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

MAY 7 1991

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#4F3121 - Pendimethalin (Prowl®) on/in Grapes.
Review of the August 10, 1990 Amendment.
(MRID Nos. 415949-01 and -02) [DEB Nos. 7045 and 7046]
(HED Project No. 0-1933)

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TO: Robert J. Taylor, PM 25
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and

Toxicology Branch II - Herbicide, Fungicide, and
Antimicrobial Support
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THRU: Richard D. Schmitt, Ph.D., Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

American Cyanamid Company has submitted this amendment consisting of a cover letter, a new Section B (new directions for use of Prowl® on grapes), and a Supplementary Section D (new crop field trial data, storage stability, and second lab validation data) in response to deficiencies outlined in our review of August 20, 1984 by E.T. Haeberer. In the interim, the Pendimethalin Registration Standard issued on May 10, 1984 and the Pendimethalin Registration Standard Update, dated March 19, 1990, identified these and additional residue chemistry deficiencies. In the cover letter, the petitioner requests reactivation of the petition, contending that all major toxicology deficiencies are resolved. The deficiencies identified in the Registration Standard are repeated below in the body of this review in the order they appeared in the Pendimethalin Registration Standard, followed by the petitioner's response, and then CBTS's comments. Our conclusions and recommendations follow.

EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

- Plant metabolism studies required.
- Poultry metabolism studies are necessary.
- Ruminant metabolism study characterization of residues is required.
- Confirmatory analytical method needed.
- Multiresidue method data are needed.
- Livestock feeding studies may be required.
- Grape processing study is necessary.
- Additional field trial residue data needed.
- PMV on method M-1623, used for residue data, is needed.

CONCLUSIONS

1. CBTS Conclusion on **Directions for Use**

The petitioner has proposed an adequate set of directions for use of Prowl® Herbicide (EPA Registration No. 241-243) in vineyards to control various grasses and broadleaf weeds.

2. CBTS Conclusion on **Nature of the Residue - Plants**

CBTS reiterates that the nature of the pendimethalin residue in plants is not adequately understood. Additional plant metabolism studies are required in which pendimethalin, radiolabeled in the phenyl ring, is applied to plants at rates equal to, or greater than, the maximum application rate. Higher application rates are preferred to increase the level of radioactive material available for analysis and identification, provided there is no phytotoxicity. One plant metabolism study should be conducted on sweet corn with analysis of vegetative parts and grain from 1) plants treated preemergence and 2) plants treated postemergence. A second plant metabolism study is needed on a plant in which the edible portion grows in the soil. The deficiency remains unsolved and continues outstanding.

3. CBTS Conclusions on **Nature of the Residue - Livestock**

a. CBTS reiterates that poultry metabolism studies are required using hens dosed with ring-labeled ^{14}C-pendimethalin for at least 3 days at a level > 1 part per million (ppm), preferably 10 ppm, sufficient to have adequate radiolabeled material available for

identification. The laying hens are to be sacrificed within 24 hours of the final dose. The distribution and characterization of at least 90+ percent of the radiolabeled residue need to be determined in eggs (white and yolk), muscle, skin, and liver. This part of the deficiency is not resolved and continues outstanding.

b. The petitioner has reported the results of a lactating caprine ^{13}C-and ^{14}C-ring-labeled pendimethalin metabolism study. Measurable residues were found only in caprine liver ranging from 0.08 to 0.17 ppm (n = 3) from a 6.5 ppm dose. Trace amounts were detected in kidney (about 0.02 ppm) and in milk (< 0.01 ppm). Fractionation of various liver extracts revealed numerous free, unbound ^{14}C-components in the 0.005 to 0.025 ppm range that were not characterized. CBTS concludes that the petitioner has not adequately identified the nature of the residue in ruminants. CBTS suggests that the petitioner repeat the HPLC identification steps for all fractions above 0.005 ppm, characterizing major peaks and using detectors that can elucidate organic structures such as, but not limited to MS, FTIR, FTUV, and NMR. The petitioner needs to confirm the presence of or absence of all metabolites identified in the rat metabolism study. Complete characterization of caprine radiolabeled residues is essential for CB to ascertain the need for a ruminant feeding study. If caprine metabolism differs significantly from that in rats, then a ^{14}C-ring- labeled pendimethalin porcine metabolism study may also be necessary. The deficiency is not resolved and continues outstanding.

4. CBTS Conclusions on **Residue Analytical Methods**

a. CBTS reiterates that a validated confirmatory method (Mass Spec is suggested) for residues of pendimethalin, per se, and its metabolites (CL-202,347) is necessary. This part of the deficiency is not resolved and continues outstanding.

b. CBTS reiterates that additional multiresidue method (MRM) validation data are necessary for the Food and Drug Administration's (FDA) MRM's A through E. Chromatographic data are required for pendimethalin and its alcohol metabolite for protocol C. Representative samples of plant and animal tissues need to be analyzed by appropriate MRM protocols B, D, and E following the FDA decision tree for MRM testing. The protocols are found in FDA's PAM-I, Appendix II. This part of the deficiency is not resolved and continues outstanding.

c. CBTS reiterates that if radiolabeled validation of existing analytical methods for plants and animals

indicated that a major portion of the total radioactive residue is not recovered and identified by these methods, then radiolabeled validation of any new proposed residue analytical method may be required. This part of the deficiency is not resolved and continues outstanding.

d. The petitioner has presented an improved method M-1623 that has been validated and is suitable to gather pendimethalin and its alcohol crop field trial residue data. However, a PMV is necessary for the procedure to be an enforcement method, and the petitioner needs to submit clean, nonconfidential copies of the method before a PMV is started.

e. The petitioner has supplied adequate second laboratory validation data for the GC method M-1623.

5. CBTS Conclusion on **Storage Stability Data**

The petitioner has presented storage stability data for wheat straw, soybeans and soybean plants, onion bulbs, potatoes, almonds and almond hulls, and for grapes and raisins to show that residues of pendimethalin and its alcohol metabolite are stable in frozen storage for at least one year. There are adequate storage stability data to support the crop field trial residue data in this petition. The deficiency is resolved.

6. CBTS Conclusion on **Magnitude of the Residue - Crop Field Trials**

After careful consideration, CB concludes the petitioner has not presented sufficient crop field trial residue data to support the proposed pendimethalin tolerance on grapes even with the results from the new field trials. CB reiterates that additional magnitude of the residue crop field trial data are necessary from all grape-growing areas. This means additional trials are needed from different areas in California, plus trials from Washington, New York, Michigan, and Pennsylvania. The petitioner needs to ensure adequate grape varietal data are included in these trials. These data should reflect the proposed use rate (and PHI). The deficiency is not resolved and continues outstanding.

7. CBTS Conclusion on **Magnitude of the Residue - Meat/ Milk/Poultry/Eggs**

a. CBTS reiterates that a conventional ruminant feeding study may be necessary, depending on the results of the ruminant metabolism study, in which lactating ruminants are dosed at 0.1, 0.3, and 1.0 ppm pendimethalin, *per se*, $\geq$ three animals per dose group in the total diet. The animals should be kept on the treated feed for 4 weeks. However, if residues have not plateaued in milk

by the end of 4 weeks, then the feeding period should continue until a plateau is reached. Milk should be collected twice daily and residues determined therein. Animals must be sacrificed within 24 hours of the final dose and residues determined in muscle, liver, kidney, and fat. The deficiency is not resolved and continues outstanding.

b. CBTS reiterates that a conventional poultry feeding study may be necessary, depending on the results of the poultry metabolism study, in which laying hens are dosed at 0.1, 0.3, and 1.0 ppm pendimethalin, per se, in the total diet, $\geq$ 10 hens per dose group. The laying hens should be kept on the treated feed for 4 weeks. However, if residues have not plateaued in eggs by the end of 4 weeks, then the feeding period should continue until a plateau is reached. Eggs should be collected at least daily and residues determined therein. The laying hens need to be sacrificed within 24 hours of the final dose and residues determined in muscle, liver, skin, and fat. The deficiency is not resolved and continues outstanding.

c. CBTS reiterates that the nature of the pendimethalin residues in livestock is not adequately understood. If the feeding studies are necessary, at this time, CBTS reiterates that we will request residue data for residues of pendimethalin, per se, and its metabolite CL-202,347 in the conventional feeding studies. CBTS points out that residue data may need to be presented for any additional metabolite(s) of toxicological concern if the requested metabolism studies so identify.

d. CBTS reiterates that the present ruminant metabolism study indicates that residues of pendimethalin may occur in meat and meat byproducts. The petitioner should be advised that tolerances need to be proposed for these animal commodities if the requested pendimethalin metabolism and feeding studies indicate the transfer of residues. The deficiency is not resolved and continues outstanding.

8. **CBTS Conclusion on Magnitude of the Residue - Processed Food/Feed**

Upon further consideration, CBTS now concludes that the petitioner needs to conduct a new pendimethalin grape-processing study using grapes bearing detectable residues, or, if no residues are detected, then using grapes treated at the highest practical application rate. The grapes are to be processed by standard commercial operations into raisins, wet and dry pomace, raisin waste, and grape juice. Pendimethalin and its metabolite residue data are needed for each of these processed grape commodities. If pendimethalin

residues concentrate, then appropriate food and/or feed additive tolerances need to be proposed.

RECOMMENDATION

CBTS cannot, at this time, recommend for the requested pendimethalin tolerance of 0.1 ppm on grapes for the reasons cited in our Executive Summary of Deficiencies and detailed in our Conclusions 2, 3, 4, 6, 7, and 8 above.

For further consideration of this petition, the petitioner needs to be advised to resolve these deficiencies.

DETAILED CONSIDERATIONS

DIRECTIONS FOR USE

Petitioner's Response

The petitioner has presented a revised label for use of Prowl® Herbicide (EPA Registration No. 241-243) containing 4 lb active ingredient/gallon, 42.3 percent of technical pendimethalin to control various grasses (e.g., barnyard grass, crabgrass, foxtail, Johnsongrass) and broadleaf weeds (e.g., carpetweed, lambsquarters, pigweed) in vineyards.

CBTS Comments

The petitioner proposes applying Prowl® Herbicide in vineyards by ground equipment in at least 20 gallons of water per acre for preemergence control of annual grasses and broadleaf weeds. The petitioner cautions that emerged weeds are not controlled. The rate of Prowl® application ranges from 2 quarts (2 lbs ai)/acre for short-term control to 4 quarts (4 lbs ai)/acre for long-term control. Prowl® is to be applied as a spray (broadcast) directly to the ground beneath the grape vines.

The petitioner cautions that Prowl® is not to be used on peat or muck soils. Prowl® should not be applied over tops of grape vines or applied to newly transplanted vines until the ground has settled and the grapevines are still dormant.

The PHI is 180 days.

Do not feed forage or graze livestock in treated fields.

Prowl® may be tank mixed with simazine, oxyfluorfen, or norflurazon. These three herbicides have established tolerances on grapes.

The petitioner has proposed an adequate set of directions for use of Prowl® Herbicide in vineyards.

NATURE OF THE RESIDUE - PLANTS

Deficiencies

The following additional data are required:

1. Data involving the reasonably complete characterization of the extractable and unextractable radioactive residues found in plant tissues as the result of the application of radiolabeled pendimethalin in a manner simulating a treatment regime registered for use. Representative crops (potatoes, soybeans, corn, etc.) for which pendimethalin formations are registered should be used.

2. Data depicting the distribution and metabolism of [^{14}C] pendimethalin in or on mature plant parts from three dissimilar food crops (e.g., a root crop, oilseed crop, and a leafy vegetable). If metabolism is not similar in the three crops, additional studies using other crops may be required. A completely characterized test substance representative of technical pendimethalin (including impurities, if appropriate) used in commercial formulations must be applied at levels sufficiently high to permit characterization of ^{14}C-residues.

3. The identities and quantities of extractable and nonextractable residues must be determined. Confirmation of the identities of residues using a suitable confirmatory method such as MS or HPLC is also required. In addition, representative samples from the tests must be analyzed using a currently accepted or proposed enforcement analytical method in order to ascertain that this method will determine all possible metabolites of concern.

Petitioner's Response

The petitioner did not respond.

CBTS Comments

After a number of consultations with the petitioner, CBTS reiterates that the registrant should be informed that the plant metabolism data base for pendimethalin is not adequate. Although the available studies indicate that low levels of radioactivity are taken up from the soil into aerial parts of plants, these studies were conducted with pendimethalin radiolabeled in side chains as opposed to in the phenyl ring. In addition, most of the studies were conducted using application rates lower than the maximum permitted on product labels.

Additional plant metabolism studies are required in which pendimethalin, radiolabeled in the phenyl ring, is applied to plants at rates equal to at least the maximum rates on product labels. Provided significant phytotoxicity does not occur, even higher application rates (2X-5X) are preferred to increase the

level of radioactivity available for analysis and identification. One study should be conducted on sweet corn with analysis of vegetative parts and grain from (1) plants treated preemergence and (2) plants treated postemergence. A second plant metabolism study is needed on a plant in which the edible portion grows in the soil (e.g., potatoes or peanuts). The petitioner's report should include the percentage of the total radioactive residue (TRR) for each plant part and the report should include the ppm value for the TRR as well as each identified component of the TRR. The petitioner is expected to identify at least 90+ percent of the TRR. The petitioner is to confirm identities of all metabolites by a second technique.

Chemistry Branch I recently concluded that deficiencies in the knowledge of plant metabolism were not applicable for use on sugarcane (PP#2F2765, R.Cook, 11/26/90). CBTS emphasizes that this decision applies only to sugarcane and is based on the low total activity (< 0.01 ppm) and long preharvest interval observed in that crop.

CBTS reiterates that the nature of the residue in plants is not adequately understood. This deficiency continues unresolved and remains outstanding.

NATURE OF THE RESIDUE - LIVESTOCK

Deficiencies

The following data are required:

1. Metabolism studies utilizing ruminants. Animals must be dosed with ring-labeled [^{14}C]pendimethalin for 3 days at a level (> 1.5 ppm) sufficient to make residue identification possible. Animals must be sacrificed within 24 hours of the final dose. The distribution and characterization of residues must be determined in milk, muscle, fat, kidney, and liver. If ruminant metabolism is found to differ significantly from that in rats, then swine metabolism data will also be required.

2. Metabolism studies utilizing poultry. Hens must be dosed with ring-labeled [^{14}C]pendimethalin for 3 days at a level (> 1 ppm) sufficient to effect residue identification. Birds must be sacrificed within 24 hours of the final dose. Residues must be characterized and quantified in eggs, muscle, fat, kidney, skin, and liver.

3. Metabolism studies utilizing ruminants and poultry. Animals must be dosed orally with ring-labeled 14C-pendimethalin for a minimum of 3 days at a level sufficient to make residue identification and quantification possible. Eggs and milk must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. The distribution and identity of residues must be

determined in eggs, milk, muscle, fat, kidney (except poultry), liver, and poultry skin. Representative samples from both of the studies must be analyzed using a suitable confirmatory method such as MS or HPLC. In addition, representative samples from these studies must be analyzed using a currently accepted or proposed enforcement analytical method in order to ascertain that the method is capable of adequately recovering and identifying all residues of concern. If the ruminant and/or poultry metabolism differs significantly from the rat data, then swine metabolism data will also be required.

Petitioner's Response

The petitioner did not respond.

CBTS Comments

CBTS reiterates that the nature of the pendimethalin residue in poultry is not adequately understood. CBTS reiterates that a poultry metabolism study using ring-labeled ^{14}C-pendimethalin is necessary. The petitioner should identify at least 90 percent of the radiolabeled material in any new poultry metabolism study. A petitioner's report should include the percentage of the total radioactive residue (TRR) for each poultry part and the ppm value for the total TRR as well as each identified component of the TRR. Current Branch policy, as outlined and explained in Attachment 3 to the "Overview of Residue Chemistry Guidelines," clearly states that CBTS now requires a poultry metabolism study whenever a pesticide is to be applied to a crop having a poultry feed commodity listed in Table II of the Residue Chemistry Guidelines. For grapes the poultry feed items listed in Table II are wet nd dry pomace. Grape pomace can be 3 to 5 percent of broilers and laying hens diets. Thus, a poultry metabolism study is necessary. CBTS reiterates that the above deficiencies remain unresolved and continues outstanding.

In a related copending petition (PP#3F2788), the petitioner presented the results of a caprine metabolism study using ^{13}C- and ^{14}C-ring-labeled pendimethalin. Measurable or detectable residues were found only in caprine liver ranging from 0.08 to 0.17 ppm from a 6.5 ppm dose. Trace amounts were also found in caprine kidney (about 0.02 ppm) and in caprine milk (< 0.01 ppm). Fractionating of various liver extracts revealed numerous free, unbound ^{14}C-components in the 0.005 to 0.025 ppm range which were not characterized. CB suggests the petitioner repeat the HPLC identification step for all fractions containing 0.005 ppm and above, characterizing the major peaks using detectors that can elucidate organic structure such as, but not limited to MS, FTIR, FTUV, NMR, etc. This information is essential for CB to ascertain the need for a ruminant feeding study. The petitioner needs to confirm the presence of or absence of all metabolites identified in the rat metabolism study. If the ruminant metabolism study differs significantly from the rat metabolism

study, then a ^{14}C-ring-labeled pendimethalin porcine metabolism study is necessary.

CBTS reiterates the above deficiencies. They remain unresolved and continue outstanding.

RESIDUE ANALYTICAL METHOD

Deficiencies

The following additional method is required:

1. A validated confirmatory method (MS is recommended) for residues of pendimethalin, per se, and its metabolite (CL-202,347).

2. Representative samples of plant and animal tissues containing residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite must be analyzed by multiresidue protocols C and E and PAM Vol. I, Appendix II.

3. If radiolabeled validation of existing analytical methodology for plants and animals (refer to "Qualitative Nature of the Residue" and "Qualitative Nature of the Residue in Animals" for additional details) indicates a major portion of the total radioactive residue is not recovered by these methods, radiolabeled validation of new proposed analytical methodology will be required.

Petitioner's Response - (see MRID No. 415949-02)

The petitioner did not respond to these deficiencies. However, the petitioner has presented second lab validation data for the method used to gather pendimethalin residue data on grapes.

CBTS Comments

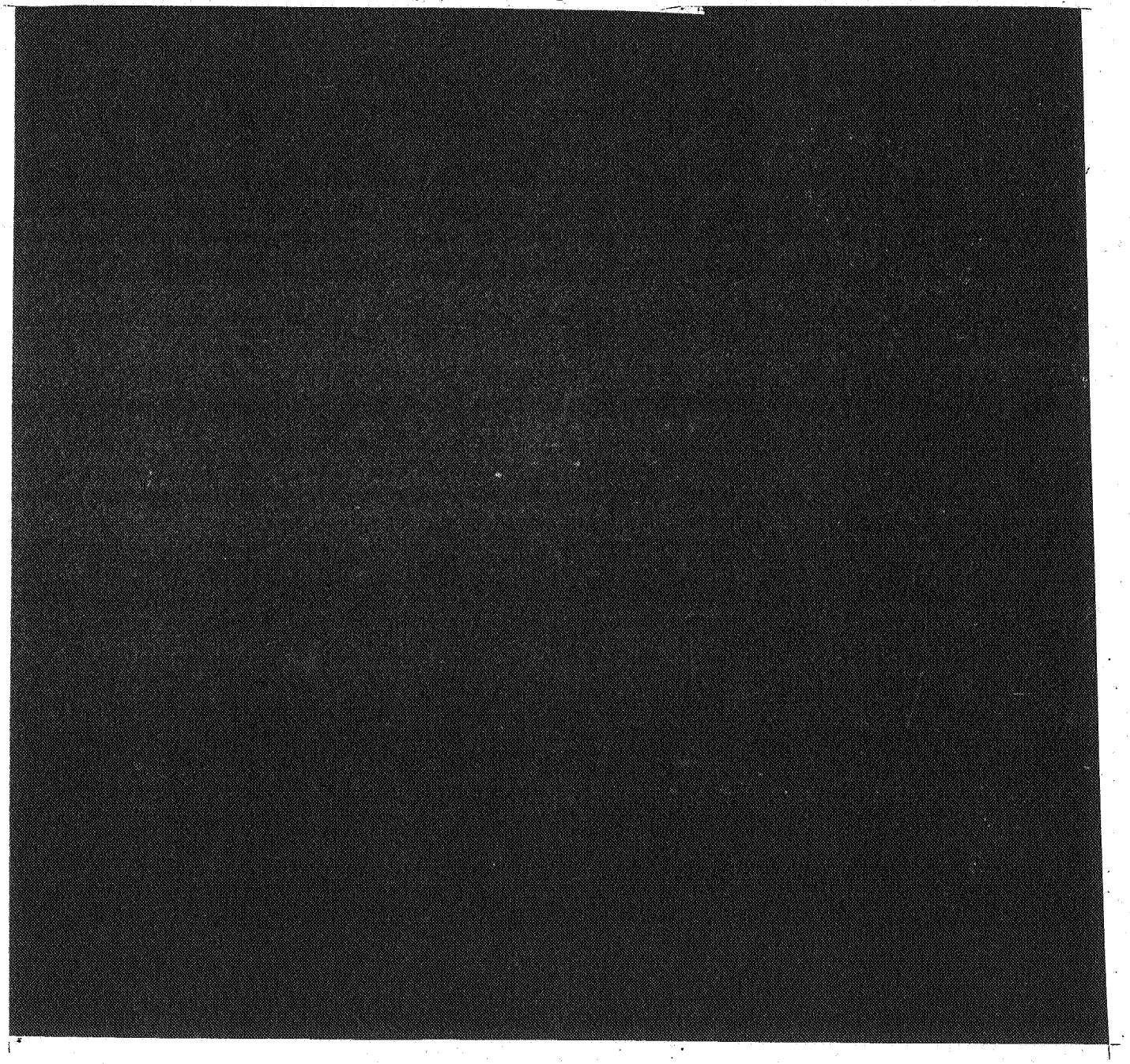
CBTS reiterates the above deficiencies. They continue unresolved and remain outstanding.

After reconsideration on the requirements for MRM testing, CB now concludes that additional MRM validation data are necessary for FDA MRM's A thru E. Chromatographic data are required for pendimethalin and its alcohol metabolite for Protocol C. Representative samples of plant and animal tissues need to be analyzed by appropriate MRM Protocols B, D, and E following FDA's decision tree for MRM testing. These protocols are found in FDA's PAM-I, Appendix II. This part of the deficiency is not resolved and continues outstanding.

The residue analytical method used to gather pendimethalin residue data on grapes is titled "Prowl® Herbicide, Pendimethalin

(CL-92,553): Determination of CL-92,553 and CL-202,347 (Metabolite) Residues on Grapes" by R. Tondreau dated May 20, 1986 and coded M-1623.

On reviewing method M-1623 and comparing it to the four enforcement methods in PAM-II, we note M-1623 is a significantly different method. Method M-1623 warrants a new petition method validation (PMV). However, the method is stamped CONFIDENTIAL and thus, CB defers initiating a new PMV request at this time. When the petitioner submits the additional pendimethalin on grapes crop field trial residue data and the results of the grape processing study, then the petitioner should submit a clean, non-confidential copy of M-1623 and a clean copy of the second lab validation data. CB considers method M-1623 to be an improved method over existing enforcement procedures.



QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED

QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED

[redacted] Adequate chromatographic supporting data have been presented.

The petitioner has submitted new method validation data. [redacted] Adequate validation data have been presented to show method M-1623 is suitable to gather pendimethalin and its alcohol metabolite grape crop field trial residue data.

The petitioner presented the second laboratory validation data for method M-1623 in a report titled "CL-92,553 (Pendimethalin): Independent Laboratory Validation of GC Method M-1623 for Determination of CL-92,553 and CL-202,347 Residues in Grapes." The second lab validation was done by Analytical Bio-Chemistry (ABC) Laboratory of Columbia, Missouri. The report was issued by ABC on July 6, 1990. ABC ran the GC method M-1623 as written without contact with American Cyanamid's chemists. ABC encountered no unusual problems and made only a minor modification in concentration in the working GC standards. CB considers this is a normal operation for a laboratory.

[redacted]

The petitioner has supplied adequate second laboratory validation data for the GC method M-1623.

STORAGE STABILITY DATA

Deficiencies

The following additional data are required:

1. Data reflecting the stability of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite (CL-202,347) in or on representative plants [such as root and tuber vegetables, legume vegetables, cereal grains, and miscellaneous crops

(e.g., cottonseed, peanuts, and sunflower seed)] and animal samples stored at freezing temperatures for time intervals approximating those of the treated samples used to determine the magnitude of the residue.

2. The sample storage conditions and intervals must be supplied for all required and previously submitted residue data for plant commodities (raw and processed foods and feeds). Storage stability data in support of previously submitted residue data are required for only those samples deemed to be useful for tolerance assessment. The purity of the reference standards used for fortification of samples and a complete description of the analytical methods (including extraction procedures) and method validation data, used to supply the data in MRID No. 405351-01, must be provided. For additional guidance on conducting storage stability studies, the registrant is referred to an August 1987 Position Document on the Effects of Storage Validity of Pesticide Residue Data available from NTIS under Order No. PB 88112362/AS.

Petitioner's Response (see MRID No. 415949-01)

The petitioner presented results of storage stability studies in a report titled "Prowl® Herbicide, Pendimethalin (CL-92,553): Summary of Ongoing Freezer Stability Studies on CL-92,553 and CL-202,347 (Metabolite) Residues in Several Different Types of Commodities" by C. Elenewski and R. Tondreau dated January 26, 1987, and coded C-2695.1.

CBTS Comments

The petitioner presented storage stability data for almond hulls, almond kernels, grapes, onion bulbs, potato tubers, raisins, soybean plants, soybean seed, tobacco, and wheat straw. All individual samples, either 10 grams or 20 grams, were spiked at 0.1 ppm or 1.0 ppm with both pendimethalin and pendimethalin alcohol. Samples were stored at -20 °F in a freezer immediately after spiking. At intervals of 1, 3, 6, and 12 months aliquots were removed for analysis.

A variety of analytical techniques was used in the analysis of the various commodities. In general they are all versions of the same basic procedure with modifications to handle high sugar (grapes and raisins), high lipid (soybeans and almonds), low moisture (straw), or high moisture (potatoes and onions). All methods used the same basic determination step, gas chromatography using a Tracor 565 GC with a nitrogen specific detector. The petitioner has also presented adequate supporting chromatographic data for all commodities in this storage stability study. Data presented are copies of chromatograms for standards, controls, and spiked controls at 0.1 ppm levels. UARs are not a problem.

Pendimethalin recoveries from almond hulls ranged from 83 percent (3 months) to 113 percent (1 month). For almond kernels spiked at 1.0 ppm pendimethalin, recoveries ranged from 79 percent (3 months) to 100 percent (1 and 6 months) averaging 90 percent for the year. Pendimethalin alcohol recoveries from almonds spiked at 0.1 ppm ranged from 41 percent (6 months) to 70 percent (3 months) and from spikes at 1 ppm recoveries ranged from 63 percent (6 months) to 107 percent (12 months). For almond kernels spiked at 1 ppm pendimethalin alcohol recoveries ranged from 83 percent (6 months) to 100 percent (1 month) and from a spike at 0.1 ppm recoveries ranged from 60 percent (3 months) to 104 percent (1 month).

Grape samples spiked at 1.0 ppm pendimethalin had initial recoveries of 81 percent. Recoveries then ranged from 74 to 90 percent over the next year. The 0.1 ppm pendimethalin spike had an initial recovery of 95 percent. Recoveries then ranged from 85 to 102 percent over the next year. For grapes spiked with pendimethalin alcohol at 1.0 ppm spike recoveries ranged from 45 percent to 89 percent. Raisins spiked at 1.0 ppm pendimethalin had initial recoveries of 81 percent. Then, over the next year recoveries ranged from 77 to 92 percent, but fell off to 57 percent at the 1-year mark. From a 0.1 ppm spike of pendimethalin in raisins residues were 91 percent, then ranged from 83 to 104 percent over the next year. Pendimethalin alcohol spiked in raisins at 0.1 ppm had a 69 percent recovery; residues then ranged from 31 percent (1 month) to 86 percent (6 months) and from the 1.0 ppm pendimethalin alcohol spike in raisins recoveries ranged from 62 to 77 percent.

From the low-moisture sample, wheat straw, spiked at 0.1 ppm or 1.0 ppm pendimethalin recoveries over the year ranged from 78 to 104 percent. For pendimethalin alcohol recoveries ranged from 75 to 114 percent on wheat straw.

For the high-moisture samples, onion bulbs and potato tubers, spiked at 0.1 ppm pendimethalin, recoveries ranged from 70 to 131 percent and from the 1.0 ppm spike, recoveries ranged from 74 to 102 percent. Pendimethalin alcohol recoveries from a 1 ppm spike over a 1-year period ranged from 79 to 145 percent. From the 0.1 ppm pendimethalin alcohol spike recoveries over 1 year ranged from 37 to 103 percent.

From soybean seed and soybean plant samples spiked at 1.0 ppm or 0.1 ppm, pendimethalin recoveries over a 1-year period ranged from 71 to 109 percent, and pendimethalin alcohol recoveries ranged from 50 to 126 percent.

The petitioner has presented an adequate amount of storage stability to show that residues of pendimethalin and its alcohol metabolite are stable in frozen storage for at least 1 year in commodities such as soybean seed and plants, onion bulbs, potatoes, wheat straw, almonds and almond hulls, and in grapes and raisins. There are adequate storage stability data to

support the crop field trial residue data in this petition. The deficiency is resolved.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Deficiency

The residue data submitted with this petition reflects five studies conducted in three States (California, Ohio, and New York) and is insufficient in number for the determination of an appropriate tolerance level in grapes. Additional residue data is needed from all grape-growing areas. These data should reflect application at the maximum proposed rate and shortest PHIs possible under the conditions of proposed use.

Petitioner's Response (See MRID No. 415949-01)

The petitioner has presented additional magnitude of the residue on grape crop field trial residue data in a study titled "Prowl® Herbicide (AC 92,553/4EC): Residues of CL-92,533 and CL-202,347 in Grapes" by R.E. Tondreu and M.A. Risley, completed on October 14, 1986 and coded C-2806, C-2807, and C-2808.

CBTS Comments

Previously the petitioner has presented results of pendimethalin on grape crop field trial residue data. In summary for the 1983 crop year, residue data were presented from California (2), New York (2), and Ohio (1). Grapes were treated at the proposed use rate of 4 lbs ai/acre (1X) and at 6 lbs ai/acre (1.5X) with PHIs ranging from 86 days to 195 days. No pendimethalin residues were detected in any samples to < 0.05 ppm. Neither were any pendimethalin alcohol residues detected in any sample to < 0.05 ppm.

In this submission the petitioner presented the results of pendimethalin on grape field trial residue data for the crop year 1985 all from California (3). The grapes were treated at either the proposed use rate of 4 lbs ai/acre or at an exaggerated rate (1.5X) of 6 lbs ai/acre and PHIs ranged from 202 days to 237 days. No residues of pendimethalin or its alcohol metabolite were detected in any of these samples to < 0.05 ppm.

Data for the new studies were generated using method M-1623 reviewed above. Adequate supporting chromatographic data were presented.

After careful consideration, CB concludes the petitioner has not presented sufficient crop field trial residue data to support the proposed tolerance even with the results from the new field trials. CB reiterates that additional magnitude of the residue crop field trial data are necessary from all grape-growing areas. This means additional trials are needed from different areas in California, plus trials from Washington, New York, Pennsylvania,

and Michigan. The petitioner needs to ensure that adequate grape varietal data are included in these trials. These data should reflect the proposed use rate (and PHI). The deficiency is not resolved and continues outstanding.

MAGNITUDE OF THE RESIDUE - MEAT/MILK/POULTRY/EGGS

Deficiencies (from the Registration Standard)

The following data are required:

1. Lactating ruminants must be dosed with 0.1, 0.3, and 1.0 ppm pendimethalin per se (≥ three animals/dose group) in the total diet until residues plateau in milk or for 28 consecutive days if no residues are detected in milk. Milk samples must be obtained twice daily. Animals must be sacrificed within 24 hours of the final dose and residues in tissues (muscle, liver, kidney, and fat) determined.

2. Poultry must be dosed with 0.1, 0.3, and 1.0 ppm pendimethalin per se (≥ 10 hens/dose group) in the total diet. Egg samples should be collected twice daily and analyzed for residues; dosing should continue until residues in eggs plateau or for 28 days if residues are nondetectable. Hens should be sacrificed within 24 hours of the final dose and residues determined in muscle, fat, kidney, liver, and other edible tissues.

3. Since the residues of concern in animal products have not been delineated, at the present time we require data reflecting residues of pendimethalin per se and its metabolite CL-202,347. Other residues may need to be sought if requested metabolism studies so indicate.

4. The available goat metabolism study (see Nature of the Residue in Animals) indicates that residues of pendimethalin may occur in meat and meat byproducts of food animals. Tolerances must be proposed for these food commodities if the above-required data so indicate.

From our review of August 20, 1984 by E.T. Haeberer:

a. The nature of the residue in animals is not adequately understood (PP#3F2792, memorandum of conference January 9, 1984, Dr. R. Perfetti). If the additional residue data discussed in conclusions 3a and 3b show real residues to be present, a metabolism study in a lactating ruminant that identifies radioactivity in tissues and milk will be needed.

b. Since grapes and grape byproducts are a major poultry feed item, any significant residues will also engender the need for a poultry metabolism study and possibly a feed study.

Petitioner's Response

The petitioner did not respond to the deficiencies raised in the Registration Standard. In the cover letter of August 10, 1990 (signed by Barbara Gingher, Product Registration Manager), the petitioner contends that no residues above the limit of detection have been seen in any of the residue trials; hence work discussed in these sections is not necessary.

CBTS Comments

After reconsideration, CBTS reiterates the above deficiencies with modifications. They continue unresolved and remain outstanding.

CBTS points out that in the "Overview of the Residue Chemistry Guidelines," current Branch policy is that animals should be kept on the treated feed for 4 weeks. However, if residues have not plateaued in eggs or milk by the end of 4 weeks, then the feeding period should continue until a plateau is reached.

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

Deficiency

No conclusions can be drawn from the grape processing study data since the grapes used for the study have < 0.05 ppm residue level, the limit of analytical method sensitivity. If the additional grape residue data requested show detectable residues on grapes, an additional processing study using grapes with residue levels of at least 0.10 ppm will be needed.

Petitioner's Response

In the cover letter of August 10, 1990 (signed by Barbara Gingher, Product Registration Manager), the petitioner contends that no residues above the limit of detection have been seen in any of the residue trials; hence work discussed in these sections is not necessary.

CBTS Comments

In our previous review by E.T. Haeberer on August 20, 1984 CBTS (aka RCB) concluded that "No conclusions can be drawn from the grape processing study data since grapes used for the study had < 0.05 ppm residue level . . . ." Upon further consideration, CBTS now concludes that a new pendimethalin grape processing study is necessary. This study should be conducted to address considerations noted below.

Based on the requirements as stated in the Overview of the Residue Chemistry Guidelines, the petitioner needs to conduct additional grape crop field trials treated with pendimethalin at

the proposed use rate and/or higher practical application rate. If detectable residues are found in the raw agricultural commodity (RAC) grapes, then a processing study is necessary; and if the data show a concentration of residues, then a Food/Feed Additive Tolerance (FAT) is required. Residue data are necessary for raisins, wet and dry grape pomace, raisin waste, and grape juice.

If "exaggerated rate" data are available and there are detectable residues, then these samples should be used for a processing study. If residues concentrate on processing, then the concentration factor should be applied to the RAC tolerance to arrive at a FAT.

If pendimethalin exaggerated rate data are available and there are no detectable residues in the RAC wheat, then no FAT is required provided that:

1. The application rate is exaggerated by at least the theoretical concentration factor,

2. The crop field trial data are sufficiently representative of major grape-growing regions so that any reasonable potential for detectable residues has been realized, and

3. The exaggerated rate was not unrealistically high.

The level of exaggerated application acceptable will depend on the use.

If application of the highest practical exaggerated pendimethalin rate results in no detectable residues and the level of exaggeration is less than the theoretical concentration factor, then the grapes are to be processed. If no detectable residues are found in the processed raisins, grape juice, wet or dry grape pomace, and raisin waste, then no FAT is required. If any of the processed commodities contain any pendimethalin and its metabolite residues, then a FAT is required. In cases where the raw grapes contain no detectable pendimethalin residue, the processing study will indicate only that the minimum concentration factor is the ratio of the concentration in the processed commodity to the limit of <u>detection</u> (not quantification) in the RAC. CBTS will evaluate all available data in determining what is the appropriate concentration factor. This will include, at a minimum, the metabolism studies and chromatographic support data for the RAC. In some cases it may be possible to estimate residue levels from chromatograms where the response is below the limit of reliable quantitation but nonetheless indicative of a "true" residue.

cc: R.F., Circ(7), Reviewer (FDG), PP#2788, 3F2844, 3F3049, and 4F3121 PIB/FOD (Furlow), R.D. Schmitt, Ph.D., Chief.

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