MEMORANDUM

Subject: **PP# 3F4231 - Imidacloprid (Admire®) on the Fruiting Vegetables and Brassica (Cole) Leafy Vegetables Crop Groups, Lettuce, Grapes and Grape Processed Commodities, Tomato Processed Commodities, Meat, Milk, Poultry, and Eggs.** Review of the Residue Data and Analytical Method.(MRID #s 428103-01, -02, -04 thru -12, -14, and 428810-01)[CBTS #s 12375 thru 12379, 13272, 13815, and 13816]{DP Barcodes D194206, D194210, D194218, D194231, D194239, D199709, D204035, and D204041}

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INTRODUCTION

Miles Inc., Agricultural Division proposes tolerances for residues of the insecticide imidacloprid, trade named Confidor®, Gaucho®, and Admire® (1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidin-imine) and its metabolites in or on the following raw agricultural commodities: fruiting vegetables crop group at 1 ppm, Brassica (cole) leafy vegetables crop at 3.5 ppm, leaf and head lettuce at 3.5 ppm, grapes at 1 ppm, milk at 0.1 ppm, meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep at 0.3 ppm, eggs at 0.02 ppm, and meat, fat, and meat by-products of poultry at 0.05 ppm. Food additive tolerances are proposed for tomato puree at 2 ppm. Feed additive tolerances are proposed for wet tomato pomace at 2 ppm, dry tomato pomace at 6 ppm, wet grape pomace at 2.5 ppm, dry grape pomace at 5 ppm, and on raisin waste at 15 ppm.

Revised tolerances and new labels were submitted in the May 25, 1994, amendment. The tolerance expression was revised and the numerical tolerances for grape juice and raisins were deleted. The petitioner added poultry and egg tolerances to this petition. Formulation names were changed and an additional use was proposed for grapes.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- Need field rotational crop studies

- Additional method validation data for all commodities at proposed tolerance

- New tomato processing study and revised tolerances for tomato processed commodities

CONCLUSIONS

1. CBTS Conclusions on **Product Chemistry/Chemical Identity**

a. Analysis of the various batches of the TGAI imidacloprid did not reveal any volatile N-nitroso amines to the limits of detection of 0.05 ppm to 0.2 ppm. However, the nitrosoimino analog was detected in all batches analyzed. The HED Metabolism Committee concluded that levels less than 40 ppm were not of toxicological concern, thus there neither is a need to change the manufacturing process to remove the nitrosoimino, nor is it necessary to list it on the Confidential Statement of Formula (CSF).

b. On review of the CSF, dated September 13, 1991, for the TGAI CBTS concludes that the impurities present in the TGAI are not expected to be a residue problem in the subject crops and crop groups when Gaucho®, Confidor®, and Admire® are used as directed.

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

The petitioner has proposed an adequate set of directions for use of imidacloprid as Gaucho 240 Flowable for seed treatment, Provado Solupak on grapes, and as Admire® 2.5 Granular and Admire® 2 Flowable on the fruiting vegetables and Brassica (cole) leafy vegetables crop groups, on leafy and head lettuce, and on grapes.

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

a. The nature of the residue in apples, potatoes, tomatoes, eggplant, and in corn grain, forage, and fodder; and cottonseed is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy, and dihydroxy imidaclo-prid followed by loss of water to

form the olefin imidacloprid,

2) reduction and loss of the nitro group on the dihydro-imidazole ring to form the nitrosimine imidacloprid, then the guanidine imidacloprid, and finally the urea imidaclo-
prid and,

3) bridge cleavage of the C-N bond to form the 6-chloro-picolyl alcohol (6-CPA) which rapidly forms the glucoside and 6-chloronicotinic acid (6-CNA) and dihydroimidazole.

b. The residues of concern are imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

c. The imidacloprid corn metabolism study confirms that from imidacloprid treated seeds residues will translocate from the seed and be detectable in the edible portion of the crop.

4. CBTS Conclusion on the **Nature of the Residue - Livestock**

a. The nature of the imidacloprid residue in ruminants is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy, plus the glucuronide conjugates of each monohydroxy metabolite, and dihydroxy imidacloprid followed by the loss of water to form the olefin imidacloprid,

2) reduction and loss of the nitro group on the dihydro-imidazole ring to form the aminoguanidine imidacloprid, then the guanidine imidacloprid, and finally the urea imidacloprid and,

3) opening of the dihydroimidazole ring with the loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine which can also form from both the guanidine imida-cloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea and picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA) and then conjugates with glycine.

b. The residues of concern in ruminants are imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

c. The nature of the imidacloprid residue in poultry is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imida-cloprid to form 4-hydroxy, 5-hydroxy, and dihydroxy imida-cloprid followed by loss of water to form the olefin imida-cloprid,

2) reduction and loss of the nitro group on the dihydro-imidazole ring to form the dihydroxyguanidine imidacloprid and,

3) opening of the dihydroimidazole ring with loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine which can also form from both the guanidine imidacloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea and picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA).

d. The residues of concern in poultry are imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

5. CBTS Conclusions on **Confined Rotational Crops**

a. CBTS reiterates that the nature of the residue in rotational crops is nearly identical to that identified in the primary crops. Imidacloprid is metabolized by the same three metabolic pathways as described for apples, eggplants, tomatoes, potatoes, and corn. The petitioner identified around 45% of the residue in the different rotational plant matrices. When the same matrices were analyzed by the common moiety method for 6-CNA, then 91-96% of the residue was recovered. This characterizes the additional components of the residues as containing the 6-chloropyridinyl moiety. The petitioner has adequately characterized and identified the nature of the imidacloprid residue in rotational crops.

b. CBTS reiterates that all 3 rotational crops in the confined study had imidacloprid residues when planted 1, 4, and 9 months after imidacloprid soil application. The total imidacloprid residues were all greater then 0.01 ppm from a 1X application. We reiterate there is potential for inadvertent imidacloprid residues to occur in non-target crops planted in rotation. Limited field rotational crops studies are necessary for a representative crop at 2 sites per crop for the following 3 crop groups: root and tuber vegetables, leafy vegetables, and cereal grains. At least 6 field trials are necessary; all at the 1X application rate.

c. We reiterate that based on the data presented from the confined imidacloprid accumulation studies CBTS anticipates that the petitioner will need to propose rotational imidacloprid tolerances. A final decision on which imidacloprid rotational tolerances will be needed as well as the need of more extensive field trial data will be based on the results of the limited field trial results.

6. CBTS Conclusions on the **Residue Analytical Methods**

a. The petitioner has conducted an adequate interference study which shows that positive interference, using Bayer method 00200, will occur from only clopyralid at 500

ppm and this is not expected to be a problem in determining total imidacloprid.

b. The petitioner has presented adequate multiresidue method recovery data for imidacloprid and its olefin, hydroxy, guanidine, and 6-chloronicotininc acid metabolites through FDA's Protocols A through E. These data have been forwarded to FDA and we expect them to be published in PAM, Vol I, Appendix I in a future update. No additional MRM recovery are necessary for other imidacloprid metabolites.

c. We reiterate that a confirmatory method is needed that precisely identifies imidacloprid and its major metabolites. The method needs to be semi-quantitative, though our choice is to have the method be quantitative. The petitioner is encouraged to continue the HPLC method development that measures imidacloprid and its major metabolites, and present the Agency with the completed validated HPLC method and accompanying ILV data as soon as possible. CBTS reiterates its observation that the petitioner needs to keep the lab time of the HPLC method under 2 days as this is necessary for the method to be an effective enforcement procedure.

d. Tentatively, for PPs # 3F4169 and 3F4231 the lack of the confirmatory procedure is not a bar to our recommendation for the proposed tolerances, provided no other compounds in this class of insecticides that determine their residues as 6-CNA are presented for registration and tolerances.

e. Method and concurrent validation data for Bayer method 00200 from tomatoes and peppers were presented. Imidacloprid and its guanidine metabolite as a mixture were spiked at various levels, but not at the proposed tolerance levels. The LOQ for peppers and tomatoes is 0.05 ppm. Recoveries are acceptable and the method has been adequately validated to gather magnitude of the imidacloprid residue on peppers and tomatoes crop field trial data.

f. For the crop group fruiting vegetables the petitioner has not presented either method validation or concurrent recovery data from the representative commodities at the proposed 1 ppm tolerance. To support a fruiting vegetables crop group tolerance the petitioner needs to generate adequate additional method validation data for imidacloprid, its guanidine and one other major metabolite in the representative commodities tomatoes and peppers at the proposed 1 ppm tolerance. CBTS suggests use of a different metabolite in peppers and tomatoes. Some additional method validation data from the representative commodities needs to be generated from a mixture of imidacloprid and its metabolites at the 1 ppm tolerance level.

g. The petitioner has presented an adequate amount of validation and concurrent recovery data for imidacloprid and its guanidine metabolite in tomato processed commodities dry pomace, puree, and juice to support the magnitude of the residue data in the tomato processing study. However, in the new imidacloprid tomato processing study to be conducted, the petitioner is reminded to generate method validation data for imidacloprid, its guanidine metabolite, and one other major imidacloprid metabolite at the proposed food/feed additive tolerances for each processed tomato commodity.

h. Method and concurrent validation data for Bayer method 00200 from cauliflower,

broccoli, cabbage, leaf lettuce, and head lettuce were presented. Imidacloprid and its guanidine metabolite as a mixture plus individual recoveries for imidacloprid, its guanidine, olefin, hydroxy, and 6-CNA metabolites were spiked at various levels. The LOQ for these commodities is 0.05 ppm. Recoveries are acceptable and the method has been adequately validated to gather magnitude of the imidacloprid residue on crop field trial data for the Brassica (cole) leafy vegetables and for lettuce.

i. For the crop group Brassica (cole) leafy vegetables the petitioner has not presented either method validation or concurrent recovery data from the representative commodities at the proposed 3.5 ppm tolerance. To support a Brassica (cole) leafy vegetables crop group tolerance the petitioner needs to generate adequate additional method validation data for imidacloprid, its guanidine and one other major metabolite in the representative commodities broccoli, cabbage, and mustard greens or leaf lettuce substituted for mustard greens at the proposed 3.5 ppm tolerance. CBTS suggests use of a different metabolite for the third fortification in cabbage, broccoli, and mustard greens or lettuce. Some additional method validation data from these representative commodities needs to be generated from a mixture of imidacloprid and its metabolites at the 3.5 ppm tolerance level. The additional method validation data are needed for lettuce as part of the Brassica (cole) leafy vegetables crop group and for the stand alone lettuce tolerance of 3.5 ppm.

j. Bayer method 00200 method has been validated for imidaclo-prid and its guanidine metabolite spiked as a mixture, plus individual recoveries of imidacloprid, its guanidine, olefin, hydroxy, and 6-CNA spiked in grapes and grape processed commodities. The LOQ for grapes and grape processed commodities is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on grapes and grape processed commodities. However, to support a grape tolerance and tolerances on grape processed commodities the petitioner needs to generate adequate additional method validation data for imidacloprid, its guanidine and one other major metabolite in grapes and each grape processed commodity; ie, at the proposed 1 ppm grape tolerance, 2.5 ppm tolerance in wet grape pomace, 5 ppm tolerance in dry grape pomace, and 15 ppm tolerance in raisin waste. CBTS suggests use of a different metabolite for the third fortification in each grape commodity. Some additional method validation data from these grape commodities needs to be generated from a mixture of imidacloprid and its metabolites at the proposed tolerance levels.

k. The petitioner presented adequate method validation data along with supporting chromatographic data for Bayer method 00191 showing recovery of imidacloprid and its major metabolites as 6-CNA from eggs, kidney, liver, milk, and muscle for test and control samples plus standards. The chromatograms showed few UARs and none that would interfere with the determination of 6-CNA. The petitioner has presented an adequately validated residue analytical method to gather the magnitude of the total imidacloprid residue data in meat, milk, poultry, and eggs.

l. TMVs were requested for Bayer method 00191 and 00200 for imidacloprid and its metabolites in milk and liver and apples and cottonseed. The results of the successful method trial 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. Based on acceptable recoveries with supporting chromatographic data there have been successful TMVs for Bayer methods 00191 and 00200. The methods are only marginally suitable to be enforcement methods with perishable commodities as both the ILV and EPA TMV 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 Pesticide Analytical Manual, Vol II.

m. The petitioner has provided accompanying recently generated ILV data for both methods. The ILV data for the plant residue method using apples were generated by Ricerca and the ILV data for the animal tissues method using liver were generated by Huntingdon Analytical Services. 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 data support the proposed tolerances. There are supplementary ILV data for the plant method at the LOQ.

7. CBTS Conclusion on **Storage Stability**

a. Imidacloprid and its major metabolites are stable under frozen conditions in corn grain, fodder, and forage for at least 24 months, and in wheat grain, forage, and straw, and in wheat processed commodities (grain dust, bran, flour, and shorts) for at least 18-20 months. CBTS concludes these storage stability data are supplementary to this petition as there are no proposed use and tolerances for any of these commodities.

b. Imidacloprid and its metabolites are stable in potatoes; apples, apple juice, and apple pomace (wet and dried); cottonseed, cottonseed hulls, soapstock, and oil under frozen conditions at -20°C for 18-20 months. These data are sufficient to support the magnitude of the residue crop field trial data on cotton, apples, and potatoes stored up to 8-11 months for harvest to analysis, and their processing studies submitted in co-pending petition PP# 3F4169.

c. While there has been a change in concentrations of the individual imidacloprid metabolites under the acidic conditions of lemon frozen storage, there has been no overall change in the total imidacloprid residue values for 2 years. These data are supplementary for this petition as there are no proposed uses and tolerances on any citrus fruits.

d. Imidacloprid and its metabolites both labeled and unlabeled are stable in lettuce under conditions of frozen storage for at least 24 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trial data reported for both head and leaf lettuce stored up to 11-12 months from harvest to analysis.

e. The petitioner has provided adequate frozen storage stability data in tomatoes and cauliflower to show that total imidaclo-prid residues are stable under frozen conditions for at least 18 months. These data are sufficient to support the magnitude of the residue crop field trial data for tomatoes (fruiting vegetables) stored up to 7 months

from harvest to analysis and for cauliflower (Brassica cole leafy vegetables) stored up to 11 months from harvest to analysis.

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

a. The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on the representative commodities peppers and tomatoes will not exceed the proposed crop group tolerance for fruiting vegetables at 1 ppm when Admire® is used at directed. Maximum residues on the representative commodities peppers and tomatoes vary by a factor of 2, thus a crop group tolerance can be supported.

b. The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on the representative commodities cabbage, broccoli, on cauliflower [a commodity of the Brassica (cole) leafy vegetables], and on leaf lettuce being substituted for mustard greens will not exceed the proposed crop group tolerance for Brassica (cole) leafy vegetables at 3.5 ppm when Admire® is used at directed.

c. The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on lettuce (head and leaf) will not exceed the proposed tolerance at 3.5 ppm when Admire® is used at directed.

d. CBTS concludes that the magnitude of the imidacloprid residue on grapes is essentially the same regardless of which formulation is used and the directions for use are followed. CBTS has no objection to the registration of the 2F and the 75WP formulations for use on grapes.

e. The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show residues of imidacloprid on grapes will not exceed the proposed tolerance at 1 ppm when either Admire® or Provado formulation is used at directed.

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

a. The tomato variety used is not a standard processing tomato variety, thus the concentration and/or decline factors reported on a fresh market tomato may not reflect the concentration/ decline factors from a processing variety tomato. CBTS cannot determine the appropriate imidacloprid tomato food and feed additive tolerances from the study results. While CBTS will not discard the results of this imidacloprid tomato processing study the petitioner will need to conduct a new imidacloprid tomato processing study using a processing variety tomato treated at an exaggerated rate to ensure there are sufficient residues for processing. The results of the present study will become supplementary and the results from the new study will be given considerable weight in determining the appropriate FATs.

b. No tomato paste was produced in this processing study. In the new imidacloprid

tomato processing study the petitioner needs to generate tomato paste as one of the tomato processed commodities.

c. The petitioner has conducted a tomato processing study using a fresh market variety tomato bearing detectable residue following an exaggerated 7.24X total imidacloprid application. Using a fresh market type tomato total imidacloprid residues concentrated 1.89X in puree, 1.57X in wet pomace, and 5X in dried pomace. While FATs are required CBTS defers judgement on the petitioner's proposed 2 ppm tolerance on puree and wet pomace, and 6 ppm tolerance in dried pomace until the petitioner completes a new imidacloprid tomato processing study using a processing variety tomato bearing detectable residues and processed into juice, puree, **paste**, and wet and dried pomace.

d. The petitioner has conducted an adequate grape processing study using grapes bearing detectable residues following an exaggerated 5X total imidacloprid application. Total imidaclo-prid residues were shown to concentrate in wet and dried grape pomace, and in raisin waste; thus feed additives tolerances (FATs) are required. The petitioner has proposed total imidacloprid FATs at 2.5 ppm on wet grape pomace, 5 ppm on dried grape pomace, and 15 ppm on raisin waste.

e. CBTS does not require tolerances on processed commodities that have small concentration factors when we are dealing with low level residues as we do not consider this to be a real concentration due to possible sample composition variations and the analytical method's inability to accurately distinguish between 0.2 and 0.23 ppm as a real difference. The revised Section F has deleted the proposed 1.5 ppm total imidacloprid tolerances on raisins and grape juice.

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

a. Based on the results of the imidacloprid bovine feeding study we reiterate that finite residues will actually occur in milk and meat from the feeding of imidacloprid treated racs or their processed feed items when Admire® is used as directed. Since this situation falls under 40 CFR §180.6(a)(1), secondary imidacloprid tolerances are required for milk and meat. CBTS concludes the imidacloprid bovine feeding study adequately supports the proposed 0.1 ppm tolerance in milk and the 0.3 ppm tolerance in meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep.

b. Based on the results of the imidacloprid poultry feeding study CBTS reiterates that finite residues will actually occur in eggs and poultry meat from feeding of imidacloprid treated racs or their processed feed commodities when Admire® is used as directed. Since this situation falls under 40 CFR §180.6(a)(1), secondary imidacloprid tolerances are required for eggs and poultry meats. CBTS concludes the imidacloprid poultry feeding study adequately supports the proposed 0.02 ppm tolerance in eggs and the 0.05 ppm tolerance in meat, fat, and meat by-products of poultry as proposed in PP#3F4169.

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

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

RECOMMENDATIONS

CBTS cannot recommend for the requested tolerances for combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, expressed as imidacloprid residues in the fruiting vegetables crop group at 1 ppm, Brassica (cole) leafy vegetables crop at 3.5 ppm, leaf and head lettuce at 3.5 ppm, grapes at 1 ppm, 0.1 ppm in milk, 0.02 ppm in eggs, 0.05 ppm in meat, fat, and meat by-products of poultry, and meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep at 0.3 ppm; food additive tolerance in tomato puree at 2 ppm; and feed additive tolerances for wet tomato pomace at 2 ppm, dry tomato pomace at 6 ppm, wet grape pomace at 2.5 ppm, dry grape pomace at 5 ppm, and on raisin waste at 15 ppm for reasons cited above in our Executive Summary and further described in the Conclusions 5b and c, 6f, g, i, and j, and 9a, b, and c above.

