CHEMISTRY BRANCH I - TOLERANCE SUPPORT, HED
DATA REVIEW QUICK FORM

MEMORANDUM

Date: FEB 22 1991

SUBJECT: Petition Review for Establishment of Tolerance(s).
         Evaluation of Analytical Method(s)
         and Residue Data.

FROM: GARY F. OTAKIE, Chemist
      Tolerance Petition Section II
      CHEMISTRY BRANCH I - TOLERANCE SUPPORT
      Hazard Evaluation Division, H7509C

THRU: ELIZABETH T. HAEBERER, SECTION HEAD
       Tolerance Petition Section II
       CHEMISTRY BRANCH I - TOLERANCE SUPPORT
       Hazard Evaluation Division, H7509C

TO: HOYT L. JAMERSON
    Registration Division, H7505C
    and
    Toxicology Branch - HFA SUPPORT
    Hazard Evaluation Division, H7509C

1. Petition No(s):    1E3926
2. DEB No(s):        7340
3. MRID No(s):       416889-00 AND 41689-01
4. Pesticide(s):     METALAXYL
5. Tolerance Proposal (RACs & Levels):    GINSENG AT 3.0 PPM

6. Petitioner:      IR-4 AND THE AGR. EXP. STATION OF
                    NEW JERSEY ON BEHALF OF AGR. EXP. STATIONS IN
                    NORTH CAROLINA AND WISCONSIN

BEST COPY AVAILABLE
7. Tolerance Expression: **METALAXYL AND ITS METABOLITES**

   **PER 40 CFR 180.408(a)**

8. Established Pesticide Tolerances: **40 CFR 180.408(a) AND (b)**

   **VARIABLES AND COMMODITIES OF ANIMAL ORIGIN FROM**
   **0.1 PPM ON BEETS, BROCCOLI, GRAIN CROPS, PINEAPPLES, ETC.**
   **TO 20.0 PPM ON PEANUT HAY, 0.05 PPM EGGS, 0.5 ppm**
   **MILK, 0.05 AND 0.4 PPM IN MEAT AND FAT RESPECTIVELY**
   **OF CATTLE GOATS, NAGS, HORSES, SHEEP AND POULTRY**


   **10 PPM IN WHEAT MILLING FRACTIONS TO 7.0 PPM**
   **IN CITRUS OIL**

10. Established Feed Additive Tolerances: **21 CFR 561.973**

    **0.4 PPM IN APPLE POMACE (WET) TO 16.0 PPM**
    **IN TOMATO POMACE (DRY)**

11. Is Pesticide a Registration Standard Chemical? **(YES/NO)**

    If yes, date Guidance Document issued:

12. Letter(s) of Authorization (if applicable): **CIBA-GEIGY TO**

    **EPA DATED OCTOBER 25, 1978 FROM HALEN S. STUMPF**

13. Formulation(s): **Ridomil**® **3E (EPA REG. NO. 100-502) WITH**

    **2 LBS A.I./GAL OR 25.1% W/W A.I.; AND Ridoromil**® **5E**

    **(EPA REG. NO. 100-638), GRANULAR, 57% W/W A.I.**

14. Inerts Status: **UNDER RD**

15. Manufacturing Process: **CONFIDENTIAL APPENDIX B TO FRS PP**

    **AND IN PP# 1F2500, 3/4/82. P.V. Enrico:**

    **DEP DOES NOT FORSEE ANY RESIDUE PROBLEMS ON FRUITING VEGETABLES**

    **FROM IMPURITIES IN THE TECHNICAL AT THE LEVELS GIVEN**

    **(SEE GF3387, 9/26/86 MEMO OF F.D. GRIFFITH).**

---

**BEST COPY AVAILABLE**
16. Proposed Use(s): As a systemic fungicide to control disease caused by members of Oomycete class of fungi. Apply metalaxyl at 0.75 lb a.i./a to soil surface in spring before plants begin growing. Make additional applications of metalaxyl at monthly intervals at 0.5 lb a.i./a, up to four supplemental applications with last application of 0.75 lb a.i./a may be made (i.e. total max. of 5 applications and 3.685 a.i./a; 9 day PHI.

