaps. UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen.	HED complete 07/11/86. HED reassess 06/12/87. HED reassess 03/30/89. EPA verified 04/20/89. On IRIS.

FOOD CODE	FOOD	FOOD FORM	PET.#	TOLERANCE (ppm)	ANTICIPATED RESIDUE (ppm)	AR STATISTIC TYPE	% CROP TREATED	RES. VALUE USED IN TAS RUN (ppm)
50000FA	MILK-FAT SOLIDS	21 COOKED-NFS	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000FA	MILK-FAT SOLIDS	51 COOKED-CANNED	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000SA	MILK SUG (LACT)	21 COOKED-NFS	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
50000SA	MILK SUG (LACT)	51 COOKED-CANNED	8F3592	P 0.005000	0.001000	EXTRAP	100.00	0.001000
53001BA	BEEF-MEAT BYP	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001BA	BEEF-MEAT BYP	26 COOKED-FRESH-PICKLED,CORNED,OR CURED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001BB	BEEF-OTH ORGAN	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001BB	BEEF-OTH ORGAN	51 COOKED-CANNED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001DA	BEEF-DRIED	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	22 COOKED-FRESH-BAKED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	23 COOKED-FRESH-BOILED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	24 COOKED-FRESH-BROILED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001FA	BEEF-FAT	25 COOKED-FRESH-FRIED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001KA	BEEF-KIDNEY	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001LA	BEEF-LIVER	25 COOKED-FRESH-FRIED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001LA	BEEF-LIVER	31 COOKED-FRESH OR CANNED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001MA	BEEF-LEAN	10 RAW-FRESH OR NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001MA	BEEF-LEAN	21 COOKED-NFS	8F3592	P 0.020000	0.020000		100.00	0.020000
53001MA	BEEF-LEAN	22 COOKED-FRESH-BAKED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001MA	BEEF-LEAN	23 COOKED-FRESH-BOILED	8F3592	P 0.020000	0.020000		100.00	0.020000
53001MA	BEEF-LEAN	24 COOKED-FRESH-BROILED	8F3592	P 0.020000	0.020000		100.00	0.020000

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Table 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 01/18/90 PAGE: 1

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: Negative- 2 species.	Incr retinal folds in weanlings, decr viability & lactation indices; decr pup body wt; incr of dead pups at birth. No evidence of oncogenicity.	ADI UF -->300 OPP RfD= 0.000400 EPA RfD= 0.000400	No data gaps. UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen.	HED complete 07/11/86. HED reassess 06/12/87. HED reassess 03/30/89. EPA verified 04/20/89. On IRIS.

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	0.000133	0.000133	33.154750	0.000000	0.000052	13.03750
U.S. POPULATION - SPRING SEASON	0.000129	0.000129	32.228500	0.000000	0.000051	12.83300
U.S. POPULATION - SUMMER SEASON	0.000129	0.000129	32.194500	0.000000	0.000051	12.78475
U.S. POPULATION - FALL SEASON	0.000136	0.000136	34.047500	0.000000	0.000053	13.24675
U.S. POPULATION - WINTER SEASON	0.000137	0.000137	34.150750	0.000000	0.000053	13.28175
NORTHEAST REGION	0.000148	0.000148	37.115000	0.000000	0.000055	13.69650
NORTH CENTRAL REGION	0.000135	0.000135	33.820250	0.000000	0.000054	13.39050
SOUTHERN REGION	0.000114	0.000114	28.380500	0.000000	0.000047	11.68925
WESTERN REGION	0.000140	0.000140	35.119250	0.000000	0.000056	13.97050
HISPANICS	0.000172	0.000172	42.902000	0.000000	0.000065	16.32275
NON-HISPANIC WHITES	0.000131	0.000131	32.669500	0.000000	0.000052	12.99725
NON-HISPANIC BLACKS	0.000123	0.000123	30.852500	0.000000	0.000046	11.55675
NON-HISPANIC OTHERS	0.000162	0.000162	40.500000	0.000000	0.000059	14.71575
NURSING INFANTS (< 1 YEAR OLD)	0.000132	0.000132	33.003500	0.000000	0.000038	9.44950
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000456	0.000456	114.108250	0.000000	0.000112	27.90150
FEMALES (13+ YEARS, PREGNANT)	0.000100	0.000100	24.979250	0.000000	0.000039	9.65825
FEMALES 13+ YEARS, NURSING	0.000110	0.000110	27.428500	0.000000	0.000042	10.45400
CHILDREN (1-6 YEARS OLD)	0.000344	0.000344	85.892500	0.000000	0.000114	28.52175
CHILDREN (7-12 YEARS OLD)	0.000210	0.000210	52.438500	0.000000	0.000078	19.52050
MALES (13-19 YEARS OLD)	0.000133	0.000133	33.351000	0.000000	0.000055	13.84750
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000111	0.000111	27.673750	0.000000	0.000045	11.22575
MALES (20 YEARS AND OLDER)	0.000085	0.000085	21.368750	0.000000	0.000041	10.22975
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000086	0.000086	21.407500	0.000000	0.000036	9.10625

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

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