For further consideration of this petition the petitioner should be advised to resolve the deficiencies described in our Executive Summary and further detailed in our conclusions above.

DETAILED CONSIDERATIONS

BACKGROUND

CBTS considers the petition is a first time, food use permanent tolerance request as there are neither temporary nor permanent established imidacloprid tolerances. There is a co-pending first time, food use permanent tolerance request for imidacloprid on apples, potatoes, and cottonseed; and their processed commodities plus meat, milk, poultry, and eggs submitted as PP# 3F4169. The petition review was completed on September 21, 1993, by F.D. Griffith, Jr. The petitioner has submitted several amendments resolving a number of deficiencies which were discussed in the June 7, 1994, review. There has been a successful tolerance method validation (TMV) for both the total imidacloprid residues in plants method and the total residue in animal tissues method. The petition is currently in reject status due to deficiencies remaining in additional residue method validation data at and above the proposed tolerances, directions for use on cotton, need field rotational crop studies, additional magnitude of the residue crop field trial data on cotton, and revised tolerances. The limited field rotational crop studies have been submitted and are currently under review.

CBTS recommended for 6 Emergency Exemptions during the 1993 crop year as follows: on broccoli, cauliflower, and cabbage (93AZ0007), on head and leaf lettuce (93AZ0005), on cotton (93AZ0003), tomatoes (94FL0001), and potatoes (94MI0002). As of March 1, 1994, CBTS has recommended for additional Emergency Exemptions as follows: 1) on cucurbits vegetables crop group (see memorandum for 94TX0004 by F. Griffith, Jr., dated

January 3, 1994), 2) on apples (see memorandum for 94WA0002 by F Griffith, Jr., dated January 3, 1994,), 3) on peppers (see memorandum for 94FL0003 by F. Griffith, Jr., dated January 5, 1994), 4) on oranges and grapefruit (citrus) (see memorandum by F. Griffith, Jr., dated January 28, 1994), and 5) on potatoes (see memorandum for 94OH0001 by F. Griffith, Jr., dated February 16, 1994).

A summary of all plant and animal (rat, ruminant, and poultry) metabolism data were presented to the HED Metabolism Committee on June 22, 1993. The Committee concluded (see memorandum by F. Griffith, Jr., dated June 24, 1993) that:

1. no additional plant or animal metabolism studies are needed at this time,

2. levels of the nitrosimino compound in the technical material were not of TOX concern, thus there is no need to change the manufacturing process to remove it, nor is it necessary to list the compound on a revised Confidential Statement of Formula (CSF),

3. residues of the guanidine and nitrosimino imidacloprid metabolites at the levels in the different metabolism studies reported are not toxicologically significant,

4. other imidacloprid metabolites at the levels reported are of no special toxicological concern, and that no additional separate regulation of residues is warranted, or are separate additional metabolism or toxicological studies warranted at this time and,

5. there are no scientific objections to the tolerance expression being for imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

No new imidacloprid product chemistry data were submitted for the technical grade active ingredient (TGAI). The product chemistry data for the TGAI were reviewed with the registration for use of imidaclo-prid on turf and ornamentals (see memorandum dated December 21, 1992, by K. Leifer). The product chemistry data for the TGAI in a first time food use petition were summarized in our reviews for PP# 3F4169 (qv).

Analysis of the various batches of the TGAI imidacloprid did not reveal any volatile N-nitroso amines to the limits of detection of 0.05 ppm to 0.2 ppm. However, the nitrosoimino analog was detected in all batches analyzed. The HED Metabolism Committee concluded that levels less than 40 ppm were not of toxicological concern, thus there neither is a need to change the manufacturing process to remove the nitrosoimino, nor is it necessary to list it on the Confidential Statement of Formula (CSF).

For the GRN 61 series review of the CSF, dated September 13, 1991, for the TGAI CBTS concludes that the impurities present in the TGAI are not expected to be a residue problem in the subject crops and crop groups when Gaucho®, Confidor®, and Admire® are used as directed.

The product is identified as required for GRN 61-1. The petitioner has adequately

described the beginning raw materials, listed the sources, 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.

For the GRN 62 series the petitioner has provided the certification of limits and described the analytical method used to establish these limits and to be used for enforcement of the label claims. The deficiency relating to method validation data for the formulation enforcement method on accuracy and precision was resolved in the April 21, 1994, amendment.

The petitioner has submitted CSFs for Confidor® 2 Flowable (EPA File Symbol 3125-URT) and Confidor® 2.5% Granular (EPA File Symbol 3125-URT) dated October 20, 1992. The CSF for Admire® Solupak was dated May 25, 1993. All CSFs were signed by J.S. Thornton. Review of the status of the inert ingredients for clearance for use on food commodities is now in the purview of the Registration Division.

DIRECTIONS FOR USE/LABELING

Imidacloprid is proposed as an insecticide to control aphids, **whiteflies** (including **Sweetpotato whiteflies** or **Silverleaf white-flies**), Colorado potato beetles, flea beetles, and thrips in eggplants, tomatoes, and peppers. Imidacloprid is proposed to control aphids and **whiteflies** in broccoli, Brussels sprouts, cabbage, cauliflower, leaf and head lettuce. Imidacloprid is proposed to control leafhoppers and mealy bugs on grapes.

In an letter dated May 25, 1994, the petitioner changed the names from Confidor to Admire for the proposed formulations for use on the leafy, fruiting, and Brassica vegetables; plus added a use for grapes for the 2F formulation; and changed the name for the formulation proposed for use on grapes from Admire to Provado. These name changes are acceptable to CBTS and we find them consistent with the formulation names proposed for co-pending petition PP# 3F4169.

For use on grapes the petitioner proposes foliar application of 0.5 oz/A to 1 oz/A Provado Solupak (EPA File Symbol 3125-EUI) which contains 75% imidacloprid active ingredient (ai) or 0.375 oz (0.023 lb) ai to 0.75 oz (0.047 lb) ai per application per acre in sufficient water to insure through foliar coverage. Two applications are permitted for a total 2 ozs maximum or 1.5 oz ai/A which is 0.094 lb/acre/ crop growing season with a 14 day repeat application interval. Application may up to and including the day of harvest for a 0 day PHI. Provado Solupak may not be applied through irrigation systems to grapes. No other restrictions are on this label for use of imidaclo-prid on grapes.

For the soil application of the 2.5% granular formulation apply 10 lbs/A to 20 lbs/A of Admire 2.5 Granular (EPA File Symbol 3125-UEG) or 0.25 lb/A ai to 0.5 lb/A ai in a narrow band on the plant row within 14 days of planting eggplant, tomato, or pepper seeds, or transplanting tomatoes, eggplants, or peppers. Application may be in-furrow at planting or as a sidedress after the plants are established. Another way to use the Admire 2.5 GR is at a rate of 6.1 oz/1000 row feet (10 lbs/A of Admire) for a 20 inch row spacing to 49 oz/1000 row feet (20 lbs/A of Admire) for a 80 inch row spacing. The maximum application rate of Confidor

2.5 Gr to eggplants, tomatoes, and peppers is 20 lbs or 0.5 lb ai imidacloprid per **year**. The PHI is 21 days and the restriction is not to apply to vegetables grown for seed.

For a soil application of Admire 2.5 GR when planting or trans-planting the Brassica (cole) leafy vegetables, and leafy and head lettuce apply 6.3 lbs/A to 20 lbs/A or 0.158 lb ai/A to 0.5 lb ai/A in a narrow band on the plant row within 14 days of planting. Application may be in-furrow at planting or as a sidedress after the plants are established. Another way to use the Admire 2.5 GR is at a rate of 3.8 ozs/1000 row feet (6.3 lbs/A of Admire) on a 38-40" double row, or 7.7 ozs/1000 row feet (6.3 lbs/A of Admire) for a single 38-40" row to 12.3 ozs/1000 row feet (20 lbs/A of Admire) on a 38-40" double row, or 24.5 ozs/1000 row feet (20 lbs/A of Admire) for a 38-40" single row. The maximum application rate of Admire 2.5 GR is 20lbs or 0.5 lb ai imidacloprid per **year**. The PHI is 21 days and the restriction is not to apply to vegetables grown for seed.

The petitioner proposed use of Gaucho® 240 Flowable, which contains 240 grams of imidacloprid ai per liter (2 pounds per gallon) or 21.4% imidacloprid ai as a seed treatment. Broccoli, cabbage, cauliflower, eggplant, lettuce, pepper, and tomatoes seeds are treated at a rate of 2.25 fl ozs per pound of seed, or 0.035 lb imidacloprid ai (15.9 grams) per lb of seed. Based on standard plant population per acre when the seeds are planted the dose of imidacloprid per acre varies from 0.79 grams/A to 2.5 grams/A or 0.0017 lb/A imidacloprid ai from lettuce seeds to 0.0055 lb/A imidacloprid ai from broccoli seeds. CBTS notes that the amount of imidacloprid on treated seeds adds very little to the total amount of imidacloprid applied per acre per crop growing season when compared to the proposed soil and foliar application rates of 0.5 lb ai/A.

Admire 2 Flowable (EPA File Symbol 3125-UEE) which contains 21.4% imidacloprid ai or 2 lbs/gallon can be applied to the fruiting vegetables crop group; ie, eggplant, tomatoes, and peppers as a soil and/or foliar spray. As a soil application the petitioner proposes use at a rate of 1 pt (16 fl ozs) to 1 qt (32 fl ozs) or 0.25 lb to 0.5 lb ai per acre in a narrow band centered on the plant row from 14 days before planting to the day of planting, at planting as an in-furrow spray at or below the seed level, as a post seeding or transplant soil drench as a side dress after the plants are established, or in drip, trickle irrigation. Another way to consider the use of Admire 2 Flowable is at a rate of 0.6 fl oz per 1000 row feet (1 pint/A of Confidor) for a single 20 inch row spacing to 5.0 fl ozs per 1000 row feet (1 quart/A of Admire) for a single 80 inch row spacing. For soil application the PHI is 21 days and the restriction is do not apply to vegetables grown for seed.

As a foliar spray to the fruiting vegetables crop group Admire 2 Flowable is applied at a rate of 3 fl ozs or 0.047 lb ai imidacloprid per acre per application for a total of 5 application or 15 fl ozs (0.234 lb ai) with a 5 day repeat application interval. As a foliar spray Admire may be applied up to and including the day of harvest for a 0 day PHI. The only restriction is not to apply to vegetables being grown for seed. Regardless of the type of application do not apply more then 0.5 lb/A/**year** ai imidacloprid to the fruiting vegetables crop group.

Admire 2 Flowable can be applied to the Brassica (cole) vegetables crop group; ie, broccoli, Brussels sprouts, cabbage, and cauli-
flower; and to head and leaf lettuce as a soil and/or foliar spray. As a soil application the petitioner proposes use at a rate of 10 fl ozs to 1 qt (32 fl ozs) or 0.156 lb to 0.5 lb ai per acre

in a narrow band centered on the plant row from 14 days before planting to the day of planting, at planting as an in-furrow spray at or below the seed level, as a post seeding or transplant soil drench as a side dress after the plants are established, or in drip, trickle irrigation. Another way to consider the use of Admire 2 Flowable is at a rate of 0.4 fl oz per 1000 row feet (10 fl oz/A of Admire) for a double 38-40" row spacing to 2.4 fl ozs per 1000 row feet (1 quart/A of Admire) for a single 38-40" row spacing. For soil application the PHI is 21 days and the restriction is do not apply to vegetables grown for seed.

As a foliar spray to the Brassica (cole) leafy vegetables crop group and leaf and head lettuce Admire 2 Flowable is applied at a rate of 3 fl ozs or 0.047 lb ai imidacloprid per acre per application for a total of 5 applications or 15 fl ozs (0.234 lb ai) with a 5 day repeat application interval. The PHI is 7 days and the only restriction is not to apply to vegetables being grown for seed. Regardless of the type of application do not apply more then 0.5 lb/A/**year** ai imidacloprid to the Brassica (cole) leafy vegetables crop group or to lettuce.

As a foliar spray to grapes Admire 2 Flowable is applied to grapes at a rate of 1.5 to 3 fl ozs or 0.024 to 0.047 lb ai imidaclo-prid per acre per application with a 14 day repeat application interval and a 0 day PHI. A maximum of 6 fl ozs of Admire or 0.094 lb ai imidacloprid may be applied to grapes per crop growing season.

The petitioner has proposed an adequate set of directions for use of imidacloprid as Provado Solupak on grapes, and as Admire 2.5 Granular and Admire 2 Flowable on the fruiting vegetables and Brassica (cole) leafy vegetables crop groups, on leafy and head lettuce, and on grapes.

NATURE OF THE RESIDUE - PLANTS

Tomatoes

The petitioner presented the results of an imidacloprid tomato metabolism study in a document titled "Investigation on the Metabolism of NTN 33893 After Application to Tomatoes." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

The petitioner conducted a two part metabolism study with one part being determining the metabolism after surface application and the other part being after stem injection. In summary for the surface application tomatoes were brushed with a 0.05% ai solution of ^{14}C-imidacloprid and mature tomatoes were harvested at 4, 7, 14, and 21 days after application. For the second part of the study, tomato plants were injected in the stems with a mixed solution of ^{12}C-, ^{13}C-, and ^{14}C-imidacloprid at a rate of 10 mg and the plants were harvested 10 days later. The mature tomatoes were separated from the vines and analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR).

In mature tomatoes the total ^{14}C-imidacloprid equivalents at 4 day PHI were 1 ppm of which 0.95 ppm (95%) was imidacloprid, per se. Other residues identified were the guanidine imidacloprid at 0.011 ppm (1.1%), the urea imidacloprid at 0.009 ppm (0.9%), the olefin imida-cloprid 0.001 ppm (0.1%), the hydroxy imidacloprid at 0.011 ppm (1.1%), the nitrosimino imidacloprid at 0.003 ppm (0.3%), and the gentiobioside of 6-CPA. The petitioner has

identified 0.986 ppm (99%) of the residue in tomatoes.

A similar metabolic profile was observed in tomatoes harvested at 7 and 14 days after application. At 7 days PHI total imidacloprid equivalents were 0.84 ppm and at 14 days PHI total imidacloprid equivalents were 0.85 ppm. Imidacloprid, per se, was 0.75 ppm (88%) of the 14 days residues. Other residues at 14 days PHI were the guanidine imidacloprid at 0.022 ppm (2.6%), the urea imidacloprid at 0.016 ppm (1.9%), the olefin imidacloprid at 0.004 ppm (0.5%), the hydroxy imidacloprid at 0.015 ppm (1.8%), the nitrosimino imidacloprid at 0.006 ppm (0.8%), the 6-CPA glucoside at 0.0008 ppm (0.1%), and the 6-CPA gentiobioside. The petitioner has identified 0.82 ppm (96.4%) out of 0.85 ppm.

At 21 days PHI the total imidacloprid residue was 0.60 ppm of which 0.51 ppm (79.4%) was imidacloprid, per se. The same imidaclo-prid metabolites were detected at 21 days PHI as were detected at 14 days PHI, only the percentages increased slightly.

Eggplant

The petitioner presented the results of an imidacloprid eggplant metabolism study titled "Metabolism of NTN 33893 in Eggplant by Planting Hole Application." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

The petitioner treated eggplants at transplanting with 2 grams per plant of a 1% ^{14}C-imidacloprid granular formulation. Edible fruits from the eggplants were harvested at PHIs of 49, 53, and 67 days. The eggplant fruit was analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR).

The total ^{14}C-imidacloprid equivalents in the edible eggplants ranged from 0.0315 ppm at 53 days PHI to 0.0534 ppm at 67 days PHI, averaging 0.0428 ppm. Since we are dealing with low levels of total radioactivity from the ^{14}C-imidacloprid application and the same metabolites were detected at all three PHIs we will review only the average residues reported. Imidacloprid, per se, was 0.0081 ppm (18.9%) of the residue. The major metabolites identified were the guanidine imidacloprid at 0.0049 ppm (14%), 6-CNA at 0.0035 ppm (13.4%), and the 6-CPA glucoside at 0.0066 ppm (13.0%). Other metabolites detected were the 5-hydroxy imidacloprid at 0.0015 ppm (3.2%), the olefin imidacloprid at <0.005 ppm (0.17%), and the nitrosimino imidacloprid at <0.005 ppm (0.093%). The urea imidacloprid was not detected. The petitioner identified 62.8% of the TRR in the eggplant fruit.

Apples

The petitioner presented the results of an imidacloprid apple metabolism study in a document titled "Metabolism of [^{14}C] NTN 33893 in Apples." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

In summary, 80 Golden Delicious apples received 3 applications one month apart of 0.299 mg of pyridinyl-^{14}C-methyl imidacloprid that had a specific activity of 92.3 uCi/mg and was formulated as a 25% WP. The apples were harvested at 0 and 14 days PHI and

analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR). Approximately 80% of the applied residue was recovered and about 70% of the recovered residue was in the peel.

The petitioner determined the residues in the wash solution (surface residues), pulp, and apple peels, then summed the results. The same metabolites were identified in each apple component, only differing in the amount detected. At 0 day PHI the total ^{14}C-imida-cloprid was 1.76 ppm of which 1.36 ppm (77%) was imidacloprid, per se, (1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-N-nitro-1H-imidazol-2-amine). Other residues identified were the 5-hydroxy imidacloprid or WAK 4103 (1-[(6-chloro-3-pyridinyl)methyl-4,5-dihydro-5-hydroxy-N-nitro-1H-imidazol-2-amine) at 0.038 ppm (2.2%), the dihydroxy imida-cloprid or WAK 3772 (1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-dihydroxy-N-nitro-1H-imidazol-2-amine) at 0.014 ppm (0.9%), the olefin imidacloprid or NTN 35884 (1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-1H-imidazol-2-amine) at 0.077 ppm (4.3%), the guanidine imidacloprid or NTN 33823/WAK 4140 (1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-1H-imidazol-2-amine) at 0.045 ppm (2.6%), the urea imidacloprid or DIJ 9817 (1-[(6-chloro-3-pyridinyl)methyl]imidazolidine-2-one) at 0.024 ppm (1.3%), the nitrosimino imidacloprid or WAK 3839 (1-[(6-chloro-3-pyridinyl)methyl]-N-nitroso-2-imino-imidazolidine) at 0.011 ppm (0.6%), and the glucoside of 6-chloropicolyl alcohol (6-CPA) or RBN 1114 at 0.021 ppm (1.3%). The petitioner has identified 1.59 ppm (90.1%) out of 1.76 ppm with 0.13 ppm being extracted, but not identified. The petitioner claims there are 26 unidentified unknowns, though reviewing the copies of the TLC chromatogram CBTS cannot confirm any of the unknowns. Only 0.037 ppm (2.1%) of the TRR was unextractable.

The residue profile on apples treated with ^{14}C-imidacloprid at 14 days PHI was nearly identical to the 0 day residue profile. The total ^{14}C-imidacloprid residue was 1.44 ppm, of which 0.99 ppm (69%) was imidacloprid, per se. The qualitative identification of imidacloprid metabolite residues for 14 days PHI was the same as at 0 days PHI; and the quantitative differences were small.

All of the identified metabolites contain the 6-chloropyridinyl moiety and all of the metabolites, except 6-CNA and 6-CPA, contain both rings of imidacloprid. The proposed residue analytical method will recover the metabolites of concern in that 85 to 90% of the residue is identified and that the proposed common moiety method recovers around 83% of the total residue. The question on whether or not the petitioner needs to do a double labeled metabolism study with a ^{14}C- label in the dihydroimidazole ring can be resolved by a logical review of the existing data. Only 1-2% (0.02-0.03 ppm) of the residue is identified as 6-CNA/6-CPA, thus it follows that only 1-2% of the residue are metabolites that contain the dihydroimidazole ring. Based on the October 1989 Overview of Residue Chemistry Guidelines the petitioner has adequately characterized and identified the total residue between 0.01 ppm and 0.05 ppm. CBTS reiterates that there are insufficient residues present to make further identification of metabolites containing only the dihydroimidazole ring.

Potatoes

The petitioner presented the results of an imidacloprid in potatoes metabolism study following a foliar application in a document titled "Study on Metabolism of NTN 33893 After Spray Application to Potatoes." The petitioner also presented the results of an imidacloprid in potatoes metabolism study following a granular application in a document tiled " Investigation of the Metabolism of NTN 33893 in Potatoes Following Granular Application." These studies have been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

The potatoes were treated at planting in-furrow at a rate of 1.52 grams per 1000 row feet (0.165X application rate) and harvested 129 days later. The mature tubers were separated from the withered vines and analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR).

The total ^{14}C-imidacloprid equivalents in the potato vines were 5.76 ppm and in potato tubers were 0.091 ppm. These residues were the sum of all of the radioresidues determined in the extracts plus the solid remainder. In the potato tubers 0.044 ppm (48.3%) was identified as the parent imidacloprid. 5-hydroxy imidacloprid was 0.007 ppm (8%) and the olefin imidacloprid was 0.003 ppm (3.1%) of the residue. 6-CNA was 0.009 ppm (9.4%) and the guanidine imidacloprid was 0.01 ppm (11.3%) of the residue. In potato tubers the petitioner identified 0.073 ppm (80.1%) of the 0.091 ppm. An additional 0.012 ppm (13.1%) was the sum of 5 unidentified metabolites and only 0.006 ppm (6.4%) of the residue was unextracted.

The residues detected in the potato vines confirm the metabolic pathway found in potato tubers. In potato vines 1.53 ppm (26.7%) of the 5.76 ppm was the parent imidacloprid. 5-hydroxy imidacloprid was 0.26 ppm (4.6%) and the olefin imidacloprid was 0.19 ppm (3.3%) of the residue. 6-CNA and the guanidine imidacloprid were each 0.48 ppm (8.3%) of the residue. Dihydroxy imidacloprid was 0.02 ppm (0.3%) and the glucoside of 6-CPA was 0.08 ppm (1.4%). Nitrosimino imidacloprid was 0.015 ppm (2.6%) of the residue. The petitioner has identified 3.19 ppm (55.4%) out of 5.76 ppm. 14 unidentified metabolites with a sum of 0.93 ppm were reported and 1.52 ppm (26.4%) was non-extract-able.

Starting with a larger total radioresidue in potato vines and identifying more metabolites helps for tentative identification of metabolites in potato tubers. CBTS feels that it is probable that the nitrosimino, dihydroxy, and 6-CPA glucoside are present in the potato tubers, only at too low a level to confirm. CBTS reiterates that since potato vines are neither a livestock feed item nor a human food commodity we do not feel additional measures are necessary to identify any of the unidentified residues in potato vines. The metabolic profile determined in potato vines supports the metabolic profile determined in potato tubers.

For the foliar part of the imidacloprid potato metabolism study the petitioner sprayed potatoes once at a rate of 0.12 lb ai/A. Samples were harvested at 7, 28, and at maturity 64 days after application. The tubers were cleaned by washing.

The total ^{14}C-imidacloprid equivalents in potato tubers were 0.009 ppm from the foliar application of which 0.007 ppm was extract-able. The parent imidacloprid was 0.001 ppm and 6-CNA was 0.003 ppm. 0.001 ppm was bound, unextractable residue. The remaining 0.004-0.005 ppm was composed of 3 metabolites and diffuse radioactivity.

The residues detected in potato vines confirm the pathway found in tubers and the metabolic pathway found from the in-furrow at panting granular application. In potato vines 0.51 ppm (37.9%) of the 1.35 ppm total residue was the parent imidacloprid. 5-hydroxy imidacloprid was 0.095 ppm (7%) and the olefin imidacloprid was 0.034 ppm (2.5%) of the residue. The major metabolite detected was the guanidine imidacloprid at 0.17 ppm (12.6%). The nitrosimino imidacloprid was 0.03 ppm (2.2%) and the dihydroxy imidacloprid was 0.036 ppm (2.7%) of the residue. 6-CNA was not detected; however the 6-CPA glucoside was found at 0.025 ppm (1.9%). One metabolite was identified that has not been reported in other metabolism studies. It is the triazinone imidacloprid or BNF 4712B at 0.014 ppm. The petitioner has identified 0.901 ppm (66.8%) of the 1.35 ppm residue in potato vines. 0.19 ppm 14.1%) remained in the vines as unextracted bound residue and 0.258 ppm (19.1%) was unidentified metabolites.

Plant Cell Suspension Cultures

The petitioner presented the results of imidacloprid metabolism in plant cell suspension cultures in a study titled "Comparative Metabolism of[pyridinyl-14C] NTN 33893 in Plant Cell Suspension Cultures."

The results of the study showed there were both qualitative and quantitative differences in cell suspension metabolism of imidaclo-prid. While imidacloprid was metabolized in all cell cultures the extent of metabolism varied widely. Imidacloprid, per se, was the dominant residue detected, except in apples, as it accounted for 77.1% to 98.5% of the recovered residues. In apples imidacloprid was only 39.4% of the residue recovered. The results of the plant cell suspension culture metabolism studies are complementary to the 14C-imidacloprid metabolism studies conducted and reported for tomatoes, corn, apples, and potatoes. This supports the conclusion that imidacloprid is metabolized by the same three pathways described in the nature of the residue summary.

Corn

The petitioner presented the results of an imidacloprid corn metabolism study in a document titled "Metabolism of NTN 33893 in Corn after Seed Dressing." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

The purpose of the study is to determine the metabolism of imidacloprid in corn after seed treatment. The ^{14}C-imidacloprid was formulated as a 70 WS and the corn seed was treated at a rate of 721 grams/100 kg seed, 1.5 ozs ai/A assuming a corn seeding rate of 15 kg corn seed/hectare. Corn plants grown from treated seed were harvested at 33 days (6-7 leaf stage) and at 61 days (9 leaf stage). At maturity or 134 days after planting the mature corn grain, fodder, husk, and cob were harvested and analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR).

At 33 days after planting the total ^{14}C-imidacloprid residue equivalents in immature corn

forage were 5.84 ppm of which 3.81 ppm (65.2%) was imidacloprid, per se. Other residues identified in corn forage at 33 days PHI were the 5-hydroxy imidacloprid at 0.41 ppm (7%), the 6-CNA at 0.04 ppm (0.7%), the olefin imidacloprid at 0.26 ppm (4.5%), the nitrosimino imidacloprid at 0.1 ppm (1.7%), the dihydroxy imidacloprid and 6-CPA at 0.03 ppm (0.5%), the ring open guanidine imidacloprid at 0.04 ppm (0.6%), the guanidine imidacloprid at 0.33 ppm (5.7%), and the urea imidacloprid at a trace. The petitioner identified 5.05 ppm (86.4%) of the 5.84 ppm residue. There are 7 other metabolites totaling 0.2 ppm and 0.44 ppm (7.6%) unextractable residue.

The same metabolites were identified in corn forage at 61 days PHI, only the amounts were different. At 61 days PHI the total 14C-imidacloprid residues were 1.52 ppm. The petitioner also presented 134 PHI residue data for corn husks at 0.21 ppm and in corn cobs at 0.12 ppm.

In 134 day PHI corn grain the total ^{14}C-imidacloprid equivalents were 0.04 ppm of which 0.01 ppm (25.2%) was imidacloprid. Other metabolites identified were 6-CNA at a trace level, the 5-hydroxy imidacloprid at 0.004 ppm (9.3%), the olefin imidacloprid 0.005 ppm (13.1%), the dihydroxy imidacloprid and 6-CPA at 0.002 ppm (4.4%) ,the guanidine imidacloprid at <0.001 ppm (2%). The petitioner has identified 0.023 ppm (58.4%) of the 0.04 ppm residue in corn grain. Two other metabolites at < 0.002 ppm (4.6%) of the residue were not identified and 0.01 ppm (26.2%) of the residue was unextracted.

In corn fodder the petitioner identified the same residues as were identified in the 33 and 61 days PHI, only the amounts were different. In 134 day PHI corn fodder only 0.68 ppm (22.2%) of the 3.08 ppm was imidacloprid. The petitioner identified 64.8% of the residue in corn fodder.

The imidacloprid corn metabolism study confirms that from imida-cloprid treated seeds residues will translocate from the seed and be detectable in the edible portion of the crop.

Summary

In summary the nature of the imidacloprid residue in apples, potatoes, tomatoes, eggplant, and in corn grain, forage, and fodder; and cottonseed is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy, and dihydroxy imidacloprid followed by loss of water to form the olefin imidacloprid,

2) reduction and loss of the nitro group on the dihydroimidazole ring to form the nitrosimine imidacloprid, then the guanidine imidacloprid, and finally the urea imidacloprid and,

3) bridge cleavage of the C-N bond to form the 6-chloro-picolyl alcohol (6-CPA) which rapidly forms the glucoside and 6-chloro-nicotinic acid (6-CNA) and dihydroimidazole.

The imidacloprid residues of concern in plants are imidacloprid and its metabolites

containing the 6-chloropyridinyl moiety.

NATURE OF THE RESIDUE - LIVESTOCK

Ruminants

The petitioner presented the results of a caprine imidacloprid metabolism study in a document titled "[pyridinyl-^{14}C-methylene] Imidacloprid: Absorption, Distribution, Excretion, and Metabolism in a Lactating Goat." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

In summary, the petitioner dosed a lactating goat for three consecutive days at a rate of 10 mg/kg body weight which is equivalent to approximately 200 ppm in the feed. Milk was collected twice daily during the test and sacrifice was 2 hours after the last dose. Samples collected were liver; both kidneys; loin, round, and flank muscle; and SC, omental, and perirenal fat. Samples were analyzed by acceptable analytical techniques to determine the total ^{14}C-imidaclo-prid and to characterize and identify the components of the total radioactive residue (TRR) in milk and caprine tissues.

Results of the total ^{14}C-imidacloprid equivalents in the tissues are 3.8 to 4.0 ppm in the different muscle samples, 1.8 to 2.2 ppm in the different fat samples, a maximum of 4.1 ppm in milk, 17.1 ppm in liver, and 13.5 ppm in kidney.

In milk the petitioner identified imidacloprid, per se, at 2.27 ppm (55.3%) out of the 4.1 ppm. Metabolites identified were nitros-imino imidacloprid at 0.014 ppm (0.3%), the glycine conjugate of 6-CNA at 0.13 ppm (3.1%), the olefin imidacloprid at 0.23 ppm (5.6%), the 4-hydroxy imidacloprid at 0.4 ppm (9.7%), and the 5-hydroxy imidacloprid at 0.29 ppm (7%) for a total of 81% of the residue. The same six metabolites were identified in all of the milk samples, only the amounts were different.

The same five compounds and at nearly the same percentages were identified in all three muscle tissue samples. In loin muscle imida-cloprid, per se, was detected at 2.65 ppm (69.8%) out of 3.8 ppm, followed by the olefin imidacloprid at 0.23 ppm (6.1%), and the 4-hydroxy imidacloprid at 0.27 ppm (7.1%). 5-hydroxy imidacloprid was detected at 0.12 ppm (3.2%) and the nitrosimino imidacloprid was at 0.02 ppm (0.6%). The petitioner identified 3.3 ppm (86.8%) out of 3.8 ppm in loin muscle.

The same five compounds and at nearly the same percentages were detected in all three fat tissue samples. In SC fat the parent imidacloprid was detected at 1.54 ppm (73.5%) out of the 2.2 ppm. Metabolites detected were the olefin imidacloprid at 0.17 ppm (7.7%), the 4-hydroxy imidacloprid at 0.12 ppm (5.8%), the 5-hydroxy imidacloprid at 0.07 ppm (3.1%), and the nitrosimino imidacloprid at 0.01 ppm (0.6%). The petitioner has identified 1.91 ppm (90.9%) out of 2.2 ppm.

In liver the petitioner identified the glycine metabolite of 6-CNA at 0.16 ppm (0.96%), the picolylic amine at 0.74 ppm (0.43%), the picolylic urea at 0.22 ppm (1.3%), the imidacloprid urea at 0.34 ppm (2%), the olefin imidacloprid at 0.54 ppm (3.2%), the aminoguanidine imidacloprid at 0.26 ppm (1.5%), the nitroguanidine imidacloprid at 0.06 ppm

(0.35%), the dihydroxy guanidine imidacloprid at 0.1 ppm (0.6%), the guanidine imidacloprid at 2.8 ppm (16.4%), and the ring open guanidine imidacloprid at 1.2 ppm (7.2%). The petitioner has identified 5.8 ppm (34%) out of 17.1 ppm. When the liver was analyzed with the common moiety method that detects all of the metabolites that can be converted to 6-CNA, then 11.8 ppm are recovered (68.7%). An additional 6 ppm of 6-CNA containing metabolites are recovered with the common moiety method that the petitioner has not identified. CBTS could consider this to be adequate characterization. Additional identification is not justified as the proposed tolerance expression is based on the common moiety method and whatever new metabolite(s) that could be identified will be determined as 6-CNA.

Residues identified in the kidney are the glycine conjugate of 6-CNA at 2.3 ppm (16.8%), 6-CNA at 0.04 ppm (0.32%), picolylic amine at 0.25 ppm (1.8%), picolylic urea at 0.03 ppm (0.2%), urea imidacloprid at 0.099 ppm (0.7%), olefin imidacloprid at 2.4 ppm (17.7%), and nitroguanidine imidacloprid at 0.11 ppm (1%). 4-hydroxy, 5-hydroxy, and dihydroxy were determined at a total of 0.26 ppm (2%). The glucu-ronide conjugates of 4-hydroxy and 5-hydroxy imidacloprid were detected at 1.9 ppm (14.1%). Dihydroxy guanidine imidacloprid was detected at 0.08 ppm (0.6%), while guanidine imidacloprid was determined at 0.8 ppm (5.9%), and ring open guanidine was at 0.6 ppm (4.2%). Imidaclo-prid, per se, was detected at 0.84 ppm (6.2%). The petitioner has identified a total of 9.7 ppm (71.6%) of the 13.5 ppm in caprine kidney.

When the kidney was analyzed with the common moiety method that detects all of the metabolites that can be converted to 6-CNA, then a total of 10.6 ppm are recovered (77.9%). An additional 0.9 ppm of 6-CNA containing metabolites are recovered with the common moiety method that the petitioner has not identified. CBTS would consider this is adequate characterization of the residue in caprine kidney.

Summary

The nature of the imidacloprid residue in ruminants is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy, plus the glucuronide conjugates of each monohydroxy metabolite, and dihydroxy imidacloprid followed by the loss of water to form the olefin imidacloprid,

2) reduction and loss of the nitro group on the dihydro-imidazole ring to form the aminoguanidine imidacloprid, then the guanidine imidacloprid. and finally the urea imidacloprid and,

3) opening of the dihydroimidazole ring with the loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine which can also form from both the guanidine imidacloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea and picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA) and then conjugates with glycine.

The residues of concern in ruminants are imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

Poultry

The petitioner presented the results of a poultry imidacloprid metabolism study in a document titled"[Methylene-^{14}C] Imidacloprid Absorption, Distribution, Excretion, and Metabolism in Laying Hens." This study has been previously reviewed in PP# 3F4169 by F. Griffith, Jr., in his September 21, 1993, memorandum (qv).

In summary, the pullets were dosed orally via a syringe daily for 3 days at a rate of 10 mg/kg body weight which is equivalent to 100 ppm in the feed. Eggs were collected throughout the test period and at sacrifice both kidneys, liver, gizzard (without lining and contents), skin (without SC fat), breast muscle, thigh muscle, and subcutaneous (SC) fat. Samples were analyzed by acceptable analytical techniques to determine the total ^{14}C-imidacloprid and to characterize and identify the components of the total radioactive residue (TRR) in milk and caprine tissues.

Results for the total ^{14}C-imidacloprid equivalents in the edible poultry tissues are 18.9 ppm in kidneys, 12.8 ppm in liver, 2.4 ppm in gizzard, 2.1 ppm in breast muscle, 2.3 ppm in thigh muscle, 3.0 ppm in skin, 1.5 ppm in SC fat, and 0.44 ppm in eggs.

In eggs nearly 97% of the residue was extracted. Residues identified were picolylic urea at 0.009 ppm (2%), the olefin imida-
cloprid at 0.14 ppm (31.8%), 4-hydroxy imidacloprid at 0.028 ppm (6.4%), 5-hydroxy imidacloprid at 0.049 ppm (11.1%), the dihydroxy imidacloprid at 0.002 ppm (0.4%), the nitroguanidine imidacloprid 0.087 ppm (19.8%), the picolylicamine at 0.019 ppm (4.3%), the dihydroxy guanidine imidacloprid at 0.004 ppm (0.9%), imidacloprid at 0.023 ppm (5.2%),and the ring open guanidine at 0.19 ppm (4.3%), and a mixture of the hydroxy imidacloprids at 0.005 ppm (1.1%).

More than 99% of the residue was extracted from the liver. Residues identified were 6-CNA at 0.31 ppm (3.2%), the picolylic urea at 0.97 ppm (7.6%), the nitroguanidine imidacloprid at 1.12 ppm (8.8%), the olefin imidacloprid at 1.91 ppm (15%), a combination of the 4-hydroxy, the 5-hydroxy, and the dihydroxy imidacloprid at 1.06 ppm (8.4%), the picolylic amine at 0.22 ppm (1.9%), the dihydroguanidine imidacloprid at 0.27 ppm (2.1%), the ring open guanidine imidacloprid at 1.99 ppm (15.6%), and an isomeric form of the dihydroxy imida-cloprid at 0.18 ppm (1.4%). The petitioner has identified 8.1 ppm (63.3%) out of 12.8 ppm of the residue in poultry liver.

About 92% of the residue was extractable from poultry muscle. Residues identified were picolylic urea at 0.08 ppm (3.7%), the nitro-guanidine at 0.15 ppm (6.7%), the olefin imidacloprid at 0.59 ppm (26.7%), the 4-hydroxy imidacloprid at 0.1 ppm (4.6%), the 5-hydroxy imidacloprid at 0.19 ppm (8.6%), picolylic amine at 0.08 ppm (3.6%), the dihydroxy guanidine at 0.03 (1.4%), imidacloprid and the ring open guanidine each at 0.14 ppm (6.3%), a mixture of the hydroxy imidaclo-prids at 0.03 ppm (1.5%), another olefinic metabolite at 0.04 ppm (1.8%), a diketo metabolite at 0.02 ppm (0.7%), and a mixture of two compounds one of which is a N-acetylpicolylic amine at 0.05 ppm (2.4%). The petitioner has identified 1.6 ppm (77.8%) out of 2.1 ppm of the residue in poultry muscle.

Approximately 73% of the residues was recovered from poultry fat. Residues identified were picolylic urea at 0.02 ppm (1.4%), 6-CNA at 0.03 ppm (1.9%), the olefin imidacloprid at 0.35 ppm (22.6%), the 4-hydroxy imidacloprid at 0.04 ppm (2.4%), the 5-hydroxy imidacloprid at 0.15 ppm (9.7%), the nitroguanidine at 0.08 ppm (5.2%), picolylic amine at 0.02 ppm (1.5%), imidacloprid at 0.19 ppm (12.4%), and the ring open guanidine at 0.07 ppm (4.2%). The petitioner has identified 0.94 ppm (62.5%) out of the 1.51 ppm of the residue in poultry fat.

Summary

The nature of the imidacloprid residue in poultry is adequately understood. Imidacloprid is metabolized by three pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imida-cloprid to form 4-hydroxy, 5-hydroxy, and dihydroxy imidacloprid followed by loss of water to form the olefin imida-cloprid,

2) reduction and loss of the nitro group on the dihydro-imidazole ring to form the dihydroxyguanidine imidacloprid and,

3) opening of the dihydroimidazole ring with loss of the ethyl group and subsequent oxidation. The first step is forming the nitro-guanidine imidacloprid, next the ring open guanidine which can also form from both the guanidine imidacloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea and picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA).

The residues of concern in poultry are imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

CONFINED ACCUMULATION STUDIES ON ROTATIONAL CROPS

The petitioner presented the results of a ^{14}C-imidacloprid confined accumulation study in rotational crops in a document titled "[Pyridinyl ^{14}C-methyl] NTN 33893 Residues in Rotational Crops" by K. Vogeler, et. al., dated August 10, 1992, coded laboratory project ID M 130 0279-2 and Miles report number 103812 (MRID # 425561-04).

Total ^{14}C-imidacloprid was determined in rotational crops following a singular spray application to sandy loam soil at a rate of 0.4 lb ai/A. 0.4 lb a.i./A is a reasonable approximation of the 0.3 lb a. i./A proposed use for cotton and potatoes and the 0.5 lb a.i./A proposed use in fruiting vegetables and Brassica (cole) leafy vegetables. The leafy vegetable used in this study was Swiss Chard; the root crop used was red beets; and the cereal grain was wheat. These crops were planted 30 days after ^{14}C-imidacloprid application. Following harvest of the crops the soil was mixed and replanted with the same crops at 120 days after the single imidacloprid application. These crops were grown to maturity and harvested. The soil was mixed a third time at 271 days after the single imidacloprid application and replanted again. The wheat was sampled at the appropriate growth stage to be considered wheat forage and at maturity the wheat was separated into grain and straw. At harvest the red beets were separated into leaves and red beet roots. All harvested samples were homogenized and

stored frozen until analysis.

The residue analytical methods used to characterize and identify imidacloprid and its metabolites are essentially the same as the methods used in other ^{14}C-imidacloprid metabolism studies which have been previously reviewed.

Total imidacloprid residues in wheat grain were 0.07 ppm (120 days), 0.06 ppm (271 days), and 0.03 ppm (408 days). The same magnitude of the imidacloprid residue was detected in beet roots at 0.07 ppm (120 days), 0.03 ppm (271 days), and 0.04 ppm (384 days). higher residues were detected in beet leaves and Swiss chard. In beet leaves total imidacloprid residue were 0.26 ppm, 0.2 ppm, and 0.17 ppm; while in Swiss chard total imidacloprid residues were 0.13 ppm (93 days), 0.24 ppm (201 days), and 0.09 ppm (345 days). Total imidacloprid residues in wheat forage were 0.48 ppm, 1 ppm, and 0.26 ppm. The highest total imidacloprid residues were detected in wheat straw at 2.5 ppm, 2.38 ppm, and 0.96 ppm.

The petitioner reported the identification of imidacloprid in samples from all 3 crop rotations in red beet roots and leaves, Swiss chard, and in wheat grain, forage, and straw. The same metabolites were identified in all 3 rotations differing only slightly in the amount reported. At the first rotation in beet roots imidacloprid was at 0.0041 ppm. Metabolites identified were the 4-hydroxy/5-hydroxy at 0.0034 ppm (4.9%), the dihydroxy and 6-CPA at 0.0004 ppm (0.5%), the olefin at 0.0009 ppm (1.3%), the nitrosimino at 0.0002 ppm (0.3%), the glucoside at 0.0001 ppm (0.2%), and 6-CNA at 0.0096 ppm (13.5%), and the ring open guanidine at 0.004 ppm (5.4%). In beet leaves imidacloprid was 0.01 ppm (3.7%). Metabolites identified were the dihydroxy at 0.003 ppm (1.3%), the 4-hydroxy/5-hydroxy at 0.021 ppm (8%), the olefin at 0.01 ppm (4%), the glucoside at 0.002 ppm (0.9%), the 6-CNA at 0.004 (1.7%), the ring open guanidine at 0.008 ppm (3.1%), and the guanidine at 0.02 ppm (8%).

In Swiss chard from the first rotation imidacloprid was 0.031 ppm (23.5%). Other metabolites were the dihydroxy at 0.002 ppm (1.2%), the 4-hydroxy/5-hydroxy at 0.011 ppm (8.1%), the olefin at 0.006 ppm (4.6%), the nitrosimino at 0.0008 (0.6%), 6-CNA at 0.012 ppm (9.3%), the glucoside at 0.003 ppm (2%), the ring open guanidine at 0.002 ppm (1.2%), and the guanidine at 0.015 ppm (11.2%).

Wheat forage samples from the first rotation contained imidacloprid at 0.2 ppm (42.1%). Other metabolites were the dihydroxy at 0.004 ppm (0.9%), the 4-hydroxy/5-hydroxy at 0.067 ppm (14%), the olefin at 0.019 ppm (4%), the nitrosimino 0.013 ppm (2.7%), 6-CNA at 0.004 ppm (0.9%), the glucoside at 0.011 ppm (2.2%), the ring opened guanidine at 0.007 ppm (1.5%), and the guanidine at 0.057 ppm (11.9%).

At the first rotation wheat grain contained imidacloprid at 0.001 ppm (1.9%). Other metabolites were the dihydroxy at 0.003 ppm (3.6%), the 4-hydroxy/5-hydroxy at 0.007 ppm (10.3%), the olefin at 0.004 ppm (5.3%), the glucoside at 0.001 ppm (1.8%), and the guanidine at 0.003 ppm (3.7%).

Wheat straw contained the highest total imidacloprid residues from each of the three rotations. Imidacloprid at the first rotation was 0.12 ppm (4.7%). Other metabolites were the

6-chloropicolyl alcohol at 0.005 ppm (0.2%), the dihydroxy at 0.065 ppm (2.6%), the 4-hydroxy/5-hydroxy at 0.17 ppm (6.8%), the olefin at 0.16 ppm (6.3%), the nitrosimino at 0.03 ppm (1%), 6-CNA at 0.02 ppm (0.6%), the glucoside at 0.12 ppm (4.4%), the ring open guanidine at 0.13 ppm (5%), and the guanidine at 0.46 ppm (18.5%).

The total extractability of imidacloprid residues from rotational crops ranged from 45% in wheat grain to 91% from Swiss chard.

CBTS reiterates that the nature of the residue in rotational crops is nearly identical to that identified in the primary crops. Imidacloprid is metabolized by the same three metabolic pathways as described for apples, cottonseed, eggplants, tomatoes, potatoes, and corn. The petitioner identified around 45% of the residue in the different rotational plant matrices. When the same matrices were analyzed by the common moiety method for 6-CNA, then 91-96% of the residue was recovered. This characterizes the additional components of the residues a containing the 6-chloropyridinyl moiety. The petitioner has adequately characterized and identified the nature of the imidacloprid residue in rotational crops.

CBTS reiterates that all 3 rotational crops in the confined study had imidacloprid residues when planted 1, 4, and 9 months after imidacloprid soil application. The total imidacloprid residues were all greater then 0.01 ppm from a 1X application. We reiterate there is potential for inadvertent imidacloprid residues to occur in non-target crops planted in rotation. Limited field rotational crops studies are necessary for a representative crop at 2 sites per crop for the following 3 crop groups: root and tuber vegetables, leafy vegetables, and cereal grains. At least 6 field trials are necessary; all at the 1X application rate.

CBTS reiterates that based on the data presented from the confined imidacloprid accumulation studies CBTS anticipates that the petitioner will need to propose rotational imidacloprid tolerances. A final decision on which imidacloprid rotational tolerances will be needed as well as the need of more extensive field trial data will be based on the results of the limited field trial results.

RESIDUE ANALYTICAL METHODS

Interference study

The petitioner presented the results of an interference study in a document titled "Interference Study of Imidacloprid Total Residue Method for Crops and Animals" by F.J.Placke dated September 4, 1992, and coded Miles report no. 103828. The petitioner tested 281 compounds having established tolerances through the total imidacloprid in plants method, Bayer method 00200. Only clopyralid at the 500 ppm showed a positive interference and this is not expected to be a problem in determining imidacloprid residues. The petitioner has conducted an interference study that shows positive interferences from other pesticides will not be a problem for the residue analytical method, Bayer method 00200.

Multiresidue method recovery data

The petitioner reported the results of multiresidue method (MRM) testing in studies titled "NTN 33893 Multiresidue Method Testing" by M. VerHey dated August 17, 1989, and

coded ID Mobay 1093; and titled "NTN 33893 Metabolites - Multiresidue Method Testing" by W. McCullough dated September 18, 192, and coded Miles - N3161602 ABC - 40082.

All of the testing was done using the FDA decision tree before starting recovery work using the FDA multiresidue method protocols A through E.

While imidacloprid standards were recovered through the columns listed in Protocol C using EC and N/P detectors it was not eluted off florisil columns, thus no additional work was done for Protocol E (MOG method). Imidacloprid is not recovered through Protocol D (Luke method), does not have a N-methyl carbamate structure (no recovery through Protocol A), and does not have a phenolic or acid structure) no recovery through Protocol B).

The imidacloprid hydroxy, guanidine, olefin, and 6-CNA metabolites were recovered through the columns listed in Protocol C using EC and N/P detectors. The responses were quite variable, low and multiple trailing peaks. None of the metabolites contained a N-methyl carbamate, thus no recovery through Protocol A. Since none of the metabolites eluted off the florisil columns no additional recovery work was done for Protocol E. Like the parent compound there was no recovery for the major metabolites through Protocol E. The methyl ester of 6-CNA was recovery quite well through Protocol B. The urea and nitrosimino imidacloprid metabolites are considered to be minor metabolites (<2% of the TRR) and no MRM recovery data are required.

CBTS concludes that the petitioner has presented adequate MRM recovery data for imidacloprid and its major metabolites through FDA Protocols A through E. All of these data have been forwarded to FDA's for more review and CBTS expects them to be published in the Pesticide Analytical Manual (PAM), Vol I, Appendix I in future update. Unless FDA finds a problem with these MRM recovery data CBTS concludes that no further data are required. CBTS does not anticipate additional MRM recovery data are required for other imidacloprid metabolites.

Residue analytical method - plants

A revised total imidacloprid in plants residue analytical method was submitted as an amendment to PP # 3F4169. The title is "Method for the Determination of Total Residues of Imidacloprid in Plant Materials and Beverages (Bayer Method 00200 - Reformatted)" by Weber and Krolski dated February 23, 1994, and coded Miles Report No. 102624-R1 (MRID # 431432-02).

Bayer method 00200 is basically a common moiety method for total imidacloprid and its metabolite residue containing the 6-chloropyridinyl moiety in plants and beverages using a methanol/sulfuric acid extraction, filtering through celite/filter paper, hexane partitioning when necessary, resin column cleanup, permanganate oxidation, silyl derivatization, and determination in a capillary GC-MS selective ion monitoring at m/z 214.

In summary, samples that contain little oil or wax; eg, lettuce, fruiting vegetables, and cole leafy vegetables, 50 grams of sample are soaked in 300 mls of CH_3OH/1% H_2SO_4 for 30 minutes then blended with a polytron for 3 minutes and filtered through 10 grams of Celite 545 in a Whatman 541 filter paper. Concentration of the filtrate is on a rotary evaporator to about

10 mls. Hexane partitioning, 3 X 100 mls, is only done with high oil samples. Sample clean-up is through a 10 gram XAD-4 resin column with imidacloprid and its metabolites eluted off in 100 mls CH_3OH.

Oxidation of the imidacloprid and its 6-chloropyridinyl metabolites to 6-CNA is done after the extract is adjusted to pH > 14 with 32% NaOH. 50 mls of $KMnO_4$ is added and the solution is refluxed for 5 minutes after brought to a rapid boil. The solution is rapidly cooled and acidified with 10% H_2SO_4 the excess permanganate is destroyed with sodium bisulfite. The solution must be clear, not purple or chocolate brown. 6-CNA is extracted with MTBE (t-butyl methyl ether) 3 X 50 mls, concentrated to just dryness, and brought back to 2.0 mls with ACN. 250 ul of this solution is added to a GC autosampler vial and derivatized with 250ul of MSTFA (N-methyl-N-(trimethyl-silyl)trifluoroacetamide. The contends are mixed and after 1 hour the derivatized sample is ready for GC-MS analysis.

Determination is by GC/MS using a Hewlett-Packard 5890 GC equipped with a 7673 autosampler. The column is a 12 m quartz capillary, 0.2 mm i.d., HP ULTRA 1 (dimethyl silicone), 0.33 um film thickness. Sample injection was in the splitless mode and the column temperature is programmed. The detector is a HP 5970 mass specific detector in the single ion monitoring (SIM) mode for detecting the m/z 214 ion and the confirmatory ions at m/z 216, 170, and 140. The petitioner propose monitoring with the m/z 214 ion at 100% and if necessary with 3 others at m/z 216 at 36-39%, m/z 170 ion at 50-51%, and the m/z 140 ion at 38-41%. These ratios will serve as an index for the determination of interferences, if and when, encountered by any of the 4 ions. The petitioner proposes that if the ratios of these 4 ions in a sample are within 10% of the ratios for the reference analytical standard, and the sample and standard peaks have the same retention time through a capillary column, then the presence of total imidacloprid is confirmed. CBTS agrees this is an acceptable procedure at this time for these 2 petitions only. The separatory power of a capillary column in identifying a compound is just as important, if not more so, than monitoring a third ion and determining its ratio. Quantitation is by peak area from a standard curve. Standards were prepared in ACN and the petitioner claims that the standards will be stable for 6 months if kept refrigerated and in the dark when not in use. Conversion factors to correct for the molecular weight differences between 6-CNA and the analyte of interest, whether it is imidacloprid or a metabolite, are listed.

The petitioner has informed us that imidacloprid is the first of a new class of insecticides. We reiterate that a confirmatory method is needed that precisely identifies imidacloprid and its major metabolites. The method needs to be semi-quantitative, though our choice is to have the method be quantitative. While the confirmatory method has not been presented the petitioner has kept CBTS informed on the progress of method development. In the EPA-Miles meeting of March 2, 1994, the petitioner described the development of a HPLC method that will measure imidacloprid as imidacloprid and separately measure several of the major metabolites. The petitioner is encouraged to continue this method development and present the Agency with the completed validated HPLC method and accompanying ILV data as soon as possible. CBTS reiterates its observation that the petitioner need to keep the lab time of the HPLC method under 2 days as this is necessary for the method to be an effective enforcement procedure.

For PPs # 3F4169 and 3F4231 the lack of the confirmatory procedure is not a bar to

our recommendation for the proposed tolerances, provided no other compounds in this class of insecticides are presented for registration and tolerances. The Branch policy is that as long as this is the only pesticide with a common moiety method that determines its residues as 6-CNA, then a confirmatory method is not required. However, if Miles or a competitor presents another chemical for registration and tolerances that measures its residues as 6-CNA, then a confirmatory method is required that accurately determines the source of the 6-CNA.

Method validation data for Bayer method 00200 from peppers were presented. Imidacloprid and its guanidine metabolite as a mixture were spiked at 0.1, 0.2, 0.5, and 2 ppm. Recoveries ranged from 85% to 103%. Concurrent recoveries from peppers spiked with a mixture of imidacloprid and its guanidine metabolite at 0.2 and 2 ppm ranged from 86% to 119%, n = 15, with only one recovery less than 100%. The LOQ for peppers is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on peppers crop field trial data.

Using Bayer method 00200 method validation data were presented for imidacloprid and its guanidine metabolite spiked as a mixture, plus individual recoveries of imidacloprid, its guanidine, olefin, hydroxy, and 6-CNA spiked at 0.05, 0.1, and 0.25 ppm in tomatoes. Recoveries ranged from 80% to 117%. Concurrent recoveries from tomatoes spiked with a mixture of imidacloprid and its guanidine metabolite at 0.1 ppm ranged from 88% to 117%, n = 16. The LOQ for tomatoes is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on tomatoes crop field trial data.

For the crop group fruiting vegetables the petitioner has not presented either method validation or concurrent recovery data from the representative commodities at the proposed 1 ppm tolerance. To support a fruiting vegetables crop group tolerance the petitioner needs to generate adequate additional method validation data for imidacloprid, its guanidine and one other major metabolite in the representative commodities tomatoes and peppers at the proposed 1 ppm tolerance. CBTS suggests use of a different metabolite in peppers and tomatoes. Some additional method validation data from the representative commodities needs to be generated from a mixture of imidacloprid and its metabolites at the 1 ppm tolerance level.

To support the tomato processing study the petitioner presented method validation data from a spike mixture of imidacloprid and its guanidine metabolite at 0.15, 0.6, and 2.5 ppm in the dry tomato pomace and tomato juice. Recoveries ranged from 88% to 120%. Concurrent recoveries from the whole fruit, dry tomato pomace, puree, and juice ranged from 93% to 121%. The petitioner has presented an adequate amount of validation and concurrent recovery data for imidacloprid and its guanidine metabolite in tomato processed commodities dry pomace, puree, and juice to support the magnitude of the residue data in the tomato processing study. However, in the new imidacloprid tomato processing study to be conducted the petitioner is reminded to generate method validation data for imidacloprid, its guanidine metabolite, and one other major imidacloprid metabolite at the proposed food/feed additive tolerances for each processed tomato commodity.

Using Bayer method 00200 method validation data were presented for imidacloprid and its guanidine metabolite spiked as a mixture, plus individual recoveries of imidacloprid, its

guanidine, olefin, hydroxy, and 6-CNA spiked at 0.1, 0.2, 1, and 10 ppm in cauliflower. Recoveries ranged from 84% to 102%. Concurrent recoveries from tomatoes spiked with a mixture of imidacloprid and its guanidine metabolite at 1 ppm and 10 ppm ranged from 87% to 116%, n = 12. The LOQ for cauliflower is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on cauli-flower crop field trial data.

Concurrent recoveries from broccoli head with stalk spiked with a mixture of imidacloprid and its guanidine metabolite at 1 and 5 ppm ranged from 97% to 120%, n = 12.

Using Bayer method 00200 method validation data were presented for imidacloprid and its guanidine metabolite spiked as a mixture, plus individual recoveries of imidacloprid, its guanidine, olefin, hydroxy, and 6-CNA spiked at 0.1, 0.2, 1, 4, and 10 ppm in head lettuce with and without leaves. Recoveries ranged from 85% to 116%. Concurrent recoveries from cabbage with the wrapper leaves spiked with a mixture of imidacloprid and its guanidine metabolite at 1 ppm, 5 ppm, and 10 ppm ranged from 97% to 120%, n = 17. Concurrent recovery data from leaf lettuce and head lettuce with and without leaves were presented for a mixture of imidacloprid and its guanidine metabolite at 1 ppm, 10 ppm, and 50 ppm. Overall recoveries ranged from 73% to 124%, n = 44, with recoveries from head lettuce alone ranged from 92% to 122%, n = 22. The LOQ for head and leaf lettuce is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on leaf lettuce and head lettuce, with and without wrapper leaves.

Concurrent recoveries from cabbage without the wrapper leaves spiked with a mixture of imidacloprid and its guanidine metabolite at 1 ppm ranged from 93% to 113 %, n = 4. The LOQ for cabbage is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on cabbage crop field trial data.

For the crop group Brassica (cole) leafy vegetables the petitioner has not presented either method validation or concurrent recovery data from the representative commodities at the proposed 3.5 ppm tolerance. To support a Brassica (cole) leafy vegetables crop group tolerance the petitioner needs to generate adequate additional method validation data for imidacloprid, its guanidine and one other major metabolite in the representative commodities broccoli, cabbage, and mustard greens or leaf lettuce substituted for mustard greens at the proposed 3.5 ppm tolerance. CBTS suggests use of a different metabolite for the third fortification in cabbage, broccoli, and mustard greens or leaf lettuce. Some additional method validation data from these representative commodities needs to be generated from a mixture of imidacloprid and its metabolites at the 3.5 ppm tolerance level. The additional method validation data are needed for lettuce as part of the Brassica (cole) leafy vegetables crop group and for the stand alone lettuce tolerance of 3.5 ppm.

Bayer method 00200 method has been validated for imidacloprid and its guanidine metabolite spiked as a mixture, plus individual recoveries of imidacloprid, its guanidine, olefin, hydroxy, and 6-CNA spiked at 0.1, 0.2, and 0.5 ppm in grapes. Recoveries ranged from 85% to 112%. Concurrent recoveries from grapes spiked with a mixture of imidacloprid and its guanidine metabolite at 0.1, 0.2, 0.4, 0.5, 0.8, 1 and 1.6 ppm ranged from 70% to 99%, n = 20. The LOQ for grapes is 0.05 ppm. The method has been adequately validated to gather magnitude of the imidacloprid residue on grapes. However, to support a grape tolerance and tolerances on grape processed commodities the petitioner needs to generate adequate

additional method validation data for imidacloprid, its guanidine and one other major metabolite in grapes and grape processed commodities; ie, at the proposed 1 ppm grape tolerance, 2.5 ppm tolerance in wet grape pomace, 5 ppm tolerance in dry grape pomace, and 15 ppm tolerance in raisin waste. CBTS suggests use of a different metabolite for the third fortification in each grape commodity., Some additional method validation data from these grape commodities needs to be generated from a mixture of imidacloprid and its metabolites at the propose tolerance levels.

To support the grape processing study the petitioner presented method validation data from 2 spike mixtures of imidacloprid and its guanidine metabolite at 0.02-0.03 and 0.35-0.4 ppm in the raisins and grape juice. Recoveries ranged from 80% to 105%. Concurrent recoveries from the whole grapes and its processed grape commodities wet and dry grape pomace, and raisin waste ranged from 93% to 121%.

The petitioner has presented a complete set of supporting chromatographic data showing each control and each fortification. Crop co-extractives as shown on the various chromatograms varied depending on the matrix. The unidentified analytical responses (UARs) do not present an interference problem for determining 6-CNA at m/ 214 in the commodities of interest.

A tolerance method validation (TMV) was requested for imidaclo-prid and its metabolites on apples and cottonseed, and in milk and beef liver (see memorandum in PP# 3F4169 by F. Griffith, Jr., dated March 3, 1993. The plant residue method, Bayer method 00200, was to be validated as a tolerance enforcement method with cottonseed fortified with imidacloprid and its olefin, hydroxy, and guanidine metabolites at 3.5 ppm and 7 ppm. Apples were fortified with the same compounds at 0.5 ppm and 1 ppm. The animal tissues method, Bayer method 00191, was to be validated as a tolerance enforcement method with milk fortified with imidacloprid and its hydroxy, guanidine, and 6-CNA metabolites at 0.05 ppm and 0.1 ppm. Liver was fortified with the same 4 compounds at 0.2 ppm and 0.5 ppm.

A TMV (tolerance method validation) was requested for Bayer method 00200 for imidacloprid and its metabolites in milk and liver (see memorandum by F. Griffith, Jr., dated March 3, 1993). The results of the successful method trial were reported by the Analytical Chemistry Branch (see memorandum in PP# 3F4169 by Stafford and Wright dated April 11, 1994). The 5 analytical method deficiencies noted in the ACB initial method screen pre-review dated April 15, 1993, are all resolved. ACB's comments on the Bayer method 00200 are considered to be minor modifications and will be forwarded to FDA to be published as the EPA addendum along with the method. While ACB did not determine the method's MDL (minimum detection limit) its estimate of 0.02 ppm in apples and cottonseed is supported by chromatographic data. Apples were spiked with imidacloprid, and its olefin, guanidine, and hydroxy metabolites at 0.5 and 1 ppm and cottonseed was spiked with the same compounds at 3.5 and 7 ppm. Based on acceptable recoveries with supporting chromatographic data there has been a successful TMV for Bayer method 00200. The method is only marginally suitable to be an enforcement method with perishable commodities as both the ILV and EPA TMV time frame to complete a set of samples takes approximately 20 hours or into a third working day. CBTS reiterates this method is quite rugged and effective as an enforcement procedure when very rapid turn around times are not required. It meets all other requirements for enforcement as described in Subdivision O and will be forwarded to FDA for publication in

the Pesticide Analytical Manual, Vol II.

Independent laboratory validation (ILV) data - plants

The accompanying independent laboratory Validation (ILV) data generated by Ricerca, Inc., for the revised plant method were presented in a study titled "Independent Laboratory Validation of Miles Method No. 102624-1, Imidacloprid Related Residues in Plants, In Compliance with PR Notice 88-5" by T. Formella dated February 28, 1994, and coded Miles Report No. 106425 (MRID # 431432-05). This study has been previously reviewed by F. Griffith, Jr., in his June 7, 1994, memorandum for PP# 3F4169.

In summary, apples were fortified with imidacloprid, its hydroxy, guanidine, olefin, and 6-CNA metabolites at 0.5 ppm (proposed tolerance) and at 2.5 ppm or 5X proposed tolerance. Ricerca made several minor modifications to the methods, all of which are acceptable. Overall recoveries ranged from 70% to 120%. Extensive supporting chromatographic data were presented which could confirm the results reported. The ILV time estimate to complete a set of samples is 18+ hours with 2 days necessary to complete the extraction and clean-up and the third day necessary for the determination step. An acceptable ILV has been conducted and these data are in agreement with the petitioner's recovery data and the Agency' own recovery data generated during the TMV. No additional ILV data are required for this petition.

Additional ILV data were presented in PP# 3F4169 and reviewed by F. Griffith, Jr., in his June 18, 1993, review. One of the studies was conducted in Germany using the original method which did not include 1% H_2SO_4 in the extraction step and used a fortified control to generate the standard curve. ILV recovery data were generated for imidacloprid and its metabolites in sunflower seeds and for imidacloprid in apples and wheat at the 0.05 ppm LOQ level. CBTS found these data difficult to interpret from the LOQ to the proposed tolerance levels. Another ILV study was done in the USA by ABC Laboratories using the current method but the fortifications for imidacloprid and its 4 major metabolites were all at 0.1 ppm in potatoes, apples, cottonseeds, hulls, oil, and soapstock. CBTS considered these ILV studies to be supplementary as none of the recovery data were generated at the proposed tolerance levels for any of the commodities.

Residue analytical method - animal tissues

The petitioner also submitted a revised total imidacloprid in animal tissues residue analytical method as an amendment to PP # 3F4169. The title is "Method for Determination of Total Residues of Imidacloprid in Animal Materials (Bayer Method 00191 M001 - Reformatted)" by Weber and Heukamp dated January 10, 1994, and coded Miles report number 103848R-1 (MRID # 431432-03).

Bayer method 00191 is also basically a common moiety method for total imidacloprid and its metabolite residue containing the 6-chloro-pyridinyl moiety in milk, eggs, and animal tissues using a methanol/ water extraction, hexane partitioning when necessary, resin column cleanup, permanganate oxidation, silyl derivatization, and determination in a capillary GC-MS selective ion monitoring at m/z 214.

In summary, 10 grams of eggs, muscle, liver, or kidney is blended with a polytron for 30 seconds, centrifuged and the extract decanted into a boiling flask. The extraction is repeated and the supernatents are combined. Concentration of the filtrate is on a rotary evaporator to about 20 mls. Milk and fat are blended in 100 mls of methanol for 30 seconds, centrifuged, and the supernatents are concentrated by rotary evaporation. Hexane partitioning, 3 X 50 mls, is only done with milk and fat samples. Sample clean-up is through a 10 gram XAD-4 resin column with imidacloprid and its metabolites eluted off in 125 mls CH_3OH.

Oxidation of the imidacloprid and its 6-chloropyridinyl metabolites to 6-CNA is done after the extract is adjusted to pH > 14 with 32% NaOH. 50 mls of $KMnO_4$ is added and the solution is refluxed for 5 minutes after brought to a rapid boil. The solution is rapidly cooled 15° and acidified with 10% H_2SO_4. The excess permanganate is destroyed with sodium bisulfite. The solution must be clear, not purple or chocolate brown. 6-CNA is extracted with MTBE (t-butyl methyl ether) 3 X 50 mls, dried through an anh. Na_2SO_4 column, concentrated to just dryness under a gentle stream of N_2, and brought back to 1 ml with ACN. 250 ul of this solution is added to a GC auto-
sampler vial and derivatized with 250 ul of MSTFA (N-methyl-N-(tri-methylsilyl) trifluoroacetamide. The contends are mixed and after 1 hour at ambient temperature the derivatized sample is ready for GC-MS analysis.

Determination is by GC/MS using a Hewlett-Packard 5890 GC equipped with a 7673 autosampler. The column is a 12 m quartz capillary, 0.2 mm i.d., HP ULTRA 1 (dimethyl silicone), 0.33 um film thickness. Sample injection was in the splitless mode and the column temperature is programmed. The detector is a HP 5970 mass specific detector in the single ion monitoring (SIM) mode for detecting the m/z 214 ion and the confirmatory ions at m/z 216, 170, and 140. The petitioner proposes monitoring with the m/z 214 ion at 100% and if necessary with 3 others at m/z 216 at 36-39%, m/z 170 ion at 50-51%, and the m/z 140 ion at 38-41%. These ratios will serve as an index for the determination of interferences, if and when, encountered by any of the 4 ions. The petitioner proposes that if the ratios of these 4 ions in a sample are within 10% of the ratios for the reference analytical standard, and the sample and standard peaks have the same retention time through a capillary column, then the presence of total imidacloprid is confirmed. CBTS agrees this is an acceptable procedure at this time for these 2 petitions only. The separatory power of a capillary column in identifying a compound is just as important, if not more so, than monitoring a third ion and determining its ratio.

Quantitation is by peak area from a standard curve. Standards were prepared in ACN and the petitioner claims that the standards will be stable for 6 months if kept refrigerated and in the dark when not in use. Conversion factors to correct for the molecular weight differences between 6-CNA and the analyte of interest, whether it is imidacloprid or a metabolite, are listed.

No new recovery data were presented for Bayer method 0019 in this petition. Extensive method validation for imidacloprid and its major metabolites in milk, liver, kidney, eggs and poultry muscle were presented in PP# 3F4169 and have been reviewed by F. Griffith, Jr., in his June 18, 1993, memorandum (q.v.).

In summary, recovery of imidacloprid and its hydroxy metabolite fortified in milk at 0.02

ppm and 0.1 ppm ranged from means of 71% to 89%. For a mixed fortification of imidacloprid, its olefin and hydroxy metabolites each at 0.03 ppm the mean recovery from milk was 88%. Liver samples fortified with imidacloprid at 0.02, 0.05, 0.25, 0.5, and 2.5 ppm had mean recoveries ranging from 71% to 80%. Additional recovery data were generated for the olefin, hydroxy, guanidine, and 6-CNA fortified at 0.02 and 0.5 ppm with mean recoveries ranging from 72% for 6-CNA to 89% for the olefin. A mixture of approximately 0.2 ppm each of imidacloprid and its major metabolites had a mean recovery of 81%. Muscle, kidney, and fat samples were fortified with the same compounds and generally at the same spiking levels. Mean recoveries were in the same range as in liver and milk with a lower recovery in kidney and some what higher recovery in fat with more spread in muscle samples.

Egg and poultry muscle samples were fortified with imidacloprid and its olefin at 0.02 and 0.1 ppm; plus a mixture of each at 0.05 ppm. Mean recoveries of imidacloprid were in the 70% range and mean recoveries of the olefin were in the 60% range. Mean recovery of the mixture was 74% in eggs and 68% in poultry muscle. Poultry fat spiked with imidacloprid and its olefin at the same levels as in eggs had mean recoveries ranging from 73% to 80%. Poultry liver samples were fortified with imidacloprid, the olefin, and guanidine at 0.02, 0.5, and 2 ppm. Recovery data for 6-CNA was reported from fortifications of 0.02 ppm and 0.3 ppm. Overall mean recoveries from poultry liver for imidacloprid and its major metabolites ranged from 85% to 111%; a higher percentage recovery for liver than any other poultry tissue.

The petitioner presented adequate supporting chromatographic data showing recovery of 6-CNA from eggs, kidney, liver, milk, and muscle for test and control samples plus standards. The chromatogram showed few UARs and none that would interfere with the determination of 6-CNA. The petitioner has presented an adequately validated residue analytical method to gather the magnitude of the residue data from meat, milk, poultry, and eggs.

A TMV (tolerance method validation) was requested for Bayer method 00191 for imidacloprid and its metabolites in milk and liver (see memorandum by F. Griffith, Jr., dated March 3, 1993). The results of the successful method trial were reported by the Analytical Chemistry Branch (see memorandum in PP# 3F4169 by Stafford and Wright dated April 11, 1994). The 5 analytical method deficiencies noted in the ACB initial method screen pre-review dated April 15, 1993, are all resolved. ACB's comments on the Bayer method 00191 are considered to be minor modifications and will be forwarded to FDA to be published as the EPA addendum along with the method. While ACB did not determine the method's MDL (minimum detection limit) its estimate of 0.02 ppm in milk and liver is supported by chromatographic data. Milk was spiked with imidacloprid, its hydroxy, guanidine, and 6-CNA metabolites at 0.05 and 0.1 ppm and beef liver was spiked with the same compounds at 0.2 and 0.5 ppm. Based on acceptable recoveries with supporting chromatographic data there has been a successful TMV for Bayer method 00191. The method is only marginally suitable to be an enforcement method with perishable commodities as both the ILV and EPA TMV time frame to complete a set of samples takes approximately 20 hours or into a third working day. CBTS reiterates this method is quite rugged and effective as an enforcement procedure when very rapid turn around times are not required. It meets all other requirements of Subdivision O and will be forwarded to FDA for publication in the Pesticide Analytical Manual, Vol II.

Independent laboratory validation (ILV) data - animal tissues

The accompanying ILV data for the animal tissues method Bayer method 00191 were generated by Huntingdon Analytical Services and presented in a study titled "An Independent Laboratory Validation for the Analysis of Imidacloprid and Metabolite Residues in Animal Tissues, Milk, and Eggs Specified in Miles Report No. 103949-R" by M. Bajzik dated January 21, 1994, and coded Miles report no. 106418 (MRID # 431432-04). This study has been previously reviewed by F. Griffith, Jr., in his June 7, 1994, memorandum for PP# 3F4169.

In summary, beef liver was fortified individually with imidaclo-prid, its hydroxy, guanidine, olefin, and 6-CNA metabolites at 0.2 ppm (proposed tolerance) and at 1 ppm or 5X proposed tolerance. Huntingdon cautions that the oxidation step to from 6-CNA is the most critical step in the method and that careful attention must be paid to the directions. Overall recoveries ranged from 76% to 105%. Extensive supporting chromatographic data were presented which could confirm the results reported. The ILV time estimate to complete a set of samples is 2 days are necessary to complete the extraction and clean-up, GC/MS overnight, and the third day necessary for the data reduction and report. An acceptable ILV for the Bayer method 00191 has been conducted and these data are in agreement with the petitioner's recovery data and the Agency' own recovery data generated during the TMV. No additional ILV data are required for this petition.

Additional ILV data were presented in PP# 3F4169 and reviewed by F. Griffith, Jr., in his June 18, 1993, review. The study was conducted in Germany using the original method. ILV recovery data were generated for imidacloprid and its guanidine and 6-CNA metabolites in milk and eggs at the 0.02 ppm LOQ level and 0.1 ppm. The fortification in liver 0.1 and 0.5 ppm. Initial CBTS concerns on whether or not the ILV in Germany was truly independent of the initial method validation have been resolved. CBTS now considered these ILV studies to be acceptable to support the proposed tolerance in eggs and milk and effectively bracket the revised tolerance in meat by-products.

STORAGE STABILITY

In an amendment to PP# 3F4169 the petitioner presented adequate storage stability data for imidacloprid in a variety of commodities. Two of these reports were updates for 6, 12, and 18 months of frozen storage data for imidacloprid and its metabolites in wheat matrices, cottonseed, tomato, cauliflower, and lettuce. Two other reports were updates for 12 and 24 months of ^{14}C-imidacloprid frozen storage in lemons, corn, and lettuce; and the last report was also an update for 6, 12, and 18 months of frozen storage in apples, potatoes, and cottonseed. These data have reviewed (see memorandum by F. Griffith, Jr., dated June 7, 1994 in PP# 3F4169).

In summary, at 12 and 24 months of storage at -20°C in corn forage recoveries ranged from 96% for the guanidine to 113% for the olefin, in fodder recoveries ranged from 92% for the guanidine to 111% for the hydroxy, and in corn grain recoveries ranged from 99% for 6-CNA to 122% for imidacloprid. Wheat commodities; grain dust, flour, bran, shorts, grain, forage, and straw spiked at 2.5 ppm and analyzed at 3, 6, 12, and around 20 months later all had acceptable total recoveries when compared to the zero day recovery and initial fortification. CBTS concludes these storage stability data are supplementary to this petition

as there are no proposed use and tolerances for any of these commodities.

In apples and the apple processed commodities; ie, wet and dried apple pomace, and juice, spiked with imidacloprid and its guanidine, olefin, hydroxy, and 6-CNA metabolites, stored frozen with aliquots analyzed at 3, 6, 12, and 18-19 months after fortification had recoveries of greater than 80% in whole apples, 80-100% in pomace, and greater than 90% in juice throughout the study. In potatoes the petitioner has provided data to show that imidacloprid and its metabolites are stable in frozen storage at -20°C for at least 19 months with recoveries ranging from greater than 90% to less than 115%. Cottonseed, cottonseed hulls, soapstock, and oil were fortified with a mixture of 0.5 ppm each of imidacloprid, its guanidine, hydroxy, olefin, and 6-CNA metabolite, placed in -20°C storage with aliquots analyzed at 3, 6, 12, and 18-20 months after the initial fortification all had recoveries greater then 80%. CBTS concludes these storage stability data are sufficient to support the magnitude of the total imidacloprid residue crop field trials that were reported for cottonseeds stored up to 8 months, apples that were stored up to 9 months, and potatoes that were stored up to 11 months from harvest to analysis.

In lemons there was a slight change in the 24 months chromato-graphic profile as would be expected under acidic conditions when the hydroxy and the nitrosimino metabolites can be converted to the olefin and guanidine metabolites. At 24 months there is essentially no change in values for imidacloprid, per se, and for 6-CNA. The 5-hydroxy and the nitrosimino both show a decline to less then 60% of the value added. There is a slight increase in the olefin and guanidine metabolite concentrations with values above 125% of that in the initial fortification. While there has been a change in concentrations of the individual imidacloprid metabolites under conditions of lemon frozen storage, there has been no overall change in concentration as the initial total imidacloprid was 5.88 ppm and 2 years later the total imidacloprid in lemons was 5.82 ppm. CBTS reiterates that total imidacloprid is stable in lemons for at least 2 years and that these data are supplementary to this petition as there are no proposed uses or tolerances for any citrus fruits.

Lettuce stored for 12 and 24 months recoveries ranged from 99% for the ^{14}C-guanidine to 108% for the ^{14}C-olefin. In a separate study the recovery of "cold" total imidacloprid from lettuce is consistent with recoveries of ^{14}C-imidacloprid and its radiolabeled metabolites from lettuce. Imidacloprid and its metabolites both labeled and unlabeled are stable under conditions of frozen storage for at least 24 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trial data reported for both head and leaf lettuce stored up to 11-12 months from harvest to analysis.

The petitioner presented the results of a frozen storage stability study for imidacloprid and its guanidine, olefin, hydroxy, and 6-CNA metabolites each at 0.5 ppm in tomatoes and cauliflower. The samples were frozen at -20°C and aliquots were removed at 3, 6, 12, and 18 months for analysis. From tomatoes recovery of total imida-
cloprid ranged from 2.35 ppm at 12 months to 2.8 ppm at 3 and 18 months. In cauliflower the recovery of total imidacloprid ranged from 2.19 ppm at 12 months to 2.87 ppm at 3 months. The petitioner has provided adequate frozen storage stability data in tomatoes and cauliflower to show that total imidacloprid residues are stable under frozen conditions for at least 18 months. These data are sufficient to support the magnitude of the residue crop field trial data for tomatoes (fruiting vegetables) stored up to 7 months from harvest to analysis and for cauliflower (Brassica cole leafy vegetables) stored up to 11 months from harvest to analysis.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Fruiting vegetables crop group

Tomatoes (MRID # 428103-01)

The petitioner presented imidacloprid magnitude of the residue data on/in tomatoes in a study titled "Imidacloprid (2.5GR and 2F) - Magnitude of the Residue on Tomato" by Burger and Lenz dated March 15, 1993, and coded Miles report number 105015.

The petitioner presented total imidacloprid magnitude of the residue data on tomatoes from 30 crop field trials in 9 states: New Jersey, Ohio, Michigan, Mississippi, California (6), Indiana (6), Kansas (6), Georgia (6), and Florida (6) all from the 1992 crop year on 8 varieties 3 of which were cherry tomatoes. Crop field trial data from these 9 states represents a fresh market tomato production on 104,100 acres out of a national fresh market tomato production on 134,290 (77.5%); and a processed tomato production on 350,650 acres out of a national processed tomato production on 354,700 acres (98.9%) [see 1991, Agr. Stat.].

Twelve of the 30 trials received a soil drench at a rate of 0.025 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 0.11 lb/acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) at 5 (± 2) day repeat application intervals. The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other studies using the 2F formulation as a soil drench only at a rate of 0.025 gram ai/plant (0.5 lb/A) 14 days after planting or transplanting. The 2F or 2.5GR formulations were used as an in-furrow application applied in, slightly above or below the seed furrow when planting at a rate of 0.03 gram ai/row meter. With a row spacing of 20-21 inches this is an application rate at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a side-dress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after transplanting.

Mature tomato samples from the soil drench plus foliar applications were harvested at 0, 3, and 7 days after the second foliar application. Mature tomato samples from the other soil applications were harvested at the earliest maturity which was 44 to 112 days after treatment. In each field trial 16 mature fruits were harvested from the 4 quarters of each vine, high and low area, and portions exposed and sheltered by the tomato foliage. Samples were frozen immediately and remained frozen until sample preparation and analysis. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data has been presented.

No total imidacloprid residues were detected in any of the control tomatoes to the LOQ level of < 0.05 ppm. At the proposed 0 day PHI following foliar applications total imidacloprid residues on tomatoes ranged from 0.05 ppm to 0.45 ppm (X = 0.15 ppm ± 0.12 ppm, n = 12) with 3 samples having residues above 0.2 ppm. There was a slight decline in total imidacloprid residues to the 3 days PHI. Total imidacloprid residues ranged from < 0.05 ppm

to 0.48 ppm (X = 0.13 ppm ± 0.12 ppm, n = 12) with 1 sample having residues above 0.2 ppm at 3 days PHI. At the 7 day PHI total imidacloprid residues ranged from < 0.05 ppm to 0.35 ppm (X = 0.11 ppm ± 0.1 ppm, n = 12) with 2 samples at or above 0.2 ppm.

Samples from the soil drench application had total imidacloprid residues ranging from < 0.05 ppm (in 7 samples) to 0.26 ppm, n = 10. From the in-furrow application total imidacloprid residues at earliest harvest ranged from < 0.05 ppm in 8 samples to 0.2 ppm. Total imida-cloprid residues from the sidedress application at the earliest harvest ranged from < 0.05 ppm to 0.26 ppm with 2 samples having total imidacloprid residues above 0.2 ppm.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show residues of imidacloprid on the representative commodity tomatoes will not exceed the proposed crop group tolerance for fruiting vegetables at 1 ppm when Admire® is used at directed.

Peppers (MRID # 428810-01)

The petitioner presented imidacloprid magnitude of the residue data on/in peppers in a study titled "Imidacloprid (2.5GR and 2F) - Magnitude of the Residue on Pepper" by Lenz and Burger dated March 19, 1993, and coded Miles report number 105016.

The petitioner presented total imidacloprid magnitude of the residue data on peppers from 25 field trials in 7 states; ie, New Mexico, California (7), New Jersey, Indiana (6), Kansas (2), Mississippi, Florida, and Georgia (6) of which 24 were from the 1992 crop year and 1 was from the 1993 crop year. Fourteen of the trials were with 5 varieties of sweet peppers and 11 of the trials were with 4 varieties of hot peppers. While there are no national pepper production figures in the 1991 Agr. Stat. the location and number of imida-cloprid pepper crop field trials will satisfy that an adequate number of crop field trials are being presented for peppers.

Eleven of the 25 trials received a soil drench at a rate of 0.025 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 0.11 lb/acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) in 8-10 GPA at 5 day repeat application intervals. The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other studies using the 2F formulation as a soil drench only at a rate of 0.025 gram ai/plant (0.5 lb/A) 14 days after transplant. The 2F or 2.5GR formulations were used as an in-furrow application applied in, slightly above or below the seed furrow when planting at a rate of 0.04 gram ai/row meter. With a row spacing of 20-21 inches this is an application rate at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a sidedress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after transplant.

Samples from the soil drench plus foliar applications were harvested at 0, 3, and 7 days after the second foliar application. Samples from the other soil applications were harvested at the earliest maturity which was 54 to 123 days after treatment. In each field trial samples were collected from at least 4 plants for 2.5 lbs plus of total harvest. Samples were frozen

immediately and remained frozen until sample preparation and analysis. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data has been presented.

No total imidacloprid residues were detected in any of the control samples to the LOQ of < 0.05 ppm. At the proposed 0 day PHI following foliar applications total imidacloprid residues ranged from 0.17 ppm to 0.96 ppm (X = 0.41 ppm $\pm$ 0.25 ppm, n = 11) with 6 samples having residues above 0.3 ppm. Samples from a 3 day PHI showed a slight declines in residues. Total imidacloprid residues ranged from 0.17 ppm to 0.39 ppm (X = 0.29 ppm $\pm$ 0.07 ppm, n = 10) with 2 samples having residues above 0.3 ppm at 3 days PHI. At the 7 day PHI total imidacloprid residues ranged from 0.13 ppm to 0.53 ppm (X = 0.23 ppm $\pm$ 0.13 ppm, n = 11) with 3 samples at or above 0.3 ppm.

Samples from the soil drench application had total imidacloprid residues ranging from < 0.05 ppm to 0.67 ppm, n = 8. From the in-furrow application total imidacloprid residues at earliest harvest ranged from < 0.05 ppm in 8 samples to 0.2 ppm. Total imidacloprid residues from the sidedress application ranged from < 0.05 ppm to 0.36 ppm.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on the representative commodity peppers will not exceed the proposed crop group tolerance for fruiting vegetables at 1 ppm when Admire® is used at directed. Maximum residues on the representative commodities peppers and tomatoes vary by a factor of 2, thus a crop group tolerance can be supported.

Brassica (cole) leafy vegetables crop group

Cabbage (MRID # 428103-6)

The petitioner presented imidacloprid magnitude of the residue data on cabbage in studies titled "Imidacloprid (2.5GR and 2F) - Magnitude of the Residue on Cabbage" by Lenz and Burger dated May 7, 1993 and coded Miles report number 105040.

The petitioner presented imidacloprid magnitude of the residue data on/in cabbage from 29 field trials in 10 states; ie, Texas (2), California (7), Florida (7), New Jersey, North Carolina, New York, Wisconsin, Mississippi, Indiana (6), and Kansas (2) with 23 trials from the 1992 crop year and 6 trials from the 1993 year on 11 varieties. While there are no national cabbage production figures in the 1991 Agr. Stat. the location and number of imidacloprid cabbage crop field trials will satisfy the requirement for an adequate number of field trials being presented for cabbage.

Thirteen of the 29 trials received a soil drench at a rate of 0.02 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 0.11 lb/acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) in 8-10 GPA at 5 day repeat application intervals. The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other studies using the 2F formulation as a soil drench only at a rate of 0.02 gram ai/plant (0.5 lb/A) 14 days after transplant. The 2F or 2.5GR formulations were used as an in-furrow at planting application applied in, slightly above or below the seed furrow when planting at a rate of 0.03 gram ai/row meter. With a row spacing of 10-40 inches this is an application at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a sidedress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after transplant.

Mature cabbage samples from the soil drench plus foliar applications were harvested at 0, 7, and 14 days after the second foliar application. Samples from the other soil applications were harvested at the earliest maturity which was 40 to 104 days after treatment. In each field trial samples were collected from at least 12 separate areas of the test plot. Samples were frozen immediately and remained frozen until sample preparation and analysis. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data has been presented.

Total imidacloprid residues were detected in only one of the 13 cabbage with leaves and without leaves control samples at 0.07 ppm. Other control cabbage samples did not have any total imidacloprid residues to the LOQ of < 0.05 ppm. The 0 days PHI total imidacloprid residues on cabbage with wrapper leaves ranged from 0.08 ppm to 4.12 ppm ($X = 1.25 \pm 1.19$ ppm, n = 13) with 4 samples having residues above 1 ppm. Cabbage with wrapper leaves from the proposed 7 day PHI showed a slight declines in residues. Total imidacloprid residues ranged from 0.05 ppm to 1.75 ppm ($X = 0.64$ ppm $\pm$ 0.53 ppm, n = 13) with 3 samples having residues above 1 ppm at 7 days PHI. At the 14 day PHI cabbage with wrapper leaves had total imidacloprid residues ranging from < 0.05 ppm to 3.25 ppm ($X = 0.68$ ppm $\pm$ 0.87 ppm, n = 13) with 3 samples above 1 ppm.

Cabbage without wrapper leaves show less total imidacloprid than did the cabbage with wrapper leaves. The 0 day PHI total imidacloprid residues on cabbage without wrapper leaves ranged from < 0.05 ppm to 1.17 ppm ($X = 0.26 \pm 0.31$ ppm, n = 13) with 2 samples having residues at or above 0.5 ppm. Cabbage without wrapper leaves from the proposed 7 day PHI showed a slight declines in residues. Total imidacloprid residues ranged from < 0.05 ppm to 0.6 ppm ($X = 0.15$ ppm $\pm$ 0.14 ppm, n = 13) with 1 sample having residues above 0.5 ppm at 7 days PHI. At the 14 day PHI cabbage without wrapper leaves had total imidacloprid residues ranging from < 0.05 ppm to 0.94 ppm ($X = 0.18$ ppm $\pm$ 0.24 ppm, n = 13) with 1 sample above 0.5 ppm.

Cabbage samples with and without wrapper leaves from the soil drench application at the earliest harvest had total imidacloprid residues ranging from < 0.05 ppm to 0.33 ppm, n = 16 with 6 samples at or above 0.2 ppm. From the in-furrow application total imidacloprid residues on cabbage with and without wrapper leaves at earliest harvest ranged from < 0.05 ppm to 0.29 ppm. Total imidacloprid residues from the sidedress application were higher then the in-furrow application. Total imidacloprid residues on cabbage with and without wapper leaves ranged from < 0.05 ppm to 0.43 ppm with 6 samples having wrapper leaves showing residues at or above 0.2 ppm and no samples without wrapper having residues at or above 0.2 ppm.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on the representative commodity cabbage will not exceed the proposed crop group tolerance for Brassica (cole) leafy vegetables at 3.5 ppm when Admire® is used at directed.

Broccoli (MRID # 428103-04)

The petitioner presented imidacloprid magnitude of the residue data on broccoli in studies titled "Imidacloprid (2.5GR and 2F) - Magnitude of the Residue on Broccoli" by Lenz and Burger dated May 7, 1993, and coded Miles report number 105019.

The petitioner presented imidacloprid magnitude of the residue data on/in broccoli from 28 field trials in 9 states; ie, Texas, Oregon, California (9), Arizona, New Jersey, Mississippi, Georgia (6), Indiana (6), and Kansas (2) with 27 trials from the 1992 crop year and 1 trial from the 1993 year on 8 varieties. Crop field trial data from these 9 states represents broccoli production on 110,800 acres out of a national broccoli production on 110,800 acres (100%) [see 1991, Agr. Stat.].

Twelve of the 28 trials received a soil drench at a rate of 0.01 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 0.11 lb/acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) in 8-10 GPA at 5 day repeat application intervals. The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other studies using the 2F formulation as a soil drench only at a rate of 0.01 gram ai/plant (0.5 lb/A) 14 days after transplant. The 2F or 2.5GR formulations were used as an in-furrow at planting application applied in, slightly above or below the seed furrow when planting at a rate of 0.03 gram ai/row meter. With a row spacing of 15-40 inches this is an application at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a sidedress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after transplant.

Mature broccoli samples from the soil drench plus foliar applications were harvested at 0, 7, and 14 days after the second foliar application. Samples from the other soil applications were harvested at the earliest maturity which was 32 to 92 days after treatment. In each field trial samples were collected from at least 12 separate areas of the test plot. Samples were frozen immediately and remained frozen until sample preparation and analysis. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data has been presented.

Fourteen control broccoli samples did not have any total imida-cloprid residues to the LOQ of < 0.05 ppm. For the soil drench plus foliar applications, the 0 days PHI total imidacloprid residues on broccoli ranged from 0.32 ppm to 3.29 ppm ($X = 1.06 \pm 0.94$ ppm, n = 12) with 5 samples having residues above 1 ppm. Broccoli from the proposed 7 day PHI showed a slight decline in residues. Total imi-
dacloprid residues ranged from 0.10 ppm to 2.25 ppm ($X = 0.47$ ppm $\pm$ 0.59 ppm, n = 12) with 3 samples having residues above 0.5 ppm at 7 days PHI. At the 14 day PHI broccoli had total

imidacloprid residues ranging from 0.07 ppm to 1.44 ppm (X = 0.35 ppm ± 0.37 ppm, n = 12) with 1 sample above 0.5 ppm.

Broccoli samples from the soil drench application at the earliest harvest had total imidacloprid residues ranging from < 0.05 ppm to 0.21 ppm, n = 7 with 2 samples at or above 0.2 ppm. From the in-furrow application total imidacloprid residues on broccoli at earliest harvest ranged from < 0.05 ppm to 0.48 ppm with 4 samples having residues above 0.2 ppm. Total imidacloprid residues from the sidedress application ranged from < 0.05 ppm to 0.36 ppm with 4 samples having at or above 0.2 ppm.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on the representative commodity broccoli will not exceed the proposed crop group tolerance for Brassica (cole) leafy vegetables at 3.5 ppm when Admire® is used at directed.

Cauliflower (MRID # 428103-05)

The petitioner presented imidacloprid magnitude of the residue data on cauliflower in studies titled "Imidacloprid (2.5GR and 2F) - Magnitude of the Residue on Cauliflower" by Lenz and Burger dated May 7, 1993, and coded Miles report number 105022.

The petitioner presented imidacloprid magnitude of the residue data on/in cauliflower from 28 field trials in 9 states; ie, Texas, Oregon, Arizona, California (10), New York, Mississippi, Florida (6), Indiana (6), and Kansas (2) with 15 trials from the 1992 crop year and 13 trials from the 1993 crop year on 7 varieties. Crop field trial data from these 9 states represents cauliflower production on 59,400 acres out of a national cauliflower production on 65,800 acres (90.3%) [see 1991, Agr. Stat.].

Twelve of the 28 trials received a soil drench at a rate of 0.02 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 0.11 lb/acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) in 8-10 GPA at 5 day repeat application intervals. The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other studies using the 2F formulation as a soil drench only at a rate of 0.02 gram ai/plant (0.5 lb/A) 14 days after transplant. The 2F or 2.5GR formulations were used as an in-furrow at transplanting treatment applied in, slightly above or below the seed furrow at a rate of 0.03 gram ai/row meter. With a row spacing of 15-40 inches this is an application at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a sidedress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after transplant.

Mature cauliflower samples from the soil drench plus foliar applications were harvested at 0, 7, and 14 days after the second foliar application. Samples from the other soil applications were harvested at the earliest maturity which was 38 to 152 days after treatment. In each field trial samples were collected from at least 12 separate areas of the test plot. Samples were frozen immediately and remained frozen until sample preparation and analysis. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method

validation and concurrent recovery data has been presented.

Twelve control cauliflower samples did not have any total imidacloprid residues to the LOQ of < 0.05 ppm. The 0 days PHI total imidacloprid residues on cauliflower ranged from 0.06 ppm to 0.88 ppm (X = 0.35 ± 0.24 ppm, n = 12) with 4 samples having residues above 0.4 ppm. Cauliflower from the proposed 7 day PHI showed a slight decline in residues. Total imidacloprid residues ranged from < 0.05 ppm to 0.39 ppm (X = 0.17 ppm ± 0.11 ppm, n = 12) at 7 days PHI. At the 14 day PHI cauliflower had total imidacloprid residues ranging from < 0.05 ppm to 0.6 ppm (X = 0.17 ppm ± 0.15 ppm, n = 12) with 1 sample above 0.4 ppm.

Cauliflower samples from the soil drench application at the earliest harvest had total imidacloprid residues ranging from 0.10 ppm to 0.25 ppm, n = 8 with 3 samples at or above 0.2 ppm. From the in-furrow application total imidacloprid residues on cauliflower at earliest harvest ranged from < 0.05 ppm to 0.09 ppm. Total imidacloprid residues from the sidedress application ranged from 0.06 ppm to 0.16 ppm with 2 samples having residues at or above 0.1 ppm.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on cauliflower, a commodity of the Brassica (cole) leafy vegetables will not exceed the proposed crop group tolerance for Brassica (cole) leafy vegetables at 3.5 ppm when Admire® is used at directed. Maximum residues on the representative commodities cabbage and broccoli tomatoes vary by a factor of 4 from cauliflower, thus a crop group tolerance can be supported. The petitioner has not supplied any magnitude of the residue data for the representative commodity mustard greens; instead requesting we substitute residue data from leaf lettuce to mustard greens. Since the proposed use pattern on lettuce is the same as for Brassica (cole) leafy vegetables and the magnitude of the residue on lettuce is similar to cabbage and broccoli we will make the translation.

Head and leaf Lettuce (MRID # 428103-07)

The petitioner presented imidacloprid magnitude of the residue data on head and leaf lettuce in a study titled "Imidacloprid (2.5 GR and 2F) - Magnitude of the Residue on Lettuce" by Burger and Lenz dated May 11, 1993, and coded Miles report number 105164.

The petitioner presented imidacloprid magnitude of the residue data on/in head and leaf lettuce from 51 total field trials in 10 states; ie, Texas (2), Washington (2), Arizona (2), California (11), New Jersey (2), Mississippi (2), Colorado (2), Georgia (12), Indiana (12), and Kansas (4) with 45 trials from the 1992 crop year and 6 trials from the 1993 crop year on 8 varieties of leaf lettuce and 9 varieties of head lettuce. Several of these trials contained head and leaf lettuce grown at the same test site. Crop field trial data from these 10 states represents head and leaf lettuce production on 227,100 acres out of a national lettuce production on 231,000 acres (98.2%) [see 1991, Agr. Stat.].

Twentyfour of the 51 trials received a soil drench at a rate of 0.01 gram ai/plant or 0.5 lb ai/acre 14 days after transplant. The 2 foliar applications using the 2 F formulation were at a rate of 1.8 oz /acre/application with a spray adjuvant (Silwet L-77, 1 pt/100 gal of spray solution) at 5 (±2) day repeat application intervals for a total foliar application of 3.6 ozs (0.23

lb ai). The total imidacloprid applied was 0.73 lb ai/A/season (1.46X exaggerated total application).

The petitioner conducted other imidacloprid in lettuce studies using the 2F formulation as a soil drench only at a rate of 0.01 gram ai/plant (0.5 lb/A) 14 days after planting. The 2F or 2.5GR formulations were used as an in-furrow at planting treatment applied in, slightly above or below the seed furrow at a rate of 0.03 gram ai/row meter. With a row spacing of 20 inches this is an application at 0.5 lb ai/A. The 2F or 2.5GR formulations were also used as a sidedress application applied 3-4" to the side of the plants and incorporated 1 or more inches into the soil at a rate of 0.5 lb ai/A 14 days after planting.

Mature lettuce samples from the soil drench plus foliar applications were harvested at 0, 7, and 14 days after the second foliar application. Samples from the other soil applications were harvested at the earliest maturity which was 12 to 133 days after treatment. In each field trial samples were collected from at least 12 separate areas of the test plot. Samples were frozen immediately and remained frozen until sample preparation and analysis at Miles laboratories. Samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data has been presented. The petitioner has provided extensive supporting chromatographic data which shows there are no interferences in the determination of 6-CNA in lettuce.

77 control lettuce samples did not have any total imidacloprid residues to the LOQ of < 0.05 ppm while only one control head lettuce showed 0.07 ppm imidacloprid equivalents. The 0 days PHI total imidacloprid residues from the soil drench plus 2 foliar applications on head lettuce with wrapper leaves ranged from 0.44 ppm to 5.1 ppm ($X = 1.82 \pm 1.30$ ppm, n = 12) with 5 samples having residues above 2 ppm, and on head lettuce without wrapper leaves ranged from < 0.05 ppm to 1.37 ppm ($X = 0.46$ ppm $\pm$ 0.41 ppm, n = 12) with 2 samples having residues above 1 ppm. Leaf lettuce at 0 day PHI had total imidaclo-prid residues ranging from 1.29 ppm to 10.6 ppm ($X = 4.24$ ppm $\pm$ 3.04 ppm, n = 12) with 8 samples having residues above 2 ppm.

Head lettuce with wrapper leaves at the proposed 7 day PHI had total imidacloprid residues ranging from 0.31 ppm to 2.13 ppm ($X = 0.87$ ppm $\pm$ 0.55 ppm, n = 12) with 1 sample having residues above 2 ppm, and lettuce without wrapper leaves had total imidacloprid ranging from < 0.05 ppm to 0.72 ppm ($X = 0.22$ ppm $\pm$ 0.22 ppm, n = 12). Leaf lettuce at the proposed 7 day PHI had total imidacloprid residues ranging from 0.09 ppm to 2.49 ppm ($X = 1.46 \pm 0.77$ ppm, n = 12) with 4 samples having residues above 2 ppm.

The petitioner continued with the imidacloprid on lettuce decline study by providing residue data at 14 days PHI. At 14-15 days PHI head lettuce with wrapper leaves had total imidacloprid residues ranging from 0.12 ppm to 0.99 ppm ($X = 0.47$ ppm $\pm$ 0.32 ppm, n = 11), and on head lettuce without wrapper leaves residues ranged from < 0.05 ppm to 0.29 ppm ($X = 0.13$ ppm $\pm$ 0.09 ppm). Leaf lettuce at 14 days PHI had total imidacloprid residues ranging from < 0.05 ppm to 2.61 ppm ($X = 0.84$ ppm $\pm$ 0.7 ppm, n = 12).

Leaf lettuce samples from the soil drench application at the earliest harvest had total imidacloprid residues ranging from 0.10 ppm to 2.06 ppm with 2 samples above 2 ppm, and

on head lettuce with and without wrapper leaves total imidacloprid residues ranged from < 0.05 ppm to 0.39 ppm at the earliest harvest. From the in-furrow application total imidacloprid residues on leaf lettuce ranged from 0.21 ppm to 0.8 ppm at earliest harvest, and ranged from < 0.05 ppm on all 4 samples of head lettuce without wrapper leaves to 0.15 ppm on the head lettuce with wrapper leaves. Total imidacloprid residues from the sidedress application on leaf lettuce ranged from < 0.05 ppm to 1 ppm with 8 samples having residues at or above 0.6 ppm. Total imidaclo-prid residues were < 0.05 ppm on all samples of head lettuce without wrapper leaves from the sidedress application to 0.13 ppm on head lettuce with wrapper leaves.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show that residues of imidacloprid on lettuce (head and leaf) will not exceed the proposed tolerance at 3.5 ppm when Admire® is used at directed.

Grapes (MRID #s 428103-02 and 428103-03)

The petitioner presented imidacloprid magnitude of the residue data on grapes in a study titled "Imidacloprid (240FS) - Magnitude of the Residue on Grape" by Lenz and Burger dated September 28, 1992, and coded Miles report number 103245. Additional imidacloprid magnitude of the residue on grapes crop field trial data were presented in a study titled "Imidacloprid (75WP and 249FS) - Magnitude of the Residue on Grape (Addendum 1)" by Burger and Lenz dated February 5, 1993, and coded Miles report number 103245-1.

The petitioner presented imidacloprid magnitude of the residue data on grapes from 7 field trials in 6 states; ie, Oregon, Washington, California (2), New York, Indiana, and North Carolina all for the 1991 crop year on 7 varieties. In the addendum the petitioner presented imidacloprid magnitude of the residue data on grapes from 9 additional field trials in 5 states; ie, Washington, California (4), New York, Michigan, Indiana (2) all from the 1992 crop year on 5 varieties. Crop field trial data from these 7 states represents grape production of 5,563,500 tons out of a national grape production of 5,659,900 tons (98.3%) [see 1991, Agr. Stat.].

All 16 grape crop field trials received 2 foliar applications. The seven 1991 trials were run using the 240FS formulation at a rate of 0.8 oz/acre/application at 14 (±3) day repeat application intervals. The six of the 1992 trials were conducted using the 75WP formulation to provide bridging data and the other 3 trials were conducted side by side with the 240FS or 2F formulation at a rate of 0.8 oz/acre/ application in 40-50 GPA or in a more dilute spray of 100-200 GPA with a 14 (± 2) days repeat application interval. The total imidacloprid applied was 1.6 oz or 0.1 lb ai/A/season (1.07X exaggerated total application). The petitioner has provided magnitude of the residue data from 10 grape field trials using the formulation for which there are other proposed uses in the current Section B, and 6 bridging studies for a new formulation which has a proposed use only on grapes.

Mature grapes samples were harvested at 0, 1, 3, 7, 14, and 21 days after the second foliar application. In each field trial samples were collected from at least 4 separate vines, talking the fruit from all sides, high and low areas, and from portions exposed and sheltered for at least 2.5 lbs of sample at each sampling date. Samples were frozen immediately and remained frozen until shipped to Miles for sample preparation and then to ABC Laboratories for analysis. Samples were analyzed by a modified version of the residue analytical method

that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data along with the chromatograms has been presented.

Sixteen control grape samples did not have any total imidacloprid residues to the LOQ of < 0.05 ppm. The 0 day proposed PHI total imidacloprid residues on grapes using the 2F formulation ranged from < 0.05 ppm to 0.61 ppm (X = 0.17 ppm ± 0.17 ppm, n = 10) with 3 samples having residues at or above 0.2 ppm. At the 0 day proposed PHI, total imidacloprid residues using the 75WP formulation ranged from 0.06 ppm to 0.17 ppm (X = 0.10 ppm ± 0.04 ppm, n = 6).

The petitioner conducted a decline study for both formulations. Grapes at the 1 day PHI had total imidacloprid residues using the 2F formulation ranging from < 0.05 ppm to 0.54 ppm (X = 0.15 ppm ± 0.15 ppm, n = 10) with only 1 sample having residues above 0.2 ppm. At the 1 day PHI, total imidacloprid residues using the 75WP formulation range from < 0.05 ppm to 0.12 ppm (X = 0.08 ppm ± 0.04 ppm, n = 6). At 3 days PHI total imidacloprid residues on grapes using the 2F formulation ranged from < 0.05 ppm to 0.51 ppm (X = 0.13 ppm ± 0.14 ppm, n = 10) again with only 1 sample having residues above 0.2 ppm. At the 3 days PHI, total imidacloprid residues using the 75WP formulation ranged from < 0.05 ppm to 0.12 ppm (X = 0.07 ppm ± 0.04 ppm, n = 6). Total imidacloprid residues on the grapes from 7 days PHI using the 2F formulation ranged from < 0.05 ppm to 0.51 ppm (X = 0.12 ppm ± 0.14 ppm, n = 10) with one sample having residues above 0.2 ppm. At the 7 days PHI total imidacloprid residues using the 75 WP formulation ranged from < 0.05 ppm to 0.11 (X = 0.06 ppm ± 0.03 ppm, n = 6). At the 14 day PHI grapes had total imidacloprid residues using the 2F formulation ranging from < 0.05 ppm (2 samples) to 0.36 ppm (X = 0.09 ppm ± 0.10 ppm, n = 10) with 1 sample above 0.2 ppm. At the 14 days PHI total imidacloprid residues using the 75 WP formulation ranged from < 0.05 ppm (3 samples) to 0.11 ppm (X = 0.06 ppm ± 0.04 ppm). After 21 days the total imidacloprid residues from the 2F formulation ranged from < 0.05 ppm (5 samples) to 0.21 ppm (X = 0.07 ppm ± 0.06 ppm, n = 10) with one sample having residues above 0.2 ppm. At the 21 days PHI total imidacloprid residues using the 75 WP formulation ranged from < 0.05 ppm to 0.11 ppm (X = 0.05 ppm ± 0.04 ppm).

There is only one field trial that consistently showed higher total imidacloprid residues. The North Carolina field trial was run using the Muscadine Carlos variety of grapes. While this is a commercial variety it is not a major commercial grape variety such as Chardenay, Catawba, Concord, or Thompson. The grape cultural practices for Muscadine Carlos are quite different from the grape varieties used in the other field trials and the proposed foliar applications of Admire or Provado would be expected to give higher total imidacloprid residues on this variety. CBTS does not consider the residues to be outliers. They will be included in our average values and will be included with the other trials to determine the appropriate total imidacloprid tolerance on grapes.

Residues from the 2 formulations are quite similar if we exclude the North Carolina field trial and compare variety to variety in the other states for which the bridging data are provided. CBTS concludes that the magnitude of the imidacloprid residue on grapes is essentially the same regardless of whether the 2F or the 75WP formulation is used and the directions for use are followed. CBTS has no objection to the registration of the 2F and the 75WP formulations for use on grapes.

The petitioner has presented an adequate amount of geographically representative and varietal crop field trial data to show residues of imidacloprid on grapes will not exceed the proposed tolerance at 1 ppm when Admire® or Provado in either formulation is used at directed.

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

Tomatoes (MRID # 428103-09)

The petitioner presented imidacloprid magnitude of the residue data on processed tomato commodities in a study titled "Imidacloprid (2F) - Magnitude of the Residue on Processed Tomato Commodities" by Burger and Lenz dated April 21, 1993, and coded Miles report number 105024.

One additional tomato field trial was conducted in California during the 1992 crop year using the variety Jackpot. The tomato variety used is not a standard processing tomato variety, thus the concentration and/or decline factors reported on a fresh market tomato may not reflect the concentration/decline factors from a processing variety tomato. CBTS cannot determine the appropriate imidacloprid tomato food and feed additive tolerances from the study results. While CBTS will not discard the results of this imidacloprid tomato processing study the petitioner will need to conduct a new imidacloprid tomato processing study using a processing variety tomato treated at an exaggerated rate to ensure there are sufficient residues for a processing study. The results of the present study will be supplementary and the results from the new study will be given considerable weight in determining the appropriate FATs.

The tomatoes were transplanted at 6 weeks after germination and using the 2F formulation were treated with a soil drench at a rate of 0.125 gram ai/plant or 2.5 lbs/Acre followed by two foliar applications at a rate of 0.56 lb ai/acre for a total exaggerated application of 3.62 lbs/A (7.24X). The second foliar imidacloprid application was with the spray adjuvant Silwet L-77 at a concentration of 1 pt/100 gal. The exaggerated application was used to ensure there was sufficient residue for a tomato processing study.

Control and treated samples were collected 14 days after the last foliar application. Approximately 700 pounds were collected for processing. 16 mature fruits were collected from the four quarters of each vine; high and low areas and portions exposed and sheltered were sampled. The samples were delivered immediately after collection to the National Food Laboratory for processing. Processing of the control and treated samples started on the day of delivery and took 3 days (July 8-10, 1992). The processing simulated commercial processing and was a material balance study. Starting with 738 lbs of control tomatoes and 784 lbs of treated tomatoes the tomatoes were washed and crushed. The 784 lbs of treated tomatoes were washed with 3030 lbs of water with 770 lbs of washed tomatoes crushed in a Reitz Grinder/Disintegrator to produce 740 lbs of juice and 9.3 lbs of wet pomace. 7.2 lbs of wet tomato pomace was placed in a harvest Maid Food Dehydrator and dried to produce 2.9 lbs of dried tomato pomace. 13.2 lbs of tomato juice were removed for canning and 727 lbs were evaporated to produce 224 lbs of puree.

All processed tomato commodities were frozen, returned to Miles, and shipped to

En-Cas Analytical Laboratories. All samples remained frozen after processing until analysis. Sample analysis of the tomato processed commodities was completed in early February 1993 or 7 months from harvest to analysis.

No tomato paste were produced. In the new imidacloprid tomato processing study the petitioner needs to generate tomato paste as one of the tomato processed commodities.

The tomato, wet and dried tomato pomace, juice, and puree samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data have been presented. Extensive supporting chromatographic data were presented. The petitioner's results can be verified from these data. While UARs were present they would not interfere with the identification and quantification of 6-CNA in any of the tomato processed commodities.

No total imidacloprid residues were detected in any of the control raw whole fruits or the tomato processed commodities to the LOQ of < 0.05 ppm. Total imidacloprid residues on the whole tomatoes before processing were 0.44 ppm. When these tomatoes were processed into tomato juice, puree, wet and dried tomato pomace total imidaclo-prid residues in juice were 0.44 ppm (1X conc. factor), in puree were 0.83 ppm (1.89 concentration factor), in wet tomato pomace at 0.69 ppm (1.57X conc. factor), and in dried tomato pomace at 2.2 ppm (5X conc. factor). Total imidacloprid residues were shown to concentrate in tomato puree, wet tomato pomace, and dried tomato pomace, thus FATs are required.

The petitioner has conducted a tomato processing study using a fresh market variety tomato bearing detectable residues following an exaggerated 7.24X total imidacloprid application. Using a fresh market type tomato total imidacloprid residues concentrated 1.89X in puree, 1.57X in wet pomace, and 5X in dried pomace. While FATs are required CBTS defers judgement on the petitioner's proposed 2 ppm tolerance on puree and wet pomace, and 6 ppm tolerance in dried pomace until the petitioner completes a new imidacloprid tomato processing study using a processing variety tomato bearing detectable residues and processed into juice, puree, **paste**, and wet and dried pomace.

Grapes (MRID # 428103-10)

The petitioner presented imidacloprid magnitude of the residue data on processed grape commodities in a study titled "Imidacloprid (2F) - Magnitude of the Residue on Processed Grape Commodities" by Burger and Lenz dated September 26, 1992, and coded Miles report number 103839.

One additional grape field trial was conducted in California during the 1991 crop year using the Thompson seedless variety. The grapes were treated twice with the 240FS formulation at a rate of 3.8 oz ai/Acre (5X exaggerated application) using an air blast sprayer with a 14 day repeat application interval and a 14 day PHI. The exaggerated application was used to ensure there was sufficient residue for a grape processing study.

264 lbs of control grapes and 299 lbs of treated grapes were collected. Samples were collected from the high and low area and portions exposed and sheltered of at least 4 vines. Samples were collected on September 10, 1991, and delivered to the National Food Laboratory on September 11. Processing started on September 12 and was competed on October 31, 1991. The processing simulated commercial processing and was a material balance study. There were 296 lbs of grapes for desteming which produce 9.2 lbs of grape stems. 20 lbs of grapes were removed for sun drying which produced 2.37 lbs of sun dried raisins and 0.12 lb of raisin waste. Another 20 lbs of grapes were removed for oven drying to produce 2.37 lbs of oven dried raisins and 0.2 lb of ovendried raisin waste. There were 240 lbs of destemed grapes left for crushing using a Reitz RP-6 disintegrator and a Langsenkamp finisher with a 0.02" screen opening to produce the grape juice and 6 lbs of wet pomace. The wet grape pomace was dried in a Harvest Maid Food Dehydrator to produce 1.4 lbs of dried grape pomace.

As the processing was completed the processed grape commodities were frozen, then shipped to Miles and forwarded to ABC Laboratories for analysis. Samples remained frozen from processing to analysis. Sample analysis of the grape processed commodities was completed in mid August 1992, or 11 months from harvest to analysis.

The whole grapes, wet and dried grape pomace, juice, raisins, and raisin waste samples were analyzed by a modified version of the residue analytical method that is reviewed above and has completed a successful TMV. Adequate supporting method validation and concurrent recovery data on the various grape processing commodities have been presented. Extensive supporting chromatographic data were presented. The petitioner's results can be verified from these data. While UARs were present they would not interfere with the identification and quantification of 6-CNA in any of the grape processed commodities.

No total imidacloprid residues were detected in any of the control raw whole grapes or in the grape processed commodities to the LOQ of < 0.05 ppm. Total imidacloprid residues on the whole grapes before processing were 0.20 ppm. When these grapes were processed into grape juice, raisins, wet and dried grape pomace, and raisin waste total imidacloprid residues in grape juice were 0.23 ppm (1.15X concentration factor), 0.2 ppm (1X conc. factor) in sun dried raisins and 0.21 ppm (1.05X conc. factor) in oven dried raisins; 0.39 ppm (1.95X conc. factor) in wet grape pomace and 0.86 ppm (4.3X conc. factor) in dried grape pomace; and 2.29 ppm (11.45X conc. factor) in sun dried raisin waste and 2.02 ppm (10.1X conc. factor) in oven dried raisin waste.

The petitioner has conducted an adequate grape processing study using grapes bearing detectable residues following an exaggerated 5X total imidacloprid application. Total imidacloprid residues were shown to concentrate in wet and dried grape pomace, and in raisin waste; thus feed additives tolerances (FATs) are required. The petitioner has proposed total imidacloprid FATs at 2.5 ppm on wet grape pomace, 5 ppm on dried grape pomace, and 15 ppm on raisin waste.

CBTS does not require tolerances on processed commodities that have small concentration factors when we are dealing with low level residues as we do not consider this to be a real concentration due to possible sample composition variations and the analytical

method's inability to accurately distinguish between 0.2 and 0.23 ppm as a real difference. The revised Section F has deleted the proposed 1.5 ppm total imidacloprid tolerances on raisins and grape juice.

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

Bovine

The petitioner presented the results of a bovine imidacloprid feeding study in a document titled "NTN 33893 - Cattle Feeding Study" by U. Heukamp dated September 10, 1992, in PP# 3F4169. This study has been reviewed in the September 21, 1993 memorandum by F. Griffith, Jr.

In summary, the petitioner conducted a bovine imidacloprid feeding study using 12 lactating dairy cows of mixed breed (German black and white X HF) that weighed 550 to 650 kg, were 2 to 4 years old and in mid lactation, but not bred. The cows were housed in normal dairy housing in Monheim, Germany for about 2 weeks prior to starting the feeding study. These housing practices are comparable to standard USA dairy practices. Each cow was given a unique identification number that followed her throughout the study.

The cows were milked twice daily with the morning and evening milk combined for each cow, but not combined for all cows in the test group. Milk production is normal and is not affected by the doses of imidacloprid.

The cows were given a salt lick and water ad libitum. The feed consisted of 8 kg hay, 20 kg of corn silage, and 8 kg of a high energy dairy concentrate which is a supplement containing 16% protein, 3.2% fat, 9% fiber, and 10% ash plus vitamins A and D. All of the cows received a daily examination by a veterinarian. The cows were dosed with either 5 mg/kg, 15 mg/kg, or 50 mg/kg imidacloprid for 28 consecutive days.

The bovine feed items associated with PP# 3F4169 are cull potatoes [20% dry matter] up to 75% in beef cattle diets and 50% in dairy cattle diets, processed potato waste [12% dry matter] up to 50% in both beef and dairy cattle diets, wet apple pomace [40% dry matter] up to 40% of beef cattle diets and up to 20% in dairy cattle diets, cottonseed meal [89% dry matter] up to 10% in beef diets and up to 15% in dairy cattle diets, undelinted seed [88% dry matter] up to 25% in both beef and dairy cattle diets, cottonseed hulls up to 20% of beef diets and up to 15% in dairy diets, cotton gin byproducts [90% dry matter] up to 30% in beef diets and up to 20% in dairy diets. From PP# 3F4231 lettuce, broccoli, cauliflower, cabbage, mustard greens, or peppers are not considered to be bovine feed items. Cull raisins [85% dry matter] can fed up 25% of beef diets and up to 20% of dairy diets. Grape pomace [wet is 15% dry matter and dried is 89% dry matter] can be fed up to 20% of beef cattle diets only and raisin waste [79% dry matter] up to 25% in beef diets and up to 10% in dairy diets. Wet tomato pomace [15% dry matter] can be fed to beef cattle up to 30% of the diet and up to 20% of the dairy cattle diet, and dried tomato pomace [92% dry matter] can be fed to beef cattle up to 25% of the diet and up to 10% in dairy cattle diets. All of the dry matter percentages and the percentages of the feed items in bovine diets are taken from Table II (June 1994).

The correct calculation of bovine dietary burden includes the conversion of the dry matter diet percentages to the as fed basis, using the moisture content of the feed. The

potential bovine dietary burden for each of these feed items is based on the proposed tolerance, percentage in the diet and percent dry matter in the particular feed item. The potential dietary burden for cull potatoes in beef cattle diets is 1.5 ppm [(0.75{% in diet}/0.2 {% DM})(0.4 {proposed tolerance}) = 1.5 ppm] and 1 ppm in dairy diets. The bovine dietary burden from processed potato waste is 3.75 ppm in dairy cattle diets and 5.63 ppm in beef cattle diets. The bovine dietary burden from wet apple pomace in beef cattle is 3 ppm and 1.5 ppm in dairy cattle. The bovine dietary burden from undelinted cottonseed in both beef and dairy diets is 1.7 ppm. The dietary burden from cottonseed meal is 1 ppm in beef diets and 1.5 ppm in dairy diets. The potential dietary burden from cull raisins fed to beef cattle is up to 0.44 ppm and up to 0.35 ppm in dairy cattle diets. Dry grape pomace fed to beef cattle only can be up to 1.35 ppm potential dietary burden and wet grape pomace fed to beef cattle only can be 2.67 ppm potential dietary burden. Raisin waste fed to beef cattle can have up to 4.57 ppm potential dietary burden and up to 1.9 ppm in dairy cattle as the potential dietary burden. The potential dietary burden from wet tomato pomace in beef cattle is up to 4 ppm and up to 2.67 ppm in dairy cattle. The potential dietary burden from feeding dried tomato pomace to beef cattle is up to 1.63 ppm and up to 0.65 ppm in dairy cattle.

The petitioner's worst case diet, while highly improbable, but which he claims none-the-less maximizes the potential imidacloprid exposure, includes grape pomace at 40% (2.8 ppm), raisin waste at 10% (0.7 ppm), potatoes at 30% (0.75 ppm), and cottonseed at 20% (0.14 ppm). We agree with the petitioner that 100% of the bovine diet can be treated with imidacloprid from the feed items in this petition and in co-pending petition PP# 3F4169. While the petitioner's worst case dietary burden at 4.4 ppm is lower then we expect from the total imidacloprid residues on bovine feed items (calculated on a % dry basis) we agree that 5 mg/kg or ppm in the feed is a reasonable 1X dose. The petitioner used 20% dry matter for apples, grapes, citrus, and potatoes and their associated processed feed items in his calculations for his probable bovine diet that is exposed to imidacloprid. CBTS does not agree with using 20% dry matter across the board for all feed items in these two petitions. Our estimate of a possible maximum imidacloprid beef cattle dietary burden is around 9.6 ppm from a highly improbable diet of 75% cull potatoes (5.6 ppm) and 25% wet tomato pomace (<4 ppm) and a dairy cattle dietary burden around 9.4 ppm from a highly improbable diet of 50% cull potatoes (3.75 ppm), 15% cottonseed meal (1.52 ppm), 20% wet tomato pomace (2.67 ppm), and 15% wet apple pomace (<1.5 ppm).

Sacrifice was 14-18 hours after the last dose. At sacrifice there were no significant morphological or pathological findings noted. The whole liver without the gall bladder, both kidneys, sufficient samples of round, flank, and loin muscle; and subcutaneous (SC), renal, and messenterial fat were collected, then cut into 2 cm cubes and frozen until analysis.

In the control milk no imidacloprid equivalents were detected to < 0.02 ppm. At the 5 mg/kg dose total imidacloprid residues in milk ranged from < 0.02 ppm to 0.023 ppm with 2 samples having residues above 0.02 ppm. At the 15 mg/kg dose total imidacloprid residues ranged from 0.02 ppm to 0.055 ppm with 5 samples having residues above 0.05 ppm. From the high dose of 50 mg/kg total imidacloprid residues ranged from 0.088 ppm to 0.177 ppm with 18 samples above 0.15 ppm.

In fat no imidacloprid equivalents were detected in the control samples and fat samples from the 5 mg/kg and 15 kg/mg doses. Only from the 50 mg/kg dose were imidacloprid

equivalents detected ranging from 0.05 ppm to 0.079 ppm.

Total imidacloprid residues were not detected in the control muscle samples or in the muscle samples from the 5 mg/kg dose. In muscle from the 15 mg/kg dose total imidacloprid residues ranged from < 0.02 ppm to 0.33 ppm and from the 50 mg/kg dose total imidacloprid ranged from 0.097 ppm to 0.192 ppm.

The control kidney samples did not have any imidacloprid equivalents to < 0.02 ppm. From the 5 mg/kg dose total imidacloprid residues ranged from 0.023 ppm to 0.032 ppm and from the 15 mg/kg dose total imidacloprid residues in kidney ranged from 0.053 ppm to 0.106 ppm. At the high dose of 50 mg/kg total imidacloprid residues ranged from 0.201 ppm to 0.384 ppm.

In control bovine liver no imidacloprid residues were detected to < 0.02 ppm. At the 5 mg/kg dose total imidacloprid residues in liver ranged from 0.041 ppm to 0.054 ppm, and from the 15 mg/kg dose total imidacloprid residues ranged from 0.084 ppm to 0.168 ppm. From the high dose 0f 50 mg/kg residues in liver ranged from 0.384 ppm to 0.566 ppm.

Based on the results of the imidacloprid bovine feeding study we reiterate that finite residues will actually occur in milk and meat from the feeding of imidacloprid treated racs or their processed feed items when Admire® is used as directed. Since this situation falls under 40 CFR §180.6(a)(1) secondary imidacloprid tolerances are required for milk and meat. CBTS concludes the imidacloprid bovine feeding study adequately supports the proposed 0.1 ppm tolerance in milk and the 0.3 ppm tolerance in meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep.

Poultry

The petitioner presented the results of a poultry feeding study in a document titled "NTN 33893 - Poultry Feeding Study" by U. Heukamp dated September 10, 1992, and submitted with PP# 3F4169. The study has been reviewed by F. Griffith, Jr., in the September 21, 1993, memorandum (qv).

In summary, the petitioner use 6 month single comb White leghorn pullets in good egg production in the feeding study. 50 pullets were assigned to one of four test groups and given a unique identification number on their individual cage and on their leg band. The feeding study was conducted in Monheim, Germany and followed accepted poultry housing practices and environmental conditions. The pullets received a daily veterinary inspection.

Eggs were collected twice daily and immediately frozen. Three eggs from the same dose group that had nearly the same feed consumption were thawed, then cracked, opened, and homogenized. The number of eggs produced in all 4 test groups does not appear the affected by the imidacloprid doses.

Water and feed were presented ad libitum throughout the study. The feed was a commercially available complete laying hen diet containing 16.5% protein, 3.5 % fat, 6% fiber, and 12 % ash plus vitamins A, D, and E fortifications. The petitioner weighed out each morning 200 grams of feed for each pullet. The amount of feed not consumed from the

previous day was collected, weighed, and recorded before the new feed was given to the pullets. Data were presented showing the amount of feed each pullet consumed each day as well as the overall average feed consumption for each pullet throughout the study were calculated and presented for review. The pullets were dosed with technical imidacloprid mixed into the feed at doses of 2 mg/kg, 6 mg/kg, and 20 mg/kg.

The poultry feed items associated with PP# 3F4169 are cottonseed meal [89 % dry matter] up to 20% of the diet. Wet apple pomace, cull potatoes and processed potato waste, undelinted cottonseed , cottonseed hulls, and cotton gin byproducts are not considered to be poultry feed items. In this petition peppers, cabbage, cauliflower, broccoli, cull raisins, grape pomace, raisin waste, lettuce, or mustard greens are not considered to be significant poultry feed items. Dried tomato pomace [92% dry matter] is a poultry feed item up to 10% of the diet. All of the dry matter percentages and the percentages of the feed items in poultry diets are taken from Table II (June 1994). The correct calculation of poultry dietary burden is on the "as-fed" basis. The potential poultry dietary burden for each of these feed items is based on the proposed tolerance and the percentage in the diet for the particular poultry feed item.

The potential poultry dietary burden from cottonseed meal is 1.8 ppm [0.2{% in diet} X 9 {proposed tolerance} = 1.8 ppm] and from dried tomato pomace is 0.6 ppm. The petitioner's worst case poultry diet, that is highly improbably, but which he claims maximizes potential imidacloprid exposure includes grape pomace at 8% (0.56 ppm), spring cereal grains (not specified) at 50% (0.025 ppm), grain dust at 4% (0.002 ppm), potatoes at 30% (0.75 ppm), cottonseed oil (soapstock) at 5% (0.175 ppm), and cottonseed meal at 3% (0.015 ppm). Based on Table II (June 1994) we no longer agree that 100% of the poultry feed items will be treated with imidacloprid as only two poultry feed items are included from these two petitions. The petitioner's worst case dietary burden is at 1.62 ppm; however our revised dietary burden is higher at 2.4 ppm. We agree that 2 ppm or mg/kg is a reasonable 1X feeding dose.

Sacrifice was after the last dose. At sacrifice no significant morphological or pathological findings were noted. The whole liver, composite thigh muscle, and breast muscle, and abdominal fat were collected, then cut roughly and immediately frozen until analysis.

In the control eggs and eggs from the 2 mg/kg dose no imidaclo-p-rid equivalents were detected to < 0.02 ppm. At the 6 mg/kg dose total imidacloprid residues ranged from 0.021 ppm to 0.056 ppm with 5 samples having residues above 0.05 ppm. From the high dose at 20 mg/kg total imidacloprid residues ranged from 0.034 ppm to 0.148 ppm with 29 samples above 0.1 ppm.

In poultry fat no imidacloprid residues were detected in the control samples and in either the 2, 6, or the 20 mg/kg doses to the LOQ of < 0.02 ppm.

Total imidacloprid residues were not detected in the control muscle samples or in the muscle samples from the 2 mg/kg dose. At the 6 mg/kg dose total imidacloprid residues ranged from < 0.02 ppm to 0.022 ppm. From the high dose of 20 mg/kg dose total imidacloprid residues in poultry muscle range from 0.031 ppm to 0.072 ppm.

In the control poultry livers no imidacloprid residues were detected to < 0.02 ppm. At

the 2 mg/kg dose total imidacloprid residues ranged from 0.035 ppm to 0.042 ppm, and from the 6 mg/kg dose ranged from 0.121 ppm to 0.16 ppm. From the 20 mg/kg dose total imidacloprid residues in poultry liver ranged from 0.235 ppm to 0.448 ppm.

Based on the results of the imidacloprid poultry feeding study CBTS reiterates that finite residues will actually occur in eggs and poultry meat from feeding of imidacloprid treated racs or their processed feed commodities when Admire® is used as directed. Since this situation falls under 40 CFR §180.6(a)(1) secondary imidacloprid tolerances are required for eggs and poultry meats. CBTS concludes the imidacloprid poultry feeding study adequately supports the proposed 0.02 ppm tolerance in eggs and the 0.05 ppm tolerance in meat, fat, and meat by-products of poultry.

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 compatibility is not a problem at this time.

cc:R.F.,Circ,Reviewer(FDG),PP#3F4231.

7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:6/6/94:edit:fdg:6/22/94.

RDI:SecHd:RSQuick:6/21/94:BrSrSci:RALoranger(byECS):6/21/94.