17. Plant Metabolism Data on: Potatoes, Grapes and Lettuce

18. Plant Residues Comprised of: Metalaxyl, and from hydrolysis of methyl ester bond, ring methyl oxidation and hydroxylation to form CGA-62826, CGA-110255 and CGA-94684 (see FRSPR PP 3-12).

19. Plant Metabolism Data Translatable Here: Potatoes, Grapes and Lettuce

20. Nature of Plant Metabolism on the Subject RAC(s) of This Petition is not adequately defined. The residue of concern is: Metalaxyl and metabolites containing 2,6-dimethylaniline moiety and N-(3-hydroxy methyl-6-methyl)-N-(methoxyacetetyl) alanine methyl ester, each expressed as metalaxyl equivalents.

BEST COPY AVAILABLE
21. Animal Metabolism Data on: RATS, GOATS AND COWS, FIRST REQUIRED NEW RUMINANT AND POULTRY METABOLISM STUDIES FOLLOWING DEB GUIDELINES, WHICH ARE CURRENTLY UNDER EPA REVIEW.

22. Animal Residues Comprised of: CURRENTLY SAME AS PLANTS. REQUIRED ANIMAL METABOLISM STUDIES IN ITEM 21 ABOVE, NOW BEING REVIEWED UNDER FIRST.

23. Animal Metabolism Data Applicable Here: GINSENG NOT AN ANIMAL FEED ITEM.

24. Nature of Animal Metabolism Data is inadequately defined. The Residue of Concern is: N/A - NO ANIMAL FEED ITEMS FROM THE PROPOSED USE ON GINSENG.

25. Analytical Method(s) (Give Reference and/or Brief Description)
   CIBA-GEIGY METHOD AG-395 (SEE PP\h 8F3617/8H554 NOVEMBER 28, 1988 MEMO OF F.D. GRIFFITH) METALAXYL AND METABOLITES CONTAINING THE 2,6-DIMETHYLANILINE MOIETY ('TOTAL' RESIDUES) ARE DETERMINED. SAMPLES EXTRACTED BY REFLUXING WITH 80% (V/V) METHANOL/WATER FOR TWO HOURS; SAMPLE EVAPORATED TO DRYNESS AND WATER ADDED, REFLUXED FOR 15 MINUTES AFTER ADDITION OF METHANESULFONIC ACID; EXTRACT BASIFIED AND 2,6-DIMETHYLANILINE FORMED IS STEAM DISTILLED AND CLEANED UP WITH SILICA SEPPAK; TRIFLUOROACETIC ACID IS ADDED TO ELUATE TO FORM SALT (DMA-TFA). CAPILLARY GAS CHROMATOGRAPHY USING NITROGEN/PHOSPHORUS DETECTOR IN NITROGEN MODE.
26. Has there been a Method Trial? (Yes No) **AG-395**
   If yes, provide details: FOR RESULTS OF MTO SEE PP# 3F294B, JULY 9, 1984 MEMO OF P. JUNGB. METHOD SUBMITTED TO FDA AS ENFORCEMENT METHOD.
   If no, is a Method Trial needed?

27. Residues Determined by Method(s): METALAXYL AND METABOLITES CONTAINING THE 2,6-DIMETHYLAMINILINE MOIETY

28. Method Validation (RACs/"spike chemical"/fortification level(s)/recovery range/average recovery):
   FRESH GINSENG FORTIFIED WITH METALAXYL FROM 0.05 TO 5.0 PPM WITH RECOVERIES FROM 71 TO 140%, N=14, MEAN 103.3%, SD = 23.7%; DRIED GINSENG WITH METALAXYL FROM 0.05 TO 5.0 PPM WITH RECOVERIES FROM 58 TO 104%, N=13, MEAN = 82.8%, SD = 14.6%

29. Method Validation (limit of detection and/or sensitivity in ppm):
   Parent: LIMIT OF DETECTION = 0.05 PPM
   Metabolite(s) (specify): PARENT AND METABOLITES DETERMINED AS ONE MOIETY.

30. Method Validation (state crops and control values reported):
   FRESH AND DRY GINSENG CONTROLS RANGED FROM 0.06 TO 0.29 PPM (N=25)

31. Adequate Analytical Method(s) are not Available for Enforcement Purposes.
   These Method(s) are located: PAM II METHOD I IS AG-348 (11/84), METHOD II IS AG-349; PAM I LUKE METHOD FOR METALAXYL, PER SE.
32. **PAM I Multiresidue Methods Data** are available for parent pesticide tested via Protocols [I II III IV] (circle, as applicable). Additional multiresidue test information for parent compound that is needed: **NONE**

33. **PAM I Multiresidue Methods Data** are available for metabolite(s) CGA-6286 and CGA-37339 tested via Protocols [I II III IV] (circle, as applicable). Additional multiresidue test information for metabolite(s) that is needed: **CGA-94684; N/A FOR MINOR USE PETITIONS**

34. **Residue Data (RAC(s) and Processed Commodities)**

<p>| Field Trials with Results from Both the 2E EC and 5G [Granular] Formulations at the 1X Rate and 5G at 2X in Wisconsin and North Carolina with Residue Results for Both Fresh and Dry Ginseng Roots at PHIs from 7 to 9 Days; Results from 1X: |</p>
<table>
<thead>
<tr>
<th>Substrate</th>
<th>Formulation</th>
<th>Range (ppm)</th>
<th>Average (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh Roots</td>
<td>2E</td>
<td>0.30 - 1.3</td>
<td>0.61 +/- 0.31 (N=10)</td>
</tr>
<tr>
<td></td>
<td>5G</td>
<td>0.18 - 2.5</td>
<td>0.95 +/- 0.78 (N=10)</td>
</tr>
<tr>
<td>Dry Roots</td>
<td>2E</td>
<td>0.31 - 1.8</td>
<td>1.0 +/- 0.59 (N=9)</td>
</tr>
<tr>
<td></td>
<td>5G</td>
<td>0.10 - 2.1</td>
<td>0.88 +/- 0.63 (N=10)</td>
</tr>
</tbody>
</table>

Results from 2X Rate

| Fresh Roots | 5G | 0.68 - 6.7 |
| Dry Roots | 5G | 0.62 - 3.2 |

**BEST COPY AVAILABLE**
35. Frozen Storage Stability Data are not Available. If yes, give RACs/fortification levels/length of storage/recovery range/conditions of storage (°C): See FRSTR PP 20-2. Data on Potatoes and Tobacco: Metalexyl residues stable for 18 months under frozen conditions. In this study residue samples were held in frozen storage from 5 to 17 months at -20.6 to -17.8 °C.

36. Regional Registration is not involved. If yes, list States in which use is sought:

37. Geographic Representation is not adequate. If no, list RAC(s) and States from which additional data are needed: Per 2/21/77 Telephone conversation, Dave Brassard, JF Bead indicated that Bead had 5/6/86 memo on file, from Dr. Jennifer Park U. of Wisconsin that 90% of U.S. Ginseng production was in Wisconsin.

38. Residues will not exceed proposed tolerance(s) on (commodities) Ginseng

but may exceed proposed tolerance(s) on (commodities) N/A

39. Livestock Feeding Studies on (species):

Dairy cattle, goats and hens

BEST COPY AVAILABLE
40. Animal Feeding Levels: Ruminants dosed at 1.5 to 25 ppm metalaaryl had residues ≤ 0.01 ppm in milk and ≤ 0.05 ppm in fat and meat, 0.23 ppm (max) in liver, and 0.83 ppm (max) in kidney. Poultry dosed at 1.5 to 5.0 ppm metalaaryl had residues ≤ 0.25 ppm in eggs, fat, liver, meat, and skin.

41. Animal Residue Ingestion Levels from Proposed RAC Tolerance(s): N/A

Levels (proposed tolerance level x percent in diet): _____ ppm in beef cattle; _____ ppm in dairy cattle/goats; _____ ppm in hogs; _____ ppm in horses; _____ ppm in sheep; _____ ppm in poultry.

42. Livestock Tolerances are Adequate in (species): N/A for this petition, no animal feed items involved, but not adequate in ____________________________

43. Livestock Tolerances Need to be Established: Yes/No. If yes, species/levels: N/A for this petition

44. Other Comments: N/A

45. Other Considerations: N/A

46. Additional Information Needed: See item 47.

BEST COPY AVAILABLE
Additional Data Needed: **A REVISED SECTION B IS NEEDED**

**THE SECTION B SUBMITTED IS INCONSISTENT WITH THE PROPOSED USE DIRECTIONS ON PAGE 12 OF THE REPORT, WHICH RECOMMENDS THAT THE FIRST APPLICATION BE MADE WITH EITHER THE 2E OR 2G FORMULATION WHILE THE REMAINING 4 SUPPLEMENTAL APPLICATIONS BE MADE WITH ONLY THE 3G FORMULATION, TO MINIMIZE THE POSSIBILITY OF RESISTANCE.**

**ALSO, IF TWO FORMULATIONS ARE PROPOSED THE LABEL MUST INCLUDE APPROPRIATE INSTRUCTIONS TO ENSURE THAT THE COMBINED APPLICATION OF THE TWO FORMULATIONS DOES NOT EXCEED THE APPROVED MAXIMUM APPLICATION RATE.**

**RECOMMENDATIONS: UPON RECEIPT OF A REVISED SECTION B, AS DESCRIBED ABOVE, CBTS CAN RECOMMEND IN FAVOR OF THE PROPOSED TOLERANCE OF 3.0 PPM FOR RESIDUES OF METALAXYL ON GINSENG.**

Other Comments Under Recommendations: **SINCE THE 2E FORMULATION IS RECOMMENDED AS AN ALTERNATIVE TO THE 2G FORMULATION FOR A SINGLE FIRST APPLICATION ONLY, FOR SIMPLICITY THE PETITIONER SHOULD CONSIDER LIMITING THE PROPOSED USE TO THE 2G FORMULATION ONLY.**

**Compatibility with Codex Tolerances? (Explain):**

**NO COMPLATIBILITY PROBLEMS EXIST SINCE THERE ARE NO MEXICAN, CANADIAN OR CODEX TOLERANCES FOR METALAXYL ON GINSENG.**

**ATTACHMENT(S): (1) International Residue Limits Status Sheet**

(2)

**CC: RE, Circ, Reviewer, PPE 1E3926, PIAB/FOD (Furrow), R. Schmitt, FDA, ORES/SALD (Kapila), E. Hauser, Approved: ET/EB/JR/2001, R. Oser, R. Loar. 3/21/91.**
# INTERNATIONAL RESIDUE LIMIT STATUS

**CHEMICAL:** *METALAXYL* (RIDOMIL)  
**CODEX NO.:** 138  
**CODEX STATUS:**  
[ ] No Codex Proposal  
[ ] Step 6 or above (or Ginseng)  

**Residue (if Step 8):**  
*METALAXYL* (or *Ginseng*)  

**Crop(s) Limit (mg/kg):**  

**PROPOSED U.S. TOLERANCES:**  
**Petition No.:** 1E3926  
**RCB Reviewer:** G. OTAKI  
**Residue:** PEP 40 CPF 180.408  
**Residue:** METALAXYL AND ITS METABOLITES CONTAINING THE 2,6-DIMETHYLAMINO MOIETY AND N-(2-HYDROXYMETHYL-6-METHYL)-N-(METHYLACETO) ALANINE METHYL ESTER  
**Crop(s) Limit (mg/kg):**  

**GINSENG**  
3.0 ppm  

**CANADIAN LIMITS:**  
[ ] No Canadian limit (or *Ginseng*)  

**Residue:**  

**Crop(s) Limit (mg/kg):**  

**MEXICAN LIMITS:**  
[ ] No Mexican limit  

**Residue:**  

**Crop(s) Limit (mg/kg):**  

## NOTES: