US EPA ARCHIVE DOCUMENT

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.
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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]<br>7.9[b] | 0.000029<br>7.3 | 0.000057<br>14.3 |
| Milk | 0.000010<br>2.6 | 0.000065<br>16.3 | 0.000031<br>7.7 |
| Citrus | 0.000010<br>2.5 | 0.000017<br>4.2 | 0.000026<br>6.4 |
| Cottonseed | < 0.000001<br>< 0.1 | < 0.000001<br>< 0.1 | < 0.000001<br>< 0.1 |
| TOTAL | 0.000052<br>13.1 | 0.000112<br>27.9 | 0.000114<br>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<br>Caswell #063AB<br>CAS No. 65195-55-3<br>A.I. CODE: 122804<br>CFR No. 180. | 2gen reprod- rat<br>NOEL= 0.1200 mg/kg<br>0.00 ppm<br>LEL= 0.4000 mg/kg<br>0.00 ppm<br>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<br>OPP RfD= 0.000400<br>EPA RfD= 0.000400 | No data gaps.<br>UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen. | HED complete 07/11/86.<br>HED reassess 06/12/87.<br>HED reassess 03/30/89.<br>EPA verified 04/20/89.<br><br>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<br>Caswell #063AB<br>CAS No. 65195-55-3<br>A.I. CODE: 122804<br>CFR No. 180. | 2gen reprod- rat<br>NOEL= 0.1200 mg/kg<br>0.00 ppm<br>LEL= 0.4000 mg/kg<br>0.00 ppm<br>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<br>OPP RfD= 0.000400<br>EPA RfD= 0.000400 | No data gaps.<br>UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen. | HED complete 07/11/86.<br>HED reassess 06/12/87.<br>HED reassess 03/30/89.<br>EPA verified 04/20/89.<br><br>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<br>Caswell #063AB<br>CAS No. 65195-55-3<br>A.I. CODE: 122804<br>CFR No. 180. | 2gen reprod- rat<br>NOEL= 0.1200 mg/kg<br>0.00 ppm<br>LEL= 0.4000 mg/kg<br>0.00 ppm<br>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<br>OPP RfD= 0.000400<br>EPA RfD= 0.000400 | No data gaps.<br>UF of 300 due pup deaths in critical study & maternal developmental toxicity in teratology studies. Mouse teratogen. | HED complete 07/11/86.<br>HED reassess 06/12/87.<br>HED reassess 03/30/89.<br>EPA verified 04/20/89.<br><br>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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