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PP#4480

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

JUN 9 1995

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: **PP# 5F4480/FAP 5H5723 - IMIDACLOPRID (ADMIRE®) ON CITRUS FRUITS CROP GROUP AND PECANS.**
Review of the Residue Data and Analytical Method.
(MRID # 435515-01 thru -04 and 435813-01)[CBTS #s 15305, 15306, 15326, 15327, 15329, and 15656]{DP Barcodes D213252, D213256, D213248, and D215794}

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INTRODUCTION

Miles Inc., Agricultural Division proposes tolerances for combined residues of the insecticide imidacloprid, trade named Gaucho® and Admire® (1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, expressed as imidacloprid in or on the raw agricultural commodities pecans at 0.05 ppm and the citrus fruits crop group at 1 ppm; and feed additive tolerances for dried citrus pulp at 5.5 ppm and molasses at 4.8 ppm.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- ADDITIONAL CROP FIELD TRIAL DATA ON ORANGES, LEMONS, AND GRAPEFRUIT
- REVISED TOLERANCES

CONCLUSIONS

1. CBTS Conclusion on Product Chemistry/Chemical Identity

CBTS concludes that after reviewing the CSF for the TGAI the impurities present in the TGAI imidacloprid are not expected to be a residue problem in the subject crop pecans and the crop group citrus fruits when Admire® is used as directed. Analysis of various batches of the TGAI imidacloprid did not reveal any volatile N-nitroso amines to the limits of detection.

2. CBTS Conclusion on Directions for Use

The petitioner has proposed an adequate set of directions for use of imidacloprid formulated as Admire® 2 Flowable for use on pecans and the crop group citrus fruits.

3. CBTS Conclusion on Nature of the Residue - Plants

The nature of the imidacloprid residue in apples, potatoes, tomatoes, eggplant, cottonseed, and in corn grain, forage, and fodder is adequately understood. The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all calculated as imidacloprid. We are translating these data to pecans and the citrus fruits crop group.

4. CBTS Conclusion on Nature of the Residue - Livestock

The nature of the imidacloprid residue in ruminants and poultry is adequately understood. The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all calculated as imidacloprid.

5. CBTS Conclusion on Confined Rotational Crops

The petitioner has adequately characterized and identified the nature of the imidacloprid residue in rotational crops. The nature of the residue in rotational crops is adequately understood and is nearly identical to that identified in the primary crops. While total imidacloprid residues were greater than 0.01 ppm from a 1X application indicating a potential for inadvertent residues to occur in non-target crops planted in rotation, CBTS concludes this is not an issue in this petition as pecan and citrus fruit trees are long lived and the groves would not be routinely rotated to other agricultural uses.

6. CBTS Conclusions on Residue Analytical Methods

a. The petitioner has presented Bayer method 00200 to gather the magnitude of the residue data and as the primary enforcement method. The method is a common moiety method.

b. Method and concurrent validation data for Bayer method 00200 from pecans, citrus fruits (oranges and orange processed commodities, lemons, and grapefruit) were presented. The limit of quantitation (LOQ) is 0.05 ppm and the minimum detection limit

(LD) is approximately 0.01 ppm. The petitioner has adequately validated the method to gather the magnitude of the total imidacloprid residue data in pecans, citrus fruits crop group and in orange processed commodities and to enforce the total imidacloprid proposed tolerance in pecans at 0.05 ppm, in the citrus fruits crop group at 1 ppm , and the FATs in dried citrus pulp at 5.5 ppm and molasses at 4.8 ppm.

c. The results of the successful method trials for Bayer methods 00191 (residues in milk and tissues) and 00200 (residues in plants) were reported by the Analytical Chemistry Branch. While ACB did not determine the methods' MDL (minimum detection limit) its estimate of 0.02 ppm in both methods is supported by chromatographic data. The methods are marginally suitable to be enforcement methods with perishable commodities as both the ILV and EPA time frame to complete a set of samples takes approximately 20 hours or into a third working day. CBTS reiterates these methods are quite rugged and effective as enforcement procedures when very rapid turn around times are not required.

d. The petitioner has presented ILV data for both primary enforcement methods. These ILV data are acceptable and are in agreement with the petitioner's method validation data as well as the data generated by the Agency's method trial.

e. The petitioner has presented the requested compound specific confirmatory method for imidacloprid and its major metabolites. Bayer method 00357 is a reverse phase HPLC-UV method that uses a 50 gram sample, methanol/sulfuric acid extraction, filtering through celite/filter paper, separation of the guanidine with weak cation exchange cartridge, 6-CNA with a strong anion exchange cartridge, CH_2Cl_2 partitioning and florisil clean-up separating the olefin from imidacloprid and the hydroxy metabolite. A TMV is necessary and will be initiated shortly for this method.

f. The petitioner has presented adequate method validation data from apples, cottonseed, and potatoes for the compound specific HPLC-UV method to show the method can gather magnitude of the residue data. Provided the TMV is successful the method is also adequate to enforce the total imidacloprid tolerances.

g. The petitioner has presented acceptable ILV data for the compound specific HPLC-UV method. These ILV data are in statistical agreement with the petitioner's method validation data.

7. CBTS Conclusion on **Storage Stability**

Imidacloprid and its metabolites are stable in potatoes, apples, apple juice, and pomace; cottonseeds, cottonseed hulls, soapstock, and oil as well as in wheat grain, forage, and straw, and in wheat processed commodities at -20°C for at least 18-20 months. There are supplementary storage stability data that shows imidacloprid and its metabolites both labeled and unlabeled are stable in lettuce under

conditions of frozen storage for at least 24 months. In lemons stored frozen under acidic conditions for 24 months there is a change in the individual concentrations of various metabolites, but no overall change in the total imidacloprid concentrations. These data are sufficient to support the magnitude of the residue crop field trial data for pecans and the citrus fruits crop group.

8. CBTS Conclusions on **Magnitude of the Residue - Crop Field Trials**

a. The petitioner has presented an adequate amount of geographically representative crop field trial data to show that combined residues of imidacloprid and its metabolites, all calculated as imidacloprid will not exceed the proposed 0.05 ppm tolerance on pecans when Admire® or Provado® is used as directed.

b. The petitioner has not provided adequate geographical representation or an adequate number of imidacloprid field trials for a citrus fruit crop group tolerance. For lemons the petitioner needs to provide at least 3 additional trials with 1 trial from Region 3 (FL) and 2 additional trials from Region 10 (CA). Additional imidacloprid on oranges field trials are necessary from Florida (6) and 1 from California. For oranges the petitioner is encouraged to improve the varietal representation in these additional field trials. To support a crop group citrus fruit tolerance the petitioner needs to present the results from an additional grapefruit field trial from Region 3. To have an imidacloprid on grapefruit only tolerance the petitioner needs to conduct 3 additional field trials in Region 3. The petitioner is reminded to treat all new citrus field trials with imidacloprid at the maximum 1X application rate with the shortest repeat application interval and harvest at the proposed PHI.

c. CBTS defers judgement on the proposed crop group tolerance of 1 ppm until all the necessary crop field trial residue data have been generated and reviewed. A revised combined residues of imidacloprid and its metabolites, all calculated as imidacloprid tolerance on citrus fruits crop group may be necessary once all of the field trial data are gathered.

9. CBTS Conclusions on **Magnitude of the Residue - Processed Food/Feed**

a. The petitioner has conducted an adequate orange (citrus) processing study using treated oranges bearing detectable residues following an exaggerated 5X total imidacloprid application. Total imidacloprid residues were shown to concentrate only in the molasses and in the dried citrus pulp; thus Feed Additive Tolerances (FATs) are required. While no residue data were presented for wet citrus pulp and wet citrus pulp is currently listed as a processed commodity in Table II we conclude a tolerance for citrus pulp (wet or dried), based on the residue data presented for dried pulp is adequate and no additional residue data are necessary for wet pulp.

b. Judgement is deferred on the adequacy of the proposed FATs at 4.8 ppm on molasses and 5.5 ppm on dried citrus pulp until the petitioner has reported the results of the requested additional crop field trials for oranges, grapefruit, and lemons and revised the proposed crop group tolerance. The petitioner is reminded that CBTS tries to avoid establishing fractional tolerances; however, we recommend for tolerances no higher than necessary.

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

Based on the results of imidacloprid bovine and poultry feeding studies, finite residues will occur in meat, milk, poultry, and eggs from the feeding of imidacloprid treated racs or their processed feed items when Admire® or Provado® is used as directed. Adequate total imidacloprid secondary tolerances have been established at 0.1 ppm in milk, 0.3 ppm in meat, fat, and meat by-products of cattle, goats, hogs horses, hogs, and sheep, 0.02 ppm in eggs, and 0.05 ppm in meat, fat, and meat by-products of poultry. These tolerance do not need to be changed with the additional proposed uses on pecans and the citrus fruits crop group. The feed stuffs associated with citrus fruits are molasses and dried citrus pulp. There are no poultry feed stuffs associated with this petition.

11. CBTS Conclusion on **Harmonization of Tolerances**

Since there are no Mexican, Canadian, or Codex MRLs/tolerances, compatibility is not a problem at this time.

RECOMMENDATION

CBTS cannot recommend for the requested tolerances for combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, expressed as imidacloprid in or on the raw agricultural commodities pecans at 0.05 ppm and the citrus fruits crop group at 1 ppm; and feed additive tolerances for dried citrus pulp at 5.5 ppm and molasses at 4.8 ppm for the reasons stated in our Executive Summary and further explained in Conclusions 8b and c, and 9b.

For further consideration of this petition the registrant should be advised to resolve the deficiencies above.

NOTE TO PM:

CBTS points out that there are no deficiencies relating to the proposed total imidacloprid tolerances on pecans.

DETAILED CONSIDERATIONS

BACKGROUND

CBTS has recommended for tolerances of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety on mangoes at 0.2 ppm (see PP# 3F4285); on apples at 0.5 ppm, cottonseeds at 6 ppm, and

potatoes at 0.3 ppm, and their processed commodities, plus meat at 0.3 ppm, milk at 0.1 ppm, poultry at 0.05 ppm, and eggs at 0.02 ppm (see PP# 3F4169); and lettuce at 3.5 ppm, grapes at 1 ppm, fruiting vegetables at 1 ppm and Brassica (cole) leafy vegetables at 3.5 ppm (see PP# 3F4231). CBTS has also recommended for time limited tolerances on sorghum grain at 0.05 ppm, and sorghum forage and fodder at 0.1 ppm (see PP# 4F4415).

There is a co-pending petition for total imidacloprid residues in/on barley, wheat, and sugarbeets and their processed commodities following seed treatment (see PP# 4F4337). This petition is in reject status with deficiencies remaining for additional crop field trial residue data, revised directions for use and revised tolerances.

CBTS recommended for imidacloprid Emergency Exemptions during 1993 and 1994 on broccoli, cauliflower, and cabbage, head and leaf lettuce, cotton, tomatoes, potatoes, the cucurbits vegetable crop group, apples, peppers, oranges and grapefruit, and hops. In 1995 additional Emergency Exemptions were recommended for use of imidacloprid on pears (95WA0014) and on leafy and Brassica vegetables crop groups (95FL0008).

A SUMMARY of all plant and animal metabolism data were presented to the HED Metabolism Committee. The Committee concluded (see memorandum by F. Griffith dated June 24, 1993) that no additional plant or animal metabolism studies are needed at this time, the levels of the nitrosimino compound in the TGAI were not of TOX concern, residues of the guanidine and nitrosimino imidacloprid metabolites plus other metabolites at the levels reported in the different metabolism studies are not toxicologically significant, no separate regulation of metabolites is warranted, and there is no scientific objections to the tolerance expression being for combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

The product chemistry data for the TGAI were summarized in our initial reviews for PP#s 3F4169 and 3F4231 (qv). The petitioner has adequately identified the active ingredient, described the starting materials and listed the sources for each, and described the manufacturing process, including the equipment used in the manufacturing process. A detailed discussion on the formation of impurities, both actual and theoretical has been presented and reviewed.

CBTS concludes that after reviewing the CSF for the TGAI the impurities present in the TGAI imidacloprid are not expected to be a residue problem in the subject crop pecans and the citrus fruits crop group when Admire® or Provado® is used as directed. Analysis of various batches of the TGAI imidacloprid did not reveal any volatile N-nitroso amines to the limits of detection.

DIRECTIONS FOR USE/LABELING

Imidacloprid is proposed as an insecticide to control aphids, spittlebugs, and phylloxera on pecans; and aphids, whiteflies,

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The nature of the imidacloprid residue in apples, potatoes, tomatoes, eggplant, cottonseed, and in corn grain, forage, and fodder is adequately understood. The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as imidacloprid. We are translating these data to pecans and the citrus fruits crop group.

NATURE OF THE RESIDUE - LIVESTOCK

No new ruminant or poultry imidacloprid metabolism studies were presented in this petition. The petitioner has presented imidacloprid metabolism studies for ruminants and poultry in PP# 3F4169.

In summary, bovine and poultry imidacloprid metabolism follows four similar, but not identical pathways as in plants: (1) hydroxylation of the dihydroimidazole ring of imidaclòprid plus glucuronide conjugate formation, (2) reduction and loss of the nitro group on the dihydroimidazole ring, (3) opening of the dihydroimidazole ring, and (4) a minor pathway of oxidative bridge cleavage.

The nature of the imidacloprid residue in ruminants and poultry is adequately understood. The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as imidacloprid.

CONFINED ACCUMULATION STUDIES ON ROTATIONAL CROPS

The petitioner has presented confined accumulation rotational crop studies using ^{14}C-imidacloprid treated soil and planted with Swiss chard as the leafy vegetable, red beets as the root crop, and wheat as the cereal grain. These studies have been previously reviewed in PP#s 3F4169 and 3F4231.

The petitioner has adequately identified around 45% of the residue from a 1X application and further characterized 91-96% of the imidacloprid residue in rotational crops. The nature of the residue in rotational crops is adequately understood and is nearly identical to that identified in the primary crops. While total imidacloprid residues were greater then 0.01 ppm from a 1X application indicating a potential for inadvertent residues to occur in non-target crops planted in rotation, CBTS concludes this is not an issue in this petition as pecan and citrus fruit trees are long lived and the groves would not be routinely rotated to other agricultural uses.

RESIDUE ANALYTICAL METHODS (MRID #s 435813-01 and 435515-04)

The petitioner has conducted an adequate interference study which shows that positive interference will occur from only clopyralid out of 281 compounds when using Bayer's method 00200.

The petitioner has presented adequate multiresidue method (MRM) recovery data for imidacloprid and its olefin, hydroxy, guanidine, and 6-chloronicotinic acid (6-CNA) metabolites through FDA's Protocols A

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blackflies, leafminers, and mealybugs on citrus fruits. For use on pecans and the citrus fruit the petitioner proposes foliar applications of either Admire® 2 Flowable (EPA Reg. No. 3125-422) containing 2 lbs imidacloprid ai/gallon or Provado® 1.6 Flowable (EPA Reg. No. 3125-457). Use on pecans may also be as a soil application.

Apply Admire to pecans at a rate of 1 pt - 1 qt (0.25-0.5 lb ai)/ acre/soil application once per year between May 15 and July 15. Admire or Provado may be applied as a foliar spray to pecans 2 times per year with a 10-14 day repeat application interval. No PHI is proposed. The first foliar application should be made before pest populations become extreme. The rate of Admire foliar application is 2.8-11.2 fl ozs (0.044-0.175 lb ai)/acre/application for a maximum of 22 fl ozs (0.35 lb ai)/year. The rate of Provado foliar application is 3.5-14 fl ozs (0.044-0.175 lb ai)/acre/application for a maximum of 28 fl ozs (0.35 lb ai)/year. Thorough uniform coverage of the pecan foliage is essential for optimum control. A foliar application in the same year following a soil application to pecans is not recommended. Regardless of which formulation is used or how it is applied; ie, soil or foliar spray do not use more than 0.5 lb ai/A/year.

Apply Admire or Provado to citrus fruits as a foliar spray 2 times per year with a 10-14 day repeat application interval and a 0 day PHI. The first foliar application should be made before pest populations become extreme and when the crawler stages are active. The rate of Admire foliar application is 2.8-4 fl ozs (0.044-0.063 lb ai)/100 gal not exceed 1 pt (0.25 lb ai)/ acre/application for a maximum of 32 fl ozs (0.5 lb ai)/year. The rate of Provado foliar application is 3.5-5 fl ozs (0.044-0.063 lb ai)/acre/application not to exceed 20 fl ozs (0.25 lb ai)/acre/application for a maximum of 40 fl ozs (0.5 lb ai)/year. Thorough uniform coverage of the citrus foliage is essential for optimum control. The petitioner recommends that use of an organosilicone based spray adjuvant not to exceed the adjuvant manufacturer's recommended use rate may improve coverage. Regardless of which formulation is used or how it is applied; ie, soil or foliar spray do not use more than 0.5 lb ai/A/year.

The petitioner has proposed an adequate set of directions for use of imidacloprid formulated as Admire® 2 Flowable or Provado® 1.6 F for use on pecans and citrus fruits crop group.

NATURE OF THE RESIDUE - PLANTS

The petitioner has presented plant imidacloprid metabolism studies for apples, potatoes, tomatoes, eggplant, cottonseed, and corn in PP# 3F4169.

In summary imidacloprid is metabolized by three pathways as follows: (1) hydroxylation of the dihydroimidazole ring, (2) reduction and loss of the nitro group on the dihydroimidazole ring, and (3) bridge cleavage of the C-N bond followed by glucoside formation.

The imidacloprid corn metabolism study confirms that from imidacloprid treated seeds residues will translocate from the seed to the edible portion of the crop.

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For the citrus fruit processing study, method and concurrent validation data for Bayer method 00200 from whole grapefruit and oranges, and from orange dried pulp, juice, oil, and molasses were presented. Preliminary method validation involved individual fortification of control matrix samples with imidacloprid and its guanidine, hydroxy, and olefin metabolites at 0.05 ppm each, except 0.25 ppm each in dried pulp and molasses. Recoveries ranged from 70 to 126%. Concurrent recovery data were generated from fortification of control samples in the processing study with an equal mixture of imidacloprid and its guanidine metabolite at 0.1 ppm, 0.2 ppm, 0.5 ppm, and 2.5 ppm (dried pulp and molasses only). Recoveries ranged from 82% to 114%. Overall recoveries from whole oranges and grapefruit, and orange dried pulp, oil, juice, and molasses averaged 93% $\pm$ 12%, n = 38. The limit of quantitation (LOQ) is 0.05 ppm and the minimum detection limit (MDL) is approximately 0.01 ppm. Extensive supporting chromatographic data were presented. These data are adequate to enable independent confirmation of all reported results. The petitioner has adequately validated the method to gather the magnitude of the total imidacloprid residue data in oranges and orange processed commodities and to enforce the total imidacloprid proposed FATs in the dried citrus pulp and molasses.

The results of the successful method trials for Bayer methods 00191 (residues in milk and tissues) and 00200 (residues in plants) were reported by the Analytical Chemistry Branch. While ACB did not determine the methods' MDL (minimum detection limit) its estimate of 0.02 ppm in both methods is supported by chromatographic data. The methods are marginally suitable to be enforcement methods with perishable commodities as both the ILV and EPA time frame to complete a set of samples takes approximately 20 hours or into a third working day. CBTS reiterates these methods are quite rugged and effective as enforcement procedures when very rapid turn around times are not required. They meet all other requirements of Subdivision O and will be forwarded to FDA for publication in the PAM, Vol II.

The petitioner has presented ILV data for both methods. The ILV data are acceptable and are in agreement with the petitioner's method validation data as well as the data generated by the Agency's method trial. The recovery data support the conclusion that method 00200 is capable of enforcing the proposed tolerances. There are supplementary ILV data for the residues in the plants method at the LOQ.

The petitioner presented the requested compound specific confirmatory method for imidacloprid and its major metabolites; ie, the olefin, guanidine, hydroxy, and 6-CNA. The method is a HPLC procedure designed to be used as a stand alone procedure, or can be used in any repeat analysis of positive findings on samples to show that the 6-CNA residues detected are due to the use/misuse of imidacloprid. The title of the method is "Residue Analytical Method for the Determination of Imidacloprid and Metabolites in Plant Matrices as Individual Components" by F.J. Placke dated August 17, 1994, and coded Miles report number 106782 and MRID # 435813-01.

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through E. These data have been forwarded to FDA to be published in a future update in PAM, Vol I, Appendix I.

The petitioner has presented Bayer method 00200 to gather the magnitude of the residue data and as the primary enforcement method. The method is a common moiety method that uses a 50 gram sample, methanol/sulfuric acid extraction, filtering through celite/filter paper, resin column cleanup, permanganate oxidation to 6-CNA, MSTFA derivatization, and determination as 6-CNA in a capillary 12m X 0.2mm id Ultra I column in a Hewlett Packard 5890 GC connected to HP 5971A MS with data acquisition by a HP G1034C MS Chemstation for selective ion monitoring at m/z 214 (primary), 216, 170, and 140.

Method and concurrent validation data for Bayer method 00200 from pecans were presented. Preliminary method validation involved individual fortification of control pecan samples with imidacloprid and its guanidine, hydroxy, olefin, and 6-CNA metabolites at 0.05 ppm each. Recoveries ranged from 86 to 118%. Validation data at 0.1 ppm were gathered using the parent imidacloprid, and the guanidine and olefin metabolites. Recoveries ranged from 88 to 120%. Concurrent recovery data were generated from fortification of control pecan samples with an equal mixture of imidacloprid and its guanidine metabolite at 0.1 ppm, 0.2 ppm, and 0.5 ppm each. Recoveries ranged from 86% to 94%. Overall method validation and concurrent recoveries from pecans averaged 98% $\pm$ 12%, n = 16. The limit of quantitation (LOQ) is 0.05 ppm and the minimum detection limit (MDL) is approximately 0.01 ppm. Extensive supporting chromatographic data were presented. These data enable independent confirmation of all reported results. The petitioner has adequately validated the method to gather the magnitude of the total imidacloprid residue data in pecans and to enforce the total imidacloprid proposed tolerance in pecans at 0.05 ppm.

Method and concurrent validation data for Bayer method 00200 from grapefruit, oranges, and lemons were presented. Preliminary method validation involved individual fortification of control grapefruit samples with imidacloprid and its guanidine, hydroxy, olefin, and 6-CNA metabolites at 0.05 ppm each. Recoveries ranged from 72 to 108%. Validation data at 1 ppm were gathered using the parent imidacloprid, and the guanidine and 6-CNA metabolites. Recoveries ranged from 97 to 119%. Concurrent recovery data were generated from fortification of control lemons, oranges, and grapefruit samples with an equal mixture of imidacloprid and its guanidine metabolite at 0.1 ppm, 0.2 ppm, 0.5 ppm, and 1 ppm (lemons only) each. Recoveries ranged from 82% to 110%. Overall method validation and concurrent recoveries from lemons, oranges, and grapefruit averaged 95% $\pm$ 12%, n = 34. The limit of quantitation (LOQ) is 0.05 ppm and the minimum detection limit (MDL) is approximately 0.01 ppm. Extensive supporting chromatographic data were presented. These data are adequate to enable independent confirmation of all reported results. The petitioner has adequately validated the method to gather the magnitude of the total imidacloprid residue data in oranges, lemons, and grapefruit and to enforce the total imidacloprid proposed tolerance in the citrus fruits crop group at 1 ppm.

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matographic conditions and the reported results. Apples were fortified with a mixed standard containing 0.1 ppm or 1 ppm of imidacloprid and its hydroxy, guanidine, olefin, and 6-CNA metabolites. Recoveries ranged from 62 to 118% with 4 below 70% (2 each for the hydroxy and 6-CNA) and 3 above 110% (2 from the olefin). The average recovery was 87 ± 20%, n = 35. Cottonseeds were fortified with the same mixed standard but at the 0.5 and 2 ppm levels. Recoveries ranged from 57 to 105% with 11 values being below 70% (4 from the hydroxy and 7 from the guanidine). The average recovery was 81.3 ± 14.4%, n = 36. Potatoes were fortified with the same mixture and at the same levels as apples; ie, 0.1 or 1 ppm. Recoveries from potatoes ranged from 75 to 97% with 3 hydroxy metabolite recoveries being below 70%. The average recovery was 85 ± 9%, n = 30. The petitioner has adequately validated his procedure to either gather magnitude of the residue data or to confirm residue values reported.

The petitioner presented the results of independent laboratory validation for the confirmatory compound specific HPLC method in a study titled "Independent Laboratory Validation of the Second Confirmatory Method for Imidacloprid and Its Metabolites in Plant Matrices (Miles Report No. 106782)" by M. Bajzik of Huntingdon Analytical Services of Middleport, NY and coded Huntingdon report number A012.007 and Miles report number 106900.

Bayer method 00357 was followed as received from the petitioner. For the determination HAS used essentially the same GC-MSD system as the petitioner. For the HPLC the ILV used a Spectra Physics SP8700 with EM LiChrospher 60 RP-Select B, 5 um, 25 X 0.4(id) cm column connected to a Waters WISP 710B autoinjector and Kratos Spectroflow 783 programmable variable wavelength detector set for 270 nm and 330 nm. Apples were spiked with imidacloprid and its guanidine, hydroxy, olefin, and 6-CNA metabolites at 0.5 and 2.5 ppm. During the first trial HAS made very minor assumptions on the method which CBTS agrees would not have changed the outcome. The results of the first ILV were unsatisfactory. Average recoveries for imidacloprid were 45 ± 3% with a range of 41.7 % to 47.7%, 138 ± 8% for the olefin with a range of 129% to 146%, 27 ± 9% for the hydroxy with a range of 15.8 to 35.9%, 83 ± 5% for the guanidine with a range of 78 to 89.7%, and 8 ± 4% for 6-CNA with a range of 3.3% to 11.1%.

HAS presented a documentation of all contacts with the petitioner. A second ILV was initiated with the same matrix and fortification levels after several changes were made to the method. The critical steps were determined to be maintaining the buffer at pH 7 to prevent the conversion of the hydroxy metabolite to the olefin, the elution rates from the SEP cartridges must be carefully monitored to be 1-2 mls/min, and ethyl acetate wash of the florisil column must be saved and analyzed for imidacloprid, per se. The results of the second ILV were satisfactory. Average recoveries using the peak height calculations for imidacloprid were 78 ± 6% with a range of 72.3 % to 83.3%, 105 ± 2% for the olefin with a range of 102% to 107%, 60 ± 9% for the hydroxy with a range of 51.2 to 68%, 81.4 ± 3% for the guanidine with a range of 78 to 84.1%, and 71 ± 29.5% for 6-CNA with a range of 41% to 111%. HAS confirmed that the analysis time for a set of samples is 2 full working day with overnight instrumental determination of the

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In summary, 50 grams of sample are mixed with 300 mls of MeOH/ACN (3:1,v/v) plus 5 mls of 10% H_2SO_4, allowed to soak for 30 minutes, then blended on a polytron for 3 minutes. The samples is filtered under vacuum through 10 grams of Celite using Whatman 541 filter paper. The extract is made to mark in a 500 ml graduate cylinder, mixed, and 100 mls (10 grams) is removed and concentrated to 10 mls using a rotary vacuum. Initial clean-up is through a 10 gram Amberlite XAD-4 resin column with imidacloprid and its metabolites being eluted off in 100 mls of CH_3OH. The pH of the eluate is critical and needs to be maintained at pH 7 by addition of a 0.1 M phosphate buffer. The extraction and initial clean-up steps in the confirmatory method are identical to the common moiety method. Again this is designated as a convenient overnight stopping point.

The guanidine metabolite is isolated from the other compounds by taking the eluant from the XAD-4 column and running it through an Isolute CBA weak cation exchange cartridge. Imidacloprid and its olefin, hydroxy, and 6-CNA metabolites are eluted off the column first with the aqueous solution used to add the sample to the cartridge. The guanidine is then eluted off with 10 mls of 0.1 N HCl. 6-CNA is isolated from imidacloprid and its olefin and hydroxy metabolites by running the first eluant from the CBA cartridge through a Mega Bond Elut SAX strong anion exchange cartridge. The eluant now contains the parent imidacloprid and its hydroxy and olefin metabolites. 6-CNA is now eluted off the SAX cartridge with 50 mls of ACN and HPLC solvent A. 6-CNA is prepared for HPLC and/or GC-MSD analysis by partitioning 2 X 60 mls MTBE drying thoroughly over anh. Na_2SO_4.

Clean-up of the fraction containing imidacloprid is by partitioning 4 X 50 mls CH_2Cl_2/ACN (4:1,v/v) with drying each organic phase thoroughly over anh. Na_2SO_4 then rotary evap to dryness and take up the residue in 3 mls of ethyl acetate. This is further cleaned-up through 10 grams of 5% water deactivated florisil eluting imidacloprid and its hydroxy metabolite with 40 mls of ACN/CH_3OH (98:2, v/v). The olefin metabolite was eluted off in 40 mls of ACN/acetic acid (98:2, v/v).

Determination of 6-CNA can be by GC-MSD using a HP 5890 II GC equipped with a 7673 auto sampler and a 12 m X 0.2 mm id HP Ultra fused silica capillary column. The detector is a HP 5971 MSD in the SIM mode for the 214 m/z ion with the 216, 170, and 140 ions as additional confirmatory ions. The data system is a HP MS ChemStation, DOS series. Quantitation is by external standard using either peak height or area. HPLC determination is with a HP 1090 equipped with a 25 X 0.4 (id) cm LiChrospher 60, RP-Select B, 5 um column. The mobile phase is a phosphate buffer plus ACN gradient elution. The HPLC detector is UV at 270 nm for imidacloprid and the guanidine, 6-CNA, and hydroxy metabolite and at 330 nm for the olefin metabolite. The procedure will take 2 full working days to prepare samples for overnight analysis.

The petitioner has presented his own method validation data for this procedure using apples, cottonseed, and potatoes. Extensive supporting chromatographic data were presented to confirm all chro-

residues. HAS provided extensive supporting chromatographic data which can confirm all reported results.

The petitioner has presented acceptable ILV data for the compound specific HPLC-UV method. These ILV data are in statistical agreement with the petitioner's method validation data. An Agency TMV is being requested for this method.

STORAGE STABILITY

The petitioner has presented frozen storage stability data for imidacloprid and its metabolites in apples, potatoes, wheat matrices, cottonseeds, tomatoes, cauliflower, and lettuce. Frozen storage at -20°C stability data were presented for various time intervals up to 24 months. Frozen storage stability data were also generated and reported using ^{14}C-imidacloprid in lemons, corn and lettuce for various time intervals to 24 months. These studies have been previously reviewed in PP#s 3F4169 and 3F4231.

Imidacloprid and its metabolites are stable in potatoes, apples, apple juice, and pomace; cottonseeds, cottonseed hulls, soapstock, and oil as well as in wheat grain, forage, and straw, and in wheat processed commodities at -20°C for at least 18-20 months. There are supplementary storage stability data that shows imidacloprid and its metabolites both labeled and unlabeled are stable in lettuce under conditions of frozen storage for at least 24 months. In lemons there is a slight change in the 24 month chromatographic profile as would be expected under acidic conditions. While there is a decline in the individual concentrations of the hydroxy and nitrosimino metabolites with a corresponding increase in the olefin and guanidine metabolite concentrations, there has been no overall change in the total imidacloprid concentrations in lemons during 24 months of frozen storage. These data are sufficient to support the magnitude of the residue crop field trial data for pecans and the citrus fruits crop group commodities.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

PECANS (MRID # 435515-03)

The petitioner presented imidacloprid magnitude of the residue data in pecans in a study titled "Admired 2F - Magnitude of the Residue on Field Treated Pecans" by C. Lenz dated Dec. 6, 1994, and coded Miles report number 106777.

The petitioner presented total imidacloprid magnitude of the residue data on pecans from 13 field trials in Texas (2), New Mexico (2), Oklahoma (2), Louisiana, Alabama (2), and Georgia (4) all from the 1993 crop year on 8 varieties of pecans. Based on our guidance document for the location and number of field trials the petitioner has provided an adequate number and geographical representation of imidacloprid pecan field trials with at least 2 trials from Region 2 (GA and AL), 1 trial from Region 4 (LA), 1 trial from Region 6 (OK), and 1 trial from Region 8 (TX and NM). Based on the 1991 Agricultural

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Statistics, crop field trial data from these 6 states represents production of 175,000,000 pounds out of a national production of 205,000,000 (85.4%).

Each of the field trials consisted of control trees and 3-6 treated trees. The pecans trees in 7 field trials were treated with 1 or 2 foliar applications starting at the fill stage for the first application and at or prior to shuck split for the second application for a repeat application interval of 10 ± 2 days. Pecan trees were treated with imidacloprid at a rate of 0.17 lb ai/acre/application and the spray adjuvant Silwet L-77 using ground airblast sprays, or approximately 11 fl ozs of the 2F formulation/application for a total application of 0.34 lb ai/acre/season. Pecans were gathered at the earliest harvest which varied from 4 to 31 days after the last Admire® application.

Pecan trees in 6 field trials were treated with imidacloprid in a single soil application at a rate of 0.5 lb ai/acre in 8-10 GPA. The PHI for the pecans from the single soil application ranged from 99 to 150 days.

At harvest the petitioner collected samples from each tree per test site for analysis. Pecans were collected by hand picking or shaking the limbs and immediately collecting the fallen nuts from the ground. After harvest these samples were shipped frozen to Miles at Stilwell, KS for sample preparation and analysis. The samples were stored frozen approximately 8 months from harvest to analysis.

Previous pesticide usage history indicates there would be no interference with the total imidacloprid results.

No total imidacloprid residues were detected in any of the control pecans to the LD of <0.01 ppm. All treated pecan samples were below the LOQ of <0.05 ppm regardless of the PHI. Total imidacloprid residues ranged from approximately 0.001 ppm to 0.005 ppm or < 1/2 the LD.

The petitioner has presented an adequate amount of geographically representative crop field trial data to show that combined residues of imidacloprid and its metabolites, all calculated as imidacloprid will not exceed the proposed tolerance on pecans at 0.05 ppm when Admire® or Provado® is used as directed.

CITRUS (MRID # 435515-01)

The petitioner presented imidacloprid magnitude of the residue data in the citrus fruits crop group in a study titled "Admire 2F - Magnitude of the Residue on Foliar Treated Citrus" by A. Maloney dated Jan. 13, 1995, and coded Miles report number 106437.

The petitioner presented total imidacloprid magnitude of the residue data on grapefruit from 5 field trials in Texas, Florida (2), and Florida (2) all from the 1993 crop year on 4 varieties. Total imidacloprid magnitude of the residue data on oranges were presented from 5 field trials in Texas, Florida (2), and California (2) all from

the 1993 crop year on 2 varieties, and on lemons from 2 field trials in California from the 1993 crop year on a single variety. Based on our June 1994 guidance document for the location and number of field trials the petitioner has not provided adequate geographical representation or an adequate number of imidacloprid field trials for a citrus fruit crop group tolerance. For lemons the petitioner needs to provide at least 3 additional trials with 1 trial from Region 3 (FL) and 2 additional trials from Region 10 (CA). Additional imidacloprid on oranges field trials are necessary from Florida (6) and 1 from California. For oranges the petitioner is encouraged to improve the varietal representation in these additional field trials. To support a crop group citrus fruit tolerance the petitioner needs to present the results from an additional grapefruit field trial from Region 3. To have an imidacloprid on grapefruit only tolerance the petitioner needs to conduct 3 additional field trials in Region 3. The petitioner is reminded to treat all new citrus field trials with imidacloprid at the maximum 1X application rate with the shortest repeat application interval and harvest at the proposed PHI.

Each citrus field trial regardless of whether it was oranges, lemons, or grapefruit was treated with 2 foliar applications to mature fruit with a repeat application interval of 10 ± 2 days. Citrus trees were treated with imidacloprid at a rate of 0.25 lb ai/acre/application and the spray adjuvant Silwet L-77 using ground airblast sprays, or 1 pint of the 2F formulation/application for a total application of 0.5 lb ai (1 qt of Admire 2F)/acre/season.

The petitioner harvested samples from each tree per test site for analysis. Citrus fruits were collected by hand picking at 0, 7, 14, and 21 days after the second application. After harvest these samples were shipped frozen to Miles at Stilwell, KS for sample preparation and analysis. The orange samples were stored frozen approximately 15 months from harvest to analysis while grapefruit samples were stored 14 months and lemons were stored 12 months from harvest until analysis.

Previous pesticide usage history on the oranges, lemons, and grapefruit indicates there would be no interference with the total imidacloprid results.

No total imidacloprid residues were detected in any of the control oranges to the LD of <0.01 ppm; however imidacloprid equivalents were detected in the control lemons and one control grapefruit at the 0.01 ppm level.

Treated grapefruit at 0 day PHI had total imidacloprid residues ranging from 0.14 to 0.32 ppm averaging 0.22 ppm ± 0.08 ppm, at 7 days PHI imidacloprid ranged from 0.14 to 0.30 ppm averaging 0.20 ± 0.07 ppm, and at 14 days PHI imidacloprid residues ranged from 0.05 to 0.23 ppm averaging 0.12 ± 0.07 ppm. Combining the 0, 7, and 14 day PHI results the average total imidacloprid residue was 0.18 ± 0.08 ppm. Thus, while there is an apparent decline in imidacloprid residues in grapefruit over 14 days, statistically the decline is not great.

Treated oranges at 0 day PHI had total imidacloprid residues ranging from 0.11 to 0.61 ppm averaging 0.31 ± 0.18 ppm, at 7 days PHI imidacloprid ranged from 0.16 to 0.41 ppm averaging 0.26 ± 0.09 ppm, and at 14 days PHI imidacloprid residues ranged from 0.09 to 0.40 ppm averaging 0.21 ± 0.13 ppm. Combining the 0, 7, and 14 day PHI results the average total imidacloprid residue was 0.26 ± 0.13 ppm. Thus, while there is an apparent slight decline in imidacloprid residues in oranges over 14 days, statistically the decline is not great.

The amount of imidacloprid residue data on lemons is limited at this time. Treated lemons at 0 day PHI had total imidacloprid residues of 0.51 and 0.31 ppm averaging 0.41 ± 0.14 ppm, at 7 days PHI imidacloprid residues were 0.62 and 0.27 ppm averaging 0.45 ± 0.25 ppm, and at 14 days PHI imidacloprid residues were 0.55 and 0.25 ppm averaging 0.40 ± 0.21 ppm. Combining the 0, 7, and 14 day PHI results the average total imidacloprid residue on lemons was 0.42 ± 0.16 ppm.

The petitioner has not presented an adequate amount of geographically representative crop field trial data on the representative commodities oranges, lemons, and grapefruit for the citrus fruits crop group to support a crop group tolerance. CBTS defers judgement on the proposed crop group tolerance of 1 ppm until all the necessary crop field trial residue data have been generated and reviewed. A revised combined residues of imidacloprid and its metabolites, all calculated as imidacloprid, tolerance on citrus fruits crop group may be necessary once all of the field trial data are gathered.

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

PECANS

Table II (June 1994) does not list any processed commodities for pecans, thus no imidacloprid in pecans processing study is required.

CITRUS (MRID # 435515-02)

The petitioner presented magnitude of the residue data in citrus processed commodities in a study titled "Admire 2F - Magnitude of the Residue on orange Processed Commodities" by A.L. Maloney dated Sept. 6, 1994 and coded Miles report number 106771.

One additional orange field trial was conducted in Florida during the 1993 crop year using the Valencia variety. The oranges were treated with 2 foliar applications from an air blast sprayer. Admire 2F was applied at a rate of 1.25 lbs ai/acre/application (5X exaggerated rate) 20 days apart for a total of 2.5 lbs ai. Harvest by hand picking was 6 days after the second application.

The unfrozen oranges, approximately 1000 lbs of control and treated, were processed by the Citrus Research and Education Center into orange juice, oil, molasses, and dehydrated pulp. The citrus processing is adequately described and is a simulated commercial citrus processing. After processing the samples were retained in frozen storage up to 301 days. Analysis of the sample were at Miles using Bayer method 00200. The petitioner has adequately validated

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this method for processed orange commodities at the LOQ of 0.05 ppm and to levels of 2.5 ppm in dried pulp and molasses. Adequate supporting chromatographic data have been presented.

No total imidacloprid residues were detected to the limit of detection (LD) of <0.005-0.01 ppm in the control oranges and in the control processed orange commodities orange juice, oil, molasses, and dried citrus pulp. Total imidacloprid residues on the whole oranges (rac) were 0.19 ppm. When the treated oranges were processed into orange juice and oil the residues were at the LD of <0.005 ppm, thus no concentration. Total imidacloprid residues in molasses were 1.23 ppm (6.47X conc. factor) and in dried citrus pulp were 1.42 ppm (7.47X conc. factor). While no residue data were presented for wet citrus pulp and wet citrus pulp is currently listed as a processed commodity in Table II we conclude a tolerance for citrus pulp (wet or dried) based on the residue data presented for dried pulp is adequate and no additional residue data are necessary for wet pulp.

The petitioner has conducted an adequate orange (citrus) processing study using treated oranges bearing detectable residues following an exaggerated 5X total imidacloprid application. Total imidacloprid residues were shown to concentrate only in the molasses and in the dried citrus pulp; thus Feed Additive Tolerances (FATs) are required.

The petitioner has proposed FATs at 4.8 ppm in molasses and at 5.5 ppm in dried citrus pulp. Judgement is deferred on the adequacy of these FATs until the petitioner has reported the results of the requested additional crop field trials for oranges, grapefruit, and lemons and revised the proposed crop group tolerance. The petitioner is reminded that CBTS tries to avoid establishing fractional tolerances; however, we recommend for tolerances no higher than necessary.

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

The petitioner has presented ruminant and poultry imidacloprid feeding studies which studies have been previously reviewed in PP#s 3F4169 and 3F4231.

In summary, for the ruminant feeding study 3 groups of 4 dairy cows were fed imidacloprid, per se, at levels of 5, 15, and 50 mg/kg in their feed for 28 consecutive days. The bovine feed items associated with this petition are dried citrus pulp [91% DM] which can be fed to beef cattle at up to 25% of their diet and up 20% of dairy cattle diets; and citrus molasses which can be fed up 10% for beef cattle diets and up to 15% of dairy cattle diets. Milk was collected twice daily and at sacrifice liver, kidney, muscle, and fat were collected and analyzed. Maximum total imidacloprid residues in milk from the 5 mg/kg dose were 0.023 ppm and from the 15 mg/kg dose were 0.055 ppm. Total imidacloprid residues in fat were detected only from the 50 mg/kg dose at 0.079 ppm. No total imidacloprid residues were detected in muscles from the 5 mg/kg dose and the maximum residues in muscle from the 50 mg/kg dose were 0.192 ppm. In liver the maximum total imidacloprid residues from the 15 mg/kg dose were 0.168 ppm. Total imidacloprid residue in ruminant kidney was 0.032 ppm from the 5 mg/kg dose and 0.106 ppm from the 15 mg/kg dose.

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There are no poultry feed items associated with this petition; thus there is little likelihood of residues in poultry tissues and eggs from the feeding of imidacloprid treated racs and their processed commodities in this petition.

Based on the results of imidacloprid bovine and poultry feeding studies, CBTS concludes that finite residues will occur in meat, milk, poultry, and eggs from the feeding of imidacloprid treated racs or their processed feed items when Admire® or Provado® is used as directed. Secondary imidacloprid tolerances are necessary since these feeding studies show transfer of residues from the treated feed items to meat, milk, poultry, and eggs. The potential dietary burden from feeding dried citrus pulp to beef cattle is 1.5 ppm and to dairy cattle is 1.2 ppm. The potential dietary burden from feeding citrus molasses to beef cattle is 0.7 ppm and to dairy cattle is 1.1 ppm. Substitution of either of these feed items into our worst case diet which is highly artificial, but none-the-less maximizes potential pesticide exposure, will not change our estimates of total imidacloprid exposure. Adequate total imidacloprid secondary tolerances have been established at 0.1 ppm in milk, 0.3 ppm in meat, fat, and meat by-products of cattle, goats, hogs horses, hogs, and sheep, 0.02 ppm in eggs, and 0.05 ppm in meat, fat, and meat by-products of poultry. These secondary tolerances do not need to be modified from the proposed additional uses on pecans and citrus fruits crop group.

HARMONIZATION OF TOLERANCES

An INTERNATIONAL RESIDUE LIMIT STATUS SHEET (IRL) is attached to this review. Since there are no Mexican, Canadian, or Codex MRLs/tolerances on pecans or the citrus fruits compatibility is not a problem at this time.

cc:ConcentrationCase:R.F.,Circu.,Reviewer(FDG),PP#5F4480,ACB(D.Marlow,Chief).
7509C:CBTS:Reviewer(FDG):CM#2:Rm804C:305-5826:FDG:5/10/95:edit:5/26/95.
RDI:SecHd:RSQuick:5/26/95:BrSrSci:RALoranger:6/2/95:BrCh:MMetzger:6/5/95.

INTERNATIONAL RESIDUE LIMIT STATUS

5/10/95
F. Griffith

CHEMICAL Imidacloprid (tam.)

CODEX NO. ____

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): ____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 4F4480 5/10/95

RCB Reviewer F. D. Griffith, Jr

Residue: Imidacloprid* and 3 other pyridinyl metabolites, all expressed as imidacloprid

Crop(s)	Limit (mg/kg)
citrus fruits crop group	1
dried citrus pulp	5.5
molasses	4.8
pecans	0.05

CANADIAN LIMITS:

☑ No Canadian limit

Residue: ____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: ____

Crop(s)	Limit (mg/kg)

NOTES:

* 1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine

Form revised 1986

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