MEMORANDUM

Subject: **PP# 3F4169/3H5655 - Imidacloprid (Admire®) on Apples, Potatoes, Cottonseed, Meat, Milk, Poultry, and Eggs.**
Review of the March 1 and April 11, 1994, Amendments.
(MRID #s 428103-11, -12, and -13, 431432-01 thru -08, 431972-01 thru -03, and 432130-01)[CBTS #s 13366 thru 13369, and 13560]{DP Barcode #s D200233, D200234, D200238, D200243, D202048, D202548, and D202897}

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6/6/94

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Thru: Esther Saito, Chief
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Background

Miles, Inc., Agriculture Division, submitted these amendments consisting of cover letters dated March 1 and April 11 and 21, 1994, and signed by J.S. Thornton, a supplementary Section A (additional validation data for the enforcement analytical for formulations), a revised Section B (new labels), supplementary Section D (Independent Laboratory Validation data and revised residue analytical methods, cottonseed metabolism, feeding studies, and storage stability), and a revised Section F (revised numerical tolerances). This amendment was submitted in response to deficiencies outlined and summarized in our September 21, 1993, review by F.D. Griffith, Jr. The deficiencies are listed and repeated in the body of this review as they appeared in our September 21 review followed by the petitioner's responses, then CBTS comments. Our conclusions and recommendations follow.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- Revise label/directions for use on cotton

- Need field rotational crop studies

- Additional residue method validation data

- Additional cotton crop field trials

- Revise tolerances

CONCLUSIONS

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

The petitioner has presented the necessary enforcement method validation data for GRN 62-3. The accuracy of this method expressed in % recovery is 100.02% and the precision of the method expressed as the variance is 0.24/0.25%. These data are presented as part of the analytical enforcement method for formulations. No further data are required for this topic. Deficiency 1 is resolved.

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

a. CBTS reiterates the petitioner has proposed an adequate set of directions for use of imidacloprid formulated as Admire® either as a granular or as a flowable for use on apples and potatoes.

b. The petitioner has submitted a new label for Gaucho® 480 to be used as a seed treatment prior to planting at a rate of 8 fl ozs Gaucho (0.25 lb imidacloprid a.i.) per 100 pounds of cottonseed, or 0.0025 lb a.i./pound of cottonseed. The proposed use matches the use in the magnitude of the residue crop field trial residue data. This part of deficiency 8a is resolved.

c. CBTS has no objections to having a lower use rate on cotton and thus a lower usage per season; however, we suggest that the petitioner consider having a maximum number of Admire applications to cotton at less than 10; ie, 8 per cotton growing season is a better approximation to the field trial data.

d. At the proposed higher use rate growers can use 4 applications per cotton growing season which more nearly approximates the use rate in the crop field trials and adequately addresses our concerns noted in deficiency 8a. This part of deficiency 8a is resolved.

e. On the revised label the petitioner proposes use of an organosilicone based spray adjuvant to improve coverage on cotton. CBTS considers this is still too general in its directions for use of adjuvants in cotton foliar applications. The petitioner needs to consider the language used in recent Emergency Exemption requests for use of adjuvants with imidacloprid on hops. In those requests we recommended for foliar applications by ground equipment in a minimum of 50 gallons of water per acre to ensure through coverage to the point of run off and that an EPA approved spray adjuvant may be added at the minimum rate as specified by the spray adjuvant manufacturer per 50 gallons. Deficiency 2a is not resolved and continues outstanding.

f. Both revised labels for use on cotton have the restriction of do not graze treated fields after any applications of Admire. This part of deficiency 8c is resolved.

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

a. Deficiency 3c is resolved. The nature of the imidacloprid residue in cottonseed is now adequately understood. Though imidacloprid is more tightly bound in cotton than in other matrices it is metabolized by the same three pathways as in apples, potatoes, tomatoes, eggplant, and corn. Using the data generated for cotton leaves and the data reported on cottonseeds both in the original submission and in this amendment the pathways are as follows:

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

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

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

b. The residues of concern in cottonseed are imidacloprid and its metabolites that contain the 6-chloropyridinyl moiety.

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

a. CBTS reiterates that all 3 rotational crops in the confined study have 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. CBTS concludes there is potential for inadvertent residues to occur in non-target crops planted in rotation. Limited field rotation crops are necessary for a representative crop at 2 sites per crop for the following 3 crops: root and tuber vegetables, leafy vegetables, and cereal grains. At least a total of 6 field trials are necessary all at the 1X application rate.

b. We reiterate that based on the data presented from the confined imidacloprid accumulation studies CBTS anticipates that the petitioner will need to propose imidacloprid tolerances for rotational crops. A final decision on the need for tolerances and more extensive field trials will be based on the results of the limited field trials.

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

a. Since the urea and nitrosimino imidacloprid constitute less then 2% of the total radioactive residue (TRR) and the HED Metabolism Committee concluded in its June 22, 1994, meeting that none of these imidacloprid metabolites were of toxicological concern that would warrant separate regulation, CBTS agrees with the petitioner that additional MRM recovery data for the urea and nitrosimino imidacloprid metabolites are not needed. Deficiency 2 is resolved.

b. The petitioner has presented acceptable ratio values for 4 selected ions for use in MS quantitation. These ratios serve as an index for the determination of interferences if and when encountered by any of the 4 ions. If the ratios of the 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 GC retention time through a capillary column, then the presence of imidacloprid is confirmed. This is adequate acceptance criteria for confirmation of residues. Deficiency 4 is resolved.

c. For Deficiencies 5 and 6 CBTS reiterates that we will need a confirmatory method that will precisely identify imidacloprid and its major metabolites, as well as be at least semi-quantitative, though we prefer the method be quantitative. CBTS reiterates our suggestion that the petitioner should continue his efforts to having the confirmatory procedure become more specific by using among other things different extraction procedure, clean-up, if necessary, different derivatization, alternate chromatographic columns, and a different detection technique. We reiterate that ILV data are necessary before a tolerance method Validation (TMV) can be started in EPA labs.

d. **Tentatively for PP# 3F4169 and PP# 3F4231 the lack of the confirmatory procedure is not a bar to our recommendation for the proposed tolerances provided no other compounds in this new class of insecticides are presented for registration and tolerances.**

e. In section 3.1.3. of the plant method, Bayer method 0200, and in section 3.1.3.1 of the animal tissues method, Bayer method 00191, the analytical reference standards for the hydroxy and olefin imidacloprid metabolites are listed as being available from Miles, Inc. They are also available from the EPA Repository in RTP-NC. Deficiency 8 is resolved.

f. The petitioner has presented the results of a new ILV study conducted in the USA using the revised and reformatted plant method, Bayer method 0200, for imidacloprid and its major metabolites individually spiked at the proposed apple tolerance and 5X tolerance. These data are in general agreement with the recovery data generated by the petitioner. They are acceptable and can support the Agency's TMV for the plant residues enforcement method. No additional ILV data are required for the plant method for this petition, PP# 3F4169, and the co-pending petition PP# 3F4231. These parts of deficiencies 7 and 9, and all of deficiency 13 are resolved.

g. Since we are no longer requiring MRM and/or method validation data for the urea and nitrosimino imidacloprid this part of deficiency 9 becomes moot and is thus resolved. We have previously concluded cotton forage is no longer a significant livestock feed item and the petitioner has proposed an acceptable feeding restriction plus withdrawn the proposed tolerance, thus additional method validation data for imidacloprid and its metabolites on cotton forage are not required. This part of deficiency 9 is resolved.

h. The petitioner has provided the requested method validation data for the

imidacloprid metabolites in apples at 0.1 and 0.5 ppm and at the 0.1 ppm level for the major imidacloprid metabolites in potatoes and cottonseed. These data validate the method at the LOQ and in the range where residues are reported for apples and potatoes. The remaining part of deficiency 9 is resolved.

i. The petitioner has provided additional copies of supporting chromatographic data for 6-CNA recoveries using the plant residue method in both the new ILV report and in the reformatted plant residue method. The supporting chromatographic data show recoveries of 6-CNA in the raw agricultural commodities (rac) and in the processed commodities. Deficiency 10 is resolved.

j. In the heading for Table 1, Appendix 12 in the revised plant method the petitioner has now clarified that the range of recovery represents only the 2 datum points used to calculate the mean with the statement that only 2 experiments were conducted for each concentration. The petitioner has presented not only a range of recoveries and a mean recovery, but also the individual datum points. Deficiency 11 is resolved.

k. The data presented do not resolve deficiency 7. It continues unresolved and remains outstanding. In 2 telcons (D. Griffith-J. Thornton on April 12 and 14) the petitioner has been notified that additional method validation data at the revised proposed tolerances levels in the rac's and processed commodities are necessary to support the plant residue method as a tolerance enforcement procedure. All of the following data are to be generated in duplicate and will be for the parent and individual metabolites as follows:

1. Apples are to be spiked at 0.5 ppm (proposed tolerance) and at a level of 2-5X the proposed tolerance (as specified in PRN 88-5) with the parent, the guanidine, and either the hydroxy, olefin, or 6-CNA. Wet apple pomace is to be spiked at 3 ppm (proposed tolerance) and at a level of 2-5X the proposed tolerance with the parent imidacloprid, the guanidine, and either 6-CNA, the olefin, or the hydroxy metabolite. CBTS suggests, for example, that if the olefin is used as the rac apple spike, then either 6-CNA, or the hydroxy be used in wet apple pomace spike.

2. In the rac potatoes the spikes should be at 0.3 ppm (proposed tolerance) and at a level 2-5X the proposed tolerance with the parent imidacloprid, the guanidine, and either 6-CNA, the hydroxy, or the olefin metabolite. The same spiking procedure should be followed for potato chips spiked at 0.4 ppm and at a level 2-5X higher and for potato waste spiked at 0.9 ppm and at a level 2-5X higher. Fortification should be for the parent imidacloprid, the guanidine, and one other metabolite. Since there are 3 commodities with potatoes to have additional method validation data, the petitioner should consider using a different metabolite for each third fortification; eg, 6-CNA in the rac, the olefin in potato chips, and the hydroxy in potato waste.

3. For the rac cottonseed the fortifications should be at 6 ppm (proposed tolerance) and at a level 2-5X the proposed tolerance with the parent, guanidine,

and 6-CNA. CBTS suggests 6-CNA be the third fortification as it is the major metabolite detected in the metabolism study. The same spiking procedure should be followed with cottonseed meal spiked at 9 ppm and at a level 2-5X the proposed tolerance. In cottonseed meal the petitioner should consider the third fortification be either the hydroxy or the olefin imidaclo-prid.

l. The petitioner has provided data to show that the ILV and the method validation were completely independent. Provisions as described in PRN 88-5 were followed. Deficiency 12 is resolved.

m. While CBTS would like to have recovery data using the methanol/1% H_2SO_4 extracting solvent the petitioner contends the data already generated are in reality a "worse case" or minimum recovery that is expected. CBTS agrees this is a minimum recovery expected, thus no additional recovery data are necessary using methanol/1% H_2SO_4 to improve the recovery of aged ^{14}C-imidacloprid residues. Deficiency 14 is resolved.

n. The petitioner has presented the results of a new ILV study conducted in the USA using the revised and reformatted animal tissues method, Bayer method 00191, for imidacloprid and its major metabolites individually spiked at the proposed meat by-products tolerance and 5X tolerance. These data are in general agreement with the recovery data generated by the petitioner. They are acceptable and can support the Agency's TMV for the animal tissues residues enforcement method. No additional ILV data are required for the animal tissues method for this petition, PP# 3F4169, and the co-pending petition PP# 3F4231. These parts of deficiency 18 and all of deficiency 19 are resolved.

o. Since we are no longer requiring MRM and/or method validation data for the urea and nitrosimino imidacloprid this part of deficiency 18 becomes moot and is thus resolved. We have previously concluded that only ruminant liver will be in our TMV. No ILV data will be required for imidacloprid and its major metabolites in beef kidney, fat, and muscle; as well as in poultry liver and muscle, thus additional ILV method validation data for imidacloprid and its metabolites are not required. Discussions with the lab indicate the initial ILV data are now sufficient to complete the TMV; thus no additional ILV data will be required for eggs and/or milk. These parts of deficiency 18 are resolved.

p. The petitioner has generated extensive method validation data for imidacloprid and its olefin guanidine, hydroxy, and 6-CNA metabolites in bovine liver, fat, muscle, and kidney, and in milk. In bovine tissues the method validation were at the LOQ, around or at the proposed tolerances and above tolerances. In poultry tissues (liver, muscle, and fat) and in eggs the petitioner has provided imidacloprid and its olefin, guanidine, and 6-CNA recovery data at the LOQ, at or near the proposed tolerances, and above the proposed tolerances. These recovery data are sufficient to show that the proposed enforcement method for animal tissues, Bayer method number 00191, is suitable to gather the magnitude of the residue data and can enforce the proposed tolerances. Deficiencies 15, 16, and 17 are resolved. No additional petitioner generated method validation data for Bayer method number 00191 are needed for

petition PP# 3F4169 and for the co-pending petition PP# 3F4231.

6. CBTS Conclusion on **Storage Stability**

a. CBTS concludes that imidacloprid and its major metabolites, both labeled and unlabeled compounds, are stable under frozen conditions in lettuce for 24 months. While these data are supplementary to PP# 3F4169 they are germane to PP# 3F4231.

b. CBTS concludes that imidacloprid and its major metabolites are stable under frozen conditions in corn grain, fodder, and forage for 24 months. These storage stability data are supplementary to PP#s 3F4169 and 3F4231.

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 concentration as the initial total imidacloprid was 5.88 ppm and 2 years later the total imidacloprid in lemons was 5.82 ppm. CBTS concludes that the total imidacloprid residues in lemons are stable for 2 years. These data are supplementary for PP#s 3F4169 and 3F4231.

d. 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 the 115% of the initial fortification. These data are sufficient to support the magnitude of the total imida-cloprid residue crop field trials data reported for potatoes stored up to 11 months from harvest to analysis.

e. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable in apples, apple juice, and apple pomace (wet and dried) for at least 19 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trials data that were reported for apples stored for up 9 months from harvest to analysis.

f. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable in cottonseed and in cottonseed hulls, soapstock, and oil for at least 18-20 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trial data that were reported for cottonseeds stored for up to 8 months from harvest to analysis.

g. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable during frozen storage in wheat grain, forage, and fodder; and in wheat processed commodities (grain dust, bran, flour, and shorts) for at least 18/20 months. CBTS concludes that these storage stability data for wheat commodities are supplementary for PPs 3F4169 and 3F4231 as there is no proposed imidacloprid tolerance on any wheat commodity.

h. The petitioner has provided adequate frozen storage stability data in tomatoes and cauliflower to show that total imidaclo-prid residues are stable for at least 18 months. While these frozen storage stability data are supplementary to PP# 3F4169 they are germane to PP# 3F4231.

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

The petitioner has been informed that at least 3 additional cotton field trials for the 1994 crop year are necessary to have adequate geographical representation. Specifically, these trials need to be in west Texas/ New Mexico/ west Oklahoma. The petitioner is reminded that he needs to have the 3 new trials, as well as a total of 12 cotton field trials all at the proposed 1X imidacloprid use rate. For the 3 new trials on cotton the petitioner needs to have imidacloprid applied at the proposed use rate; ie, treated seed plus soil drench plus 4 foliar applications all at the proposed 1X application rate. Deficiency 8a is not resolved and continues outstanding.

8. CBTS Conclusions on the **Proposed Tolerances**

a. The petitioner will need to modify the proposed tolerance expression in a revised Section F to reflect what is actually measured by the residue analytical enforcement method. The expression should read "tolerances of combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as imidacloprid on the following commodities:"

b. CBTS reiterates that at this time the petitioner's cotton crop field trial residue data do not support the proposed 6 ppm tolerance on cottonseeds as there are insufficient geographical representation of cotton field trials. The results from the additional crop field trials are necessary before a decision can be made on the adequacy of the proposed 6 ppm tolerance. This part of deficiency 8a remains unresolved and continues outstanding.

c. CBTS reiterates that while an imidacloprid FAT is required for cottonseed meal, judgement is deferred on the proposed FAT as there are insufficient geographically representative crop field trial data available from the proposed imidacloprid use to determine the proper imidacloprid tolerance on cottonseed, and thus the FAT for cottonseed meal. Deficiency 9a is not resolved and continues outstanding.

d. The petitioner has proposed a 0.5 ppm total imidacloprid tolerance on apples. The petitioner has presented sufficient varietal and geographically representative magnitude of the residue crop field trial residue data to show that when Admire® is used as directed residues are not expected to exceed the proposed 0.5 ppm tolerance on apples. Deficiency 8e is resolved.

e. The petitioner has proposed a 3 ppm tolerance on apple pomace (wet and dried) which helps avoids proliferation of tolerances as suggested by CBTS. CBTS reiterates that the petitioner has conducted an apple processing study using apples bearing detectable total imidacloprid residues following an exaggerated imidacloprid application. The results of the study show a 6X concentration factor for apple pomace; thus a feed additive tolerance of 3 ppm for apple pomace (wet and dried) is necessary. Deficiency 9b is resolved.

f. The petitioner proposes a 0.3 ppm total imidacloprid tolerance for potatoes

pointing out that the highest residue is due to mainly soil application. After reconsideration CBTS agrees. The petitioner has presented an adequate amount of varietal and geographically representative magnitude of the residue crop field trial residue data that shows when Admire® is used as directed total residues of imidacloprid are not expected to exceed the 0.3 ppm tolerance. Deficiency 8g is resolved.

g. In the revised Section F the petitioner has proposed new tolerances for potato chips and potato waste based on the new tolerance proposed for the rac potatoes. CBTS reiterates that the petitioner has conducted an adequate potato processing study using potatoes bearing detectable residue from an exaggerated application. Total imidacloprid residues were shown to concentrate in potato chips 1.3X requiring a revised FAT of 0.4 ppm and to concentrate in dry potato peels at 2.9X requiring a revised FAT of 0.9 ppm for potato waste. Deficiency 9c is resolved.

h. CBTS reiterates that based on the results of the imidaclo-prid bovine feeding study CBTS concludes that finite residues will actually occur in milk and 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 in meat and milk. The proposed limit of detection secondary tolerances are not acceptable. CBTS suggests the petitioner propose in a new Section F revised milk and meat tolerances at the levels submitted with PP# 3F4231; that is, 0.1 ppm in milk and at 0.3 ppm in the meat, fat, meat by-products of cattle, goats, hogs, horses, and sheep. These levels include all livestock feed items reviewed in this petition and in the co-pending petition currently under review. Deficiency 10a is not resolved and continues outstanding.

i. CBTS reiterates that based on the results of the imidaclo-prid poultry feeding study we conclude that finite residues will actually occur in eggs and poultry meat from feeding of imidacloprid treated racs, or their processed fees commodities when Admire® is used as directed. Since this situation falls under 40 CFR 180.6(a)(1) secondary imidacloprid tolerances are required in eggs and poultry. The proposed limit of detection secondary tolerances in poultry are not acceptable. CBTS suggests that the petitioner propose in a new Section F revised tolerances at 0.02 ppm for eggs and at 0.05 ppm (assuming the cottonseed tolerance will not be significantly different as a result of the new field trials residue data) for poultry meat, fat, and meat by-products. These levels include all poultry feed items reviewed in this petition and in the co-pending petition currently under review. Deficiency 10c is not resolved and continues outstanding.

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

a. The petitioner provided the ages of the cows in the feeding study and the source of the cows. The petitioner has provided a description of the housing practices as used in Germany for conducting the bovine feeding study. The daily housing practices are similar in Germany to those in the USA. The petitioner provided an English translation

of the label for the feed used in the bovine feeding study showing that it is a supplementary feed which contains 16% protein, 3.2% fat, 9% fiber, and 10% ash; plus vitamin supplements. The type of hay used was from a grass meadow which had no history of any chemical treatment. The petitioner has the quality assurance data from the German feed producing plant, daily health report for each cow from the attending veterinarian, plus a weekly intensive examination for each cow. This is sufficient data for CBTS to conclude the cow feed was free from significant contamination from other pesticides, mycotoxin, and heavy metals. Deficiency 10b is resolved.

b. The petitioner provided an English translation of the label for the poultry feed which shows the poultry feed is a complete laying hen diet containing 16.5% protein, 3.5% fat, 6% fiber, and 12% ash, plus vitamin fortifications. The petitioner has the quality assurance data from the German feed producing plant and daily health report for each hen from the attending veterinarian. This is sufficient data for CBTS to conclude the poultry feed was free from significant contamination from other pesticides, mycotoxin, and heavy metals. Deficiency 10d is resolved.

c. The breed used in the poultry feeding study was Lohmann Single Comb White Leghorn. This is a commercial poultry breed. Deficiency 10e is resolved.

RECOMMENDATION

CBTS cannot recommended for the requested tolerances for residues of imidacloprid and its metabolites containing the 6-clororpyridinyl moiety in apples at 0.5 ppm, apple pomace (wet and dried) at 3 ppm, in cottonseed at 6 ppm, in cottonseed meal at 9 ppm, in potatoes at 0.3 ppm, in potato chips at 0.4 ppm in potato waste at 0.9 ppm, and in milk, eggs, meat, fat, meat by-products of cattle, goats, hogs, horses, poultry, and sheep at < 0.02 ppm for the reasons cited in our Executive Summary and further described in Conclusions 2c and e, 4a and b, 5k, 7, and 8a, b, c, h and i.

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

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

Deficiency

1. CBTS reiterates that validation data, although alluded to in the description of the analytical method provided for the preliminary analysis has not been presented and needs to be presented. These validation data should be presented as part of the analytical method used to verify the certified limits for the active ingredient. The petitioner is reminded that the analytical method will be validated as the formulation enforcement method.

Petitioner's response

The petitioner submitted the requested product chemistry method validation data for GRN 62-3 in a study titled "Product Chemistry of Bay NTN 33893 Technical" by L. Fontaine dated April 15, 1994, and coded Miles report number 106286 (MRID # 432130-01).

CBTS Comments

Accuracy is defined as the closeness of agreement between a test result and an accepted reference value. The petitioner conducted a series of tests to determine accuracy by using an internal standard at 3 different levels and express the results in terms of percent recovery. 2.5115 grams of imidacloprid was weighed into a 250 ml flask to serve as an internal standard and the internal standard, propiophone, was to be the sample. Propiophone weights were 0.94, 0.99, and 1.06 of the standard weights. The average percent recovery using reverse phase HPLC-UV was 100.02% $\pm$ 0.23%, COV = 0.23% with individual recoveries ranging from 98.80% to 100.25%.

The precision of the method is based on three analyses of two samples of imidacloprid technical using the same reverse phase HPLC-UV equipment. The results for one sample ranged from 96.94% to 97.37%, X = 97.20% $\pm$ 0.23%, COV = 0.24% and the results for the other sample ranged from 98.40% to 98.89%, X = 98.64%, $\pm$ 0.25%, COV = 0.25%. The petitioner also conducted UV scans to determine if interferences were present. The upward side, apex, and downward side were compared for all three scans on a sample. Since the spectra for all three scans matched there were no interferences present. The petitioner presented copies of the UV spectra and CBTS agrees with the petitioner's findings of no interferences present.

The petitioner has presented the necessary enforcement method validation data for GRN 62-3. The accuracy of this method expressed in % recovery is 100.02% and the precision of the method expressed as the variance is 0.24/0.25%. These data were presented as part of the enforcement analytical method. No further data are required for this topic. Deficiency 1 is resolved.

DIRECTIONS FOR USE/LABELING

Deficiencies

2. The petitioner needs to more narrowly define on a revised Confi-dor® 2 Flowable label which spray adjuvants are acceptable. The present revised label is too general in its instructions for use of the spray adjuvants in foliar applications to cotton since field trial data show the use of an adjuvant in the crop field trials essentially doubled the total imidacloprid residues in cottonseed.

8a. The petitioner has the option of either generating all new cotton field trial residue data at the proposed use, or proposing a new set of directions for use in which accurately reflect the use pattern for generating the magnitude of the residue data, namely adding a use for treating cotton seed and having only 2 foliar applications at a rate of 0.24 lb a.i., 7 day repeat

application interval with a 14 day PHI plus the use of the spray adjuvant Silwet 77.

8c. While cotton forage is listed currently in Table 2 as a rac and a cattle feed item CBTS does not feel this is a significant feed item at this time. Information we have received indicates cotton forage is not used as a feed item and, if it is, then cotton forage has a very limited use. CBTS will not require any additional crop field trial residue data for imidacloprid on cotton forage. We suggest the petitioner submit a revised label prohibiting the possible use of cotton forage as a feed and also propose a revised Section F deleting the proposed total imidacloprid tolerance on cotton forage.

Petitioner's response

The petitioner has submitted new labels for imidacloprid formulated as Admire® 2 Flowable Systemic Insecticide (EPA File Symbol No. 3125-UEE) containing 2 lbs per gallon or 21.4% ai imidacloprid. Another new label was submitted for imidacloprid formulated as Admire® 2.5 Granular Systemic Insecticide (EPA File Symbol No. 3125-UEG) containing 2.5% ai. imidacloprid. With these new labels the petitioner has changed the trade name from Confidor to Admire. In future reviews relating to the commodities in this petition CBTS will refer to the formulations as Admire and will drop Confidor. The petitioner has also submitted a new label for Gaucho® 480 proposing a seed treatment use on cottonseed.

CBTS Comments

There has been no change in the proposed use as an insecticide to control aphids, leafhoppers, leafminers in apples; **whiteflies**, aphids, thrips, and plantbugs on cotton; and aphids, leafhoppers, flea
beetles, and Colorado potato beetles on potatoes.

Review of the revised label for Admire® 2.5 Granular formulation for use on potatoes and on cotton at planting shows there are no significant changes from the use initially proposed. Comments from our September 21, 1993, review on the proposed use of the 2.5% granular formulation are now incorporated herein by reference.

Review of the revised label for use of Admire® 2 Flowable on apples shows there are no significant changes to the proposed use. Likewise, the revised label contains no significant changes in direct-ions for use of Admire® 2 Flowable on potatoes. Comments from our September 21, 1993, review on the proposed use of the 2 lbs/gal formulation for use on potatoes and apples are incorporated herein by reference.

CBTS reiterates the petitioner has proposed an adequate set of directions for use of imidacloprid formulated as Admire either as a granular or as a flowable on apples and potatoes.

The petitioner has submitted a new label for Gaucho® 480 which contains imidacloprid at 40.7% or 480 grams/liter (equivalent to 4 lbs per gallon) to be used as a seed treatment prior to planting. Cottonseeds are to be treated at a rate of 8 fl ozs Gaucho (0.25 lb imidacloprid a.i.) per 100 pounds of cottonseed, or 0.0025 lb a.i./pound of cottonseed. The product is for use only in liquid or slurry treaters, not for use on agricultural establishments in

hopper boxes, slurry boxes, or in any other seed treatment applications at planting. The proposed use matches the use in the magnitude of the residue crop field trial data. This part of deficiency 8a is resolved.

The petitioner has revised the directions for use on cotton for Admire® 2 F. There is still a soil application at planting at a rate of 1.3 fl ozs per 1000 row feet as a narrow band in furrow spray at or below the seed line for rows 42 to 34 inches apart. If these directions are followed, then the grower will apply from 0.25 lb ai imida-cloprid for a 42 inch row spacing to 0.31 lb ai imidacloprid for a 34 inch row spacing. For soil application to cottonseed at planting the petitioner has proposed a maximum of 0.3 lb ai imidacloprid per season. The is also a proposed foliar application to cotton at a rate of 3 fl ozs to 7.5 fl ozs (0.05 lb ai to 0.125 ai) per application with a 7 day repeat application interval and a 21 day PHI. Foliar applications to cotton may be by ground or air. For foliar application the petitioner may use a maximum of 0.5 lb ai per acre per growing season. At the proposed higher use rate growers can use 4 applications per season which more nearly approximates the use rate in the metabolism study and adequately addresses our concerns noted in deficiency 8a. This part of deficiency 8a is resolved. At the lower use rate 10 applications may be made. CBTS has no objections to having a lower use rate and thus a lower usage per season; however, we suggest that the petitioner consider having a maximum number of Admire applications to cotton at less than 10; ie 8 per cotton growing season which is a better reflection of the residue data. With a maximum of 0.5 lb ai imidacloprid being applied to cotton, growers have the option to use all foliar applications, or to split the applications between soil at planting and foliar applications as long as no more then 0.5 lb ai are applied in a single cotton growing season.

On the revised label the petitioner proposes use of an organo-silicone based spray adjuvant to improve coverage. CBTS considers this is still too general in its directions for use of adjuvants in cotton foliar applications. The petitioner needs to consider the language used in recent Emergency Exemption requests for use of adjuvants with imidacloprid on hops. In those requests we recommended for foliar applications by ground equipment in a minimum of 50 gallons of water per acre to ensure through coverage to the point of run off and that an EPA approved spray adjuvant may be added at the minimum rate as specified by the spray adjuvant manufacturer per 50 gallons. Deficiency 2a is not resolved and continues outstanding.

Both revised labels for use on cotton have the restriction of do not graze treated fields after any applications of Admire. This part of deficiency 8c is resolved.

NATURE OF THE RESIDUE - PLANTS

Cottonseed

Deficiency

3c. The nature of the imidacloprid residue in cottonseed is not adequately understood when 56% of the residue is unidentified metabolites and is compared to the proposed 6 ppm tolerance for cottonseed. The petitioner is reminded that he is expected to identify at least 90% of the radioactive residue. The petitioner needs to provide additional identification of radiolabeled residues in cottonseeds, either from reserve ^{14}C-imidacloprid cottonseed

samples not analyzed, or from reanalysis of extracts from cottonseeds from the soil drench part of the metabolism study. CBTS feels that the unidentified metabolite which is 1.62 ppm imidacloprid equivalents should be easily identified. The petitioner also has the option of repeating the ^{14}C-imidacloprid cotton metabolism study using an exaggerated application rate that approximates the proposed in-furrow, banded at planting application plus 4 foliar applications to generate sufficient radio-labeled residues for identification of metabolites.

Petitioner's response (MRID # 431432-01)

The petitioner has provided the results of additional characterization and identification of radiolabeled residues in the cottonseed metabolism study in a document titled "Addendum 1 Metabolism of NTN 33893 in Cotton After Seed Treatment" by K. Vogeler and A. Brauner dated December 7, 1993, and coded Miles report number 103818-1.

CBTS Comments

The petitioner noted that all of the cottonseeds from the exaggerated rate application were used in the initial extractions. However, the petitioner did not use all of the original extracts and adequate amounts of the methanol/water phase, methanol reflux extract, and methanol/6N HCL reflux extract were still available for further characterization and identification of radioresidues.

The initial part of the experiment was to repeat the TLC analysis of these extracts and compare the plates to see if there were any qualitative and/or quantitative changes during the 3 years of storage. The TLC plates used were Merck's Kiesselgel 60 F_{254}. Known reference compounds of the plant metabolites were co-chromatographed and visualized by UV at 254 nm. The radioresidues were detected using a BAS 2000 Bio-Imaging Analyzer. This instrument uses ultra sensitive imaging plates which when exposed to the TLC plates containing the radiolabeled compounds accumulates and stores irradiated radioactive energy. This plate is scanned with a fine laser and emits luminescence in proportion to the recorded radiation intensity. The were no significant changes in the chromatographic profile in the methanol/ water phase and in the methanol reflux extract. In the methanol/6N HCl extract the chromatographic profile was unchanged, but there were minor quantitative changes.

CBTS's major concern was the identification of the 1.62 ppm unknown. The petitioner refers to this compound as Metabolite 15. The petitioner used HPLC to separate metabolite 15 from the reflux
extract. The HPLC was a Hewlett-Packard 1090 LC with a diode array detector set at 265nm and a Ramona D radioactivity flow through detector which were connected to a Gilson 202 fraction collector. The columns were either a LiChrosorb RP 18, 25 cm X 4mm, or a LiChrosorb RP 8, 25 cm X 4 mm. Then, using 2 dimensional TLC with an authentic reference standard the unknown was identified as 6-hydroxynicotinic acid methyl ester. The structure was confirmed using GC/MS. The GC was a Hewlett-Packard 5880A GC connected to mass selective detector, HP 5970, in the EI mode, using a 15m capillary SE 54 column with splitless injection.

Another major unidentified metabolite which was 0.44 ppm in the original extract is referred to as metabolite 16. Using 2 dimensional TLC with an authentic reference standard

this metabolite was identified as 6-hydroxynicotinic acid. The third major unidentified metabolite was 0.33 ppm in the original extract is referred to as metabolite 19. Additional TLC using different solvent systems shows the metabolite was really two compounds, one of which was the 6-chloronicotinic acid methyl ester.

The petitioner has provided extensive supporting chromatographic data showing how the metabolites were identified in cottonseed. Copies of 10 TLC plates were presented. CBTS concurs with the petitioner's conclusions on identification of the unknowns after our review of the TLC plates. The petitioner also presented the HPLC chromato-grams showing separation of the 6-hydroxynicotinic acid methyl ester from the cottonseed matrix as well as the MS spectra confirming the identification of the metabolite.

The concern at this point is why are there no 6-hydroxynicotinic acid residues reported in other imidacloprid metabolism studies. The petitioner notes these residues were detected in only the 6 hour methanol/6N HCl reflux. CBTS agrees this is a harsh condition, one that could break molecular bonds. Other imidacloprid metabolites identified in the methanol/water phase and in the methanol reflux were subjected to the 6 hour methanol/6N HCl reflux and all metabolites previously identified converted to the 6-hydroxynicotinic acid derivatives. We agree that these newly identified metabolites are, in fact, artifacts of the procedure used to free imidacloprid metabolites from cottonseed. They are not the result of the normal expected metabolic process in cotton.

To complete the characterization of metabolites the petitioner analyzed the methanol/water phase and the methanol reflux extracts using the common moiety method which converts imidacloprid and all of its metabolites that contain the 6-chloropyridinyl moiety to 6-CNA.
In the methanol/water phase 91% of the residue contains 6-CNA and in the methanol reflux 87% of the residue contained 6-CNA. This characterizes the additional components of the residues as containing the 6-chloropyridinyl moiety. The petitioner has now adequately characterized the radioactive residue in cottonseeds.

The nature of the imidacloprid residue in cottonseed is now adequately understood. Though imidacloprid is more tightly bound in cotton then in other matrices it is metabolized by the same three pathways as in apples, potatoes, tomatoes, eggplant, and corn. Using the data generated for cotton leaves and the data reported on cottonseeds both in the original submission and in this amendment the pathways are as follows:

1) hydroxylation of the dihydroimidazole ring to form the monohydroxy and dihydroxy imidacloprid followed by the loss of water to form the olefin imidacloprid,

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

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

The residues of concern in cottonseed are imidacloprid and its metabolites that contain

the 6-chloropyridinyl moiety. Deficiency 3c is resolved.

ROTATIONAL CROPS

Deficiency

5b. All 3 rotational crops in the confined study have 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. CBTS concludes there is potential for inadvertent residues to occur in non-target crops planted in rotation. Limited field rotation crops are necessary for a representative crop at 2 sites per crop for the following 3 crops: root and tuber vegetables, leafy vegetables, and cereal grains. At least a total of 6 field trials are necessary all at the 1X application rate.

5c. 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 the need for tolerances and more extensive field trials will be based on the results of the limited field trials.

Petitioner's response

The petitioner did not respond in this amendment.

CBTS comments

While the petitioner did not respond CBTS is aware that extensive work has been done on rotational crops. After our meeting with representatives of Miles on March 2, 1994, we expect a completed rotational crops field trials residue data report will be submitted by the end of April 1994. Prior to the submission of the report CBTS requested that the petitioner generate additional method validation data at the LOQ of 0.01 ppm as required by the Guidelines, Subdivision N. Method validation data at 0.01 ppm gives us greater confidence for the proper plant back intervals. CBTS reiterates that no additional ILV data are required.

Until we have received and reviewed the new rotational crops field trial residue data deficiencies 5b and 5c are reiterated. They are not resolved and continue outstanding.

RESIDUE ANALYTICAL METHODS

Deficiencies

2. The petitioner has presented adequate multiresidue method (MRM) recovery data for imidacloprid and its olefin, hydroxy, guanidine, and 6-chloronicotinic acid (6-CNA metabolites through FDA protocols A through E. These data will be forwarded to FDA for more review and will be printed in FDA's PAM, Vol. I, Appendix I in a future update. Additional MRM recovery data should be presented for the urea and nitrosimino imidacloprid metabolites through Protocols A through E, as appropriate.

4. The confirmation procedure in both plant and animal tissue methods use only one additional ion for identification of the common moiety. Monitoring with less then 3 ions for confirmation can lead to misidentification. The methods should state criteria for relative response ratios of sample ions compared with relative ratios for analytical standards. The petitioner needs to provide an acceptable ratio value for the selected ions used for mass spectrometric quantitation as an index for determination of interference when encountered with either ion.

5. CBTS concludes that the petitioner has not presented an adequate imidacloprid confirmatory procedures for both the residue plant and animal methods. Since the primary detection system is GC/MS the confirmatory procedure should use an alternative detection system. The petitioner needs to have a different confirmatory procedure than that proposed in which only another ion is measured. CBTS suggests that a different imidacloprid confirmatory procedure be presented which has enhanced specificity using different extraction and clean-up techniques, derivatization reagents, and alternate GC columns. The confirmatory method should be at least semi-quantitative, though we would prefer the confirmatory method be quantitative. In either case additional petitioner generated validation data as well as ILV data are necessary. An additional TMV may be requested for the confirmatory procedure.

6. **The petitioner has informed CBTS that imidacloprid is the first of a new class of insecticides. We have concluded the confirmatory method needs to precisely identify imidacloprid and its major metabolites, as well as be at least semi-quantitative, though our choice would be to have the confirmatory method be quantitative. CBTS suggests that the petitioner direct his efforts toward developing a confirmatory method that can adequately identify residues of imidaclo-prid and its major metabolites, not just measuring another ion from the spectrum of a derivatized common moiety entity.**

7. The recovery data presented do not adequately validate the imidacloprid plant residue method to gather the magnitude of the residue data, or to enforce the proposed tolerances. The petitioner has not presented any recovery data for imidacloprid fortifications at the proposed tolerance levels for apples; cottonseed, cottonseed meal, and cotton forage; potatoes, potato chips, and potato flakes. The petitioner needs to present imidacloprid recovery data at levels appropriate to the proposed tolerances, including ILV data requirements and at levels that encompass the residue data reported.

8. The olefin imidacloprid and hydroxy imidacloprid metabolite standards are not listed as being available in the write-up of the methods. Standards for which we have requested and received MRM recovery data as well as petitioner generated recovery data are to be supplied to the EPA Repository as appropriate. CBTS requests that the petitioner note in the revised method that standards for the olefin, hydroxy, urea, and nitrosimino imidacloprid metabolites are also available.

9. In addition the petitioner needs to generate imidacloprid recovery data for the imidacloprid olefin and the 5-hydroxy metabolites in apples at the 0.05-0.5 ppm level (the level where most of the residue data are reported), and at levels appropriate to the proposed tolerances, including ILV data requirements. Complete imidacloprid metabolite recovery data for the olefin, guanidine, 5-hydroxy, and urea metabolites are needed from cottonseed, cotton

forage, and potatoes.

10. The petitioner needs to present additional supporting chromatographic data for the plant residue method showing recovery of 6-CNA at levels appropriate to the proposed tolerances, including ILV requirements in each raw agricultural commodity and processed commodity for which a tolerance is proposed.

11. Additional recovery data for the plant method are required. The petitioner has presented his recovery data showing only the range of recoveries and the mean recovery. The raw data showing each individual recovery datum point, as well as the total number of analyses that went into determining the mean recovery were not presented. These individual recovery datum points for imidacloprid and its metabolites are required.

12. The ILV data for both the plant method and the animal tissue method from Germany appear to have been generated at the same testing facility as were the petitioner's original method validation data. CBTS cannot ascertain from the material presented whether or not the same facilities, equipment/instrumentation, reagents, and personnel were used to generate the method validation data and ILV data. The petitioner needs to provide proof the ILV data were generated separately in every respect from the petitioner's method validation data.

13. The German ILV data were generated using the original version of the Bayer plant residue method No. 00200. Since there were major changes to the method, none of these ILV recovery data can be used as ILV data for the enforcement method. Only the ILV data on apples can be used from this study and only to give further confidence on the magnitude of the residue data.

14. CBTS defers judgement on the ^{14}C-imidacloprid recovery data using the proposed enforcement and residue gathering method to support the method as adequate for recovery of total imidacloprid residues from crop field trials and to enforce the proposed imidacloprid tolerances. We would prefer recovery data of aged radiolabeled residues be presented using the methanol/1% H_2SO_4 instead of the methanol/water extracting solvent, and that the recovery data be from ^{14}C-imidacloprid treated apples, potato tubers, cottonseeds and cotton forage; not from other commodities for which there are no tolerance proposals.

15. Additional petitioner generated animal tissues method recovery data are required. Again, the petitioner has presented his recovery data showing only the range of recoveries and the mean recovery. The raw data showing each individual recovery datum point were not presented. These individual recovery datum points for imidacloprid and its metabolites are required.

16. These recovery data presented do not adequately validate the imidacloprid animal tissues method to enforce the proposed secondary tolerances. The petitioner has not presented any recovery data for imidacloprid, per se, and its significant metabolites fortifications at the proposed tolerances in milk, eggs, liver, kidney, fat, and various muscles from ruminants and poultry. The petitioner needs to present imidacloprid, per se, and its significant metabolites recovery data at all proposed meat, milk, poultry, and egg tolerance levels.

17. Based on the ruminant and poultry metabolism studies the petitioner needs to generate imidacloprid metabolite recovery data for the imidacloprid metabolites listed in the following conclusion, in addition to the data already presented for the olefin, hydroxy, and 6-CNA metabolites. Recovery data are also needed for 6-CNA in milk before the TMV can be started.

18. The petitioner has not presented acceptable ILV data for the proposed imidacloprid animal tissues enforcement method. ILV data are required for imidacloprid, per se, and its olefin, hydroxy, urea, WAK 3583, nitrosimino, and 6-CNA in ruminants liver, kidney, fat, muscle, and milk at the proposed tolerances and 2-5 times the proposed tolerances. ILV data are also required for imidacloprid, per se, and its olefin, hydroxy, dihydroxy, DIJ 10739, WAK 4126, 6-CNA, and WAK 4230 in eggs, poultry liver, and muscle tissues at levels appropriate to the proposed tolerances, including ILV data requirements. The petitioner is reminded that the TMV for milk cannot be completed without these additional ILV data. Based on the new recovery ILV data the milk and tissues TMV may be modified.

19. None of the additional ILV data recently generated in the USA are suitable to support the proposed enforcement method for imidaclo-prid and its metabolites containing the 6-chloropyridinyl moiety because these data were not generated at the proposed tolerance levels and at levels above the proposed tolerances. These recovery data are suitable to provide further confidence in the petitioner's method to generate magnitude of the residue data.

Petitioner's response

The petitioner submitted a detailed response to all of our questions on the residue analytical methods in a document titled "Replies to Comments and Questions from the EPA Concerning the Analytical Methodology Used for Imidacloprid Residues in Crops and Animal Tissues" by J.J. Murphy dated March 15, 1994, and coded Miles Report No. 106427 (MRID # 431432-08).

The petitioner submitted a revised residue analytical method in a document titled "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). 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).

The petitioner submitted another revised residue analytical method in a document titled "Method for the Determination of Total Residues of Imidacloprid in Animal Materials (Bayer Method 0091 M001 - Reformatted)" by Weber and Heukamp dated January 10, 1994, and coded Miles Report No. 103848R-1 (MRID # 431432-03). The accompanying ILV data generated by Huntingdon Analytical Services for the revised animal tissues method were 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).

CBTS comments

The petitioner proposes that because the urea and nitrosimino imidaclo-prid are very minor metabolites they need not be evaluated through the FDA multiresidue method (MRM) protocols. Since they constitute less then 2% of the total radioactive residue (TRR) and the HED Metabolism Committee concluded in its June 22, 1994, meeting that none of these imidacloprid metabolites were of toxicological concern that would warrant separate regulation, CBTS agrees with the petitioner that additional MRM recovery data for the urea and nitrosimino imida-cloprid metabolites are not needed. Deficiency 2 is resolved.

Initially the petitioner proposed determining the residues by monitoring at m/z 214 and confirmation at m/z 170. The petitioner now proposes monitoring with the m/z ion of 214 as 100% and 3 additional ions at m/z 216, 170, and 140. With the ratio of m/z 214 at 100% the ratios for m/z 216 is 36-37% in apples and cottonseed, and 38-39% in potatoes. The m/z 170 ratio is 50-51% in all 3 matrices and the m/z 140 ratio is 38-41% in all 3 matrices. The petitioner has presented acceptable ratio values for 4 selected ions for use in MS quantitation. These ratios serve as an index for the determination of interferences if and when encountered by any of the 4 ions.

The proposed interim confirmation of imidacloprid related residues is to monitor the 4 ions of m/z 214, 216, 179, and 140. The petitioner proposes the following criteria for confirmation using SIM: if the ratios of the 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 GC retention time through a capillary column then the presence of imidacloprid is confirmed. This is acceptable to CBTS. Deficiency 4 is resolved.

CBTS agrees with the petitioner that 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 response ratio. We envision that most monitoring and enforcement actions will initially use 1-2 ions. Only in cases that involve court appearance will it be necessary to monitor all 4 ions and have an alternate confirmatory procedure.

The petitioner did not present a separate confirmatory procedure as suggested in deficiencies 5 and 6. In the EPA-Miles conference of March 2, 1994, we were informed of the progress being made in developing a HPLC method that will measure imidacloprid as imidacloprid and separately measure several of the major imidacloprid metabolites. The petitioner is encouraged to continue this development and present the Agency with the completed HPLC method and accompanying ILV data as soon as possible. Our only observation is to keep the confirmatory method under 2 working days as this is necessary for the method to be an effective enforcement procedure.

For deficiencies 5 and 6, CBTS reiterates that we will need a confirmatory method that will precisely identify imidacloprid and its major metabolites, as well as be at least semi-quantitative, though we prefer the method be quantitative. CBTS reiterates our suggestion that the petitioner should continue his efforts to having the confirmatory procedure

become more specific by using among other things different extraction procedure, clean-up, if necessary, different derivatization, alternate chromatographic columns, and a different detection technique. We reiterate that ILV data are necessary before a tolerance method Validation (TMV) can be started in EPA labs.

Tentatively for PP# 3F4169 and PP# 3F4231 the lack of the confirmatory procedure is not a bar to our recommendation for the proposed tolerances provided no other compounds in this new class of insecticides are presented for registration and tolerances.

In section 3.1.3. of the plant method, Bayer method 0200, and in section 3.1.3.1 of the animal tissues method, Bayer method 00191, the analytical reference standards for the hydroxy and olefin imidacloprid metabolites are listed as being available from Miles, Inc. They are also available from the EPA Repository in RTP-NC. Deficiency 8 is resolved. The petitioner has deleted the urea and nitrosimino imidacloprid metabolites as being available. CBTS agree that these are minor metabolites and they need not be listed for routine recovery work.

The petitioner has presented the results from a new ILV study generated in the USA using the revised and reformatted plant method for the Bayer method 0200. The study was performed by Ricerca, Inc., using the method as received, without any consultation with the petitioner and standards as supplied by Miles, Inc. The study used control McIntosh apples fortified individually with imidacloprid, the hydroxy, guanidine, olefin, and 6-CNA metabolites at the proposed apples tolerance of 0.5 ppm and at 5X or 2.5 ppm. In the first analyses Ricerca had 6-CNA recoveries generally less then 50%. After consultation with Miles the following minor modifications were made. Ricerca used oven dried Na_2SO_4 and the evaporation of the t-butyl ether was rotary evaporation, not a transfer to a 5 ml centrifuge tube with subsequent evaporation. These changes are acceptable to CBTS. ILV recoveries of 6-CNA spiked at 0.5 and 2.5 ppm ranged from 80% to 110% (X = 95% $\pm$ 16%). Imidacloprid ILV recoveries from 0.5 ppm and 2.5 ppm ranged from 82% to 115% (X = 98% $\pm$ 18%) and the guanidine imidacloprid recoveries from the 0.5 ppm and 2.5 ppm spike ranged from 70% to 92% (X = 81% $\pm$ 9%). Recovery of the olefin metabolite from the 0.5 and 2.5 ppm spike ranged from 73% to 121% (X = 98% $\pm$ 22%) and the for the hydroxy imidacloprid spiked at 0.5 ppm and 2.5 ppm recoveries ranged from 95% to 109% (X = 102% $\pm$ 6%). Ricerca provided the petitioner with extensive supporting chromatographic data. These chromatographic data are acceptable. The ILV time estimate for 6 samples is 2 working days to complete the extraction and cleanup to the point of GC/MS injection. A third day is required for the determination step. A total time estimate is 18+ hours to run a set of 6 samples.

In summary, the petitioner has presented the results of a new ILV study conducted in the USA using the revised and reformatted plant method, Bayer method 0200, for imidacloprid and its major metabolites individually spiked at the proposed apple tolerance and 5X tolerance. These data are in general agreement with the recovery data generated by the petitioner. They are acceptable and can support the Agency's TMV for the plant residues enforcement method. No additional ILV data are required for the plant method for this petition, PP# 3F4169, and the co-pending petition PP# 3F4231. These parts of deficiencies 7 and 9, and all of deficiency 13 are resolved.

Since we are no longer requiring MRM and/or method validation data for the urea imidacloprid this part of deficiency 9 becomes moot and is thus resolved. We have previously concluded cotton forage is no longer a significant livestock feed item and the petitioner has proposed an acceptable feeding restriction plus withdrawn the proposed tolerance, thus additional method validation data for imidacloprid and its metabolites in cotton forage are not required. This part of deficiency 9 is resolved.

In the ILV the petitioner generated recovery data using apples for the olefin imidacloprid at 0.5 ppm which were 110% and 121% and for the hydroxy metabolite which were 105% and 109%. The petitioner has compiled recovery data for the hydroxy and olefin metabolites spiked in apples at 0.1 ppm showing recoveries at 103% and 89% respectively. In potatoes fortifications were at 0.1 individually for the guanidine, olefin, and hydroxy imidacloprid metabolites with recoveries ranging from 75% (olefin) to 108% (guanidine). In cottonseed spiked individually at 0.1 ppm with the guanidine, hydroxy, and olefin metabolites recoveries ranged from 79% (hydroxy) to 93% (guanidine). The petitioner has provided the requested method validation data for the imidacloprid metabolites in apples at 0.1 and 0.5 ppm and at the 0.1 ppm level for the major imidacloprid metabolites in potatoes and cottonseed. These data validate the method at the LOQ and in the range where residues are reported for apples and potatoes. The remaining part of deficiency 9 is resolved.

The petitioner has provided additional copies of supporting chromatographic data for 6-CNA recoveries using the plant residue method in both the new ILV report and in the reformatted plant residue method. The supporting chromatographic data show recoveries of 6-CNA in the raw agricultural commodities (rac) and in the processed commodities. Deficiency 10 is resolved.

In the original method recovery data were generated in Germany and presented to the Agency as a range with the mean. The petitioner points out that in reality there are only 2 datum points and the mean was calculated using the two reported datum points. In the heading for Table 1, Appendix 12 in the revised plant method this has now been clarified with the statement that only 2 experiments were conducted for each concentration. The petitioner has presented not only a range of recoveries and a mean recovery, but also the individual datum points. Deficiency 11 is resolved.

The petitioner has compiled all of the method validation and concurrent recovery data into individual tables per commodity. The recovery data presented in Tables 1, 2, 3, and 4 in the revised and reformatted plant residue method are adequate to show the method can generate magnitude of the residue data presented in this petition. In general, these recovery data were for an equal mixture of the parent plus the guanidine metabolite; plus several recoveries of an equal mixture of parent, guanidine, hydroxy, olefin, and/or 6-CNA.

The data presented do not resolve deficiency 7. It continues unresolved and remains outstanding. In 2 telcons (D. Griffith-J. Thornton on April 12 and 14) the petitioner has been notified that additional method validation data at the revised proposed tolerance levels in the rac's and processed commodities are necessary to support the plant residue method as a tolerance enforcement procedure. All of the following data are to be generated by the petitioner in duplicate and will be for the parent and individual metabolites:

1. Apples are to be spiked at 0.5 ppm (proposed tolerance) and at a level of 2-5X the proposed tolerance (as specified in PRN 88-5) with the parent, the guanidine, and either the hydroxy, olefin, or 6-CNA. Wet apple pomace is to be spiked at 3 ppm (proposed tolerance) and at a level of 2-5X the proposed tolerance with the parent imidacloprid, the guanidine, and either 6-CNA, the olefin, or the hydroxy metabolite. CBTS suggests, for example, that if the olefin is used as the rac apple spike, then either 6-CNA, or the hydroxy be used in wet apple pomace spike.

2. In the rac potatoes the spikes should be at 0.3 ppm (proposed tolerance) and at a level 2-5X the proposed tolerance with the parent imidacloprid, the guanidine, and either 6-CNA, the hydroxy, or the olefin metabolite. The same spiking procedure should be followed for potato chips spiked at 0.4 ppm and at a level 2-5X higher, and for potato waste spiked at 0.9 ppm and at a level 2-5X higher. Fortification should be for the parent imidacloprid, the guanidine, and one other metabolite. Since there are 3 commodities with potatoes to have additional method validation data, the petitioner should consider using a different metabolite for each third fortification; eg, 6-CNA in the rac, the olefin in potato chips, and the hydroxy in potato waste.

3. For the rac cottonseed the fortifications should be at 6 ppm (proposed tolerance) and at a level 2-5X the proposed tolerance with the parent, guanidine, and 6-CNA. CBTS suggests 6-CNA be the third fortification in the rac, cottonseed as it is the major metabolite detected in the metabolism study. The same spiking procedure should be followed with cottonseed meal spiked at 9 ppm and at a level 2-5X the proposed tolerance. In cottonseed meal the petitioner should consider the third fortification be either the hydroxy imidacloprid or the olefin imidacloprid.

The petitioner acknowledges that the original method validation data and the IV data were generated in Germany at the same testing facility. However, the petitioner has provided the names of the analysts, the serial number of the test instruments, and the room numbers where the ILV and method validation tests were conducted. The petitioner has provided data to show that the ILV and the method validation were completely independent. Provisions as described in PRN 88-5 were followed. Deficiency 12 is resolved.

The ^{14}C-imidacloprid recovery data using the proposed enforcement method were generated with the methanol/water extracting solvent. While CBTS would like to have recovery data using the methanol/1% H_2SO_4 extracting solvent the petitioner contends the data already generated are in reality a "worse case" or a minimum recovery that can be expected. CBTS agrees this is a minimum recovery expected, thus no additional recovery data are necessary using methanol/1% H_2SO_4 to improve the recovery of aged ^{14}C-imidacloprid residues. Deficiency 14 is resolved.

The petitioner has presented a new ILV study generated in the USA using the revised and reformatted animal tissue method for the Bayer method 00191. The study was preformed by Huntingdon Analytical Services using the method as received, without any consultation with the petitioner and standards as supplied by Miles, Inc. The study used control beef liver fortified individually with imidacloprid, the 5-hydroxy, guanidine, olefin, and 6-CNA metabolites at the proposed meat by-product tolerance of 0.2 ppm and at 5X or 1 ppm. ILV recoveries of

6-CNA spiked at 0.2 and 1 ppm ranged from 83% to 98% (X = 90% ± 7%) using the 214 ion and from 84% to 99% using the 140 ion. Imida-cloprid ILV recoveries from 0.2 ppm and 1 ppm fortifications ranged from 84% to 101% (X = 92% ± 9%) using the 214 ion and from 87% to 105% using the 170 ion. The guanidine imidacloprid recoveries from the 0.2 ppm and 1 ppm spike ranged from 76% to 97% (X = 86% ± 9%) using the 214 ion and from 76% to 93% using the 170 ion. Recovery of the olefin metabolite from the 0.2 and 1 ppm spike ranged from 80% to 105% (X = 93% ± 13%) using the 214 ion and from 80% to 102% using the 170 ion. For the 5-hydroxy imidacloprid spiked at 0.2 ppm and 1 ppm recoveries ranged from 80% to 99% (X = 86% ± 9%) using the 214 ion and from 82% to 97% using the 170 ion. Huntingdon provided the petitioner with extensive supporting chromatographic data. These chromatographic data are acceptable. Huntingdon cautions the petitioner that the oxidation step to form 6-CNA is the most critical step in the method and careful attention must be paid to the directions. The ILV time estimate for 6 samples is the same as in the plant method ILV. It requires 2 working days to complete the extraction and cleanup to the point of GC/MS injection. The GC/MS runs over night, and the data reduction and the report are completed in the third day. A total time estimate is around 20 hours to run a set of 6 samples.

In summary, the petitioner has presented the results of a new ILV study conducted in the USA using the revised and reformatted animal tissues method, Bayer method 00191, for imidacloprid and its major metabolites individually spiked at the proposed meat by-products tolerance and 5X tolerance. These data are in general agreement with the recovery data generated by the petitioner. They are acceptable and can support the Agency's TMV for the animal tissues residues enforcement method. No additional ILV data are required for the animal tissues method for this petition, PP# 3F4169, and the co-pending petition PP# 3F4231. These parts of deficiency 18 and all of deficiency 19 are resolved.

Since we are no longer requiring MRM and/or method validation data for the urea and nitrosimino imidacloprid this part of deficiency 18 becomes moot and is thus resolved. We have previously concluded that only ruminant liver will be in our TMV, thus no ILV data will be required for imidacloprid and its major metabolites in beef kidney, fat, and muscle; as well as in poultry liver and muscle, thus additional ILV method validation data for imidacloprid and its metabolites are not required. Discussion with the lab indicate the initial ILV data are now sufficient to complete the TMV; thus no additional ILV data will be required for eggs and/or milk. These parts of deficiency 18 are resolved.

The petitioner has provided additional method validation data from bovine tissues for the revised animal tissues method, Bayer method, 00191. Milk was spiked with imidacloprid, the olefin, and hydroxy metabolites at 0.02 ppm and 0.1 ppm plus a mixture of all three at 0.033 ppm each, n = 67. Recoveries ranged from 61% (imida-cloprid at 0.02 ppm) to 111% (hydroxy at 0.1 ppm). Ruminant muscle was spiked with imidacloprid, the olefin, and the hydroxy metabolites at 0.02 ppm and 0.6 ppm plus a mixture of all three compounds at 0.2 pm each. Recoveries ranged from 69% (hydroxy at 0.6 ppm) to 103% (imidacloprid at 0.02 ppm). Fat was spiked with the same three compounds at 0.02 ppm to 0.3 ppm plus a mixture of imidacloprid, the hydroxy, and olefin metabolites each at 0.1 ppm, n = 42. Recoveries from fat ranged from 81% (imidacloprid at 0.3 ppm) to 125% (mixture).

Liver was fortified with imidacloprid at 0.02 ppm, 0.05 ppm, 0.25 ppm, 0.5 ppm, and at 2.52 ppm; with the olefin, 6-CNA, and the hydroxy at 0.02 ppm and at 0.5 ppm. Liver was also fortified with the guanidine at 0.02 ppm and 0.42 ppm plus a mixture of imidacloprid, the olefin,

hydroxy, 6-CNA each at 0.2 plus the guanidine metabolite at 0.17 ppm, n = 46. Recoveries ranged from 69% (imidacloprid at 0.02 ppm) to 99% (olefin at 0.5 ppm). Kidney was fortified with imidaclo-prid at 0.02 ppm, 0.5 ppm, and 2 ppm; with the olefin, 6-CNA, and the hydroxy metabolites at 0.02 ppm and at 0.5 ppm plus a mixture of imidacloprid and the olefin, hydroxy, and 6-CNA each at 0.25 ppm, n = 30. Recoveries from kidney ranged from 62% (6-CNA at 0.02 ppm) to 89% (hydroxy at 0.5 ppm).

The petitioner has provided additional method validation from poultry tissues for the Bayer method 00191. Eggs were fortified with imidacloprid and the olefin at 0.02 ppm and at 0.1 ppm plus a mixture of these each at 0.05 ppm, n = 54. Recoveries from eggs ranged from 55% (olefin at 0.02 ppm) to 102 % (imidacloprid at 0.02 ppm). Poultry muscle was fortified with imidacloprid and the olefin separately at 0.02 ppm and 0.1 ppm, plus a mixture of these each at 0.05 ppm, n = 32. Recoveries ranged from 64% (olefin at 0.1 ppm) to 90% (imidacloprid at 0.1 ppm). Poultry fat was fortified with imidacloprid and its olefin metabolite each at 0.02 ppm and 0.1 ppm plus a mixture of these each at 0.05 ppm, n = 29.

Poultry liver was spiked with imidacloprid at 0.02 ppm, 0.5 ppm, and 2 ppm; with the olefin and guanidine at 0.02 ppm and 0.5 ppm, and 6-CNA at 0.02 ppm and 0.3 ppm plus a mixture of these each at 0.125 ppm, n = 37. Recoveries ranged from 77% (olefin at 0.02 ppm) to 117% (imidacloprid at 0.02 ppm).

Since most of the method validation for Bayer method 00191 was done in Germany the petitioner provided a comparison of recoveries with standards in the matrix and standards in solvents. Recoveries from eggs using standards in the matrix were 67% while the same recoveries from eggs were 65% using standards in the solvent. Recoveries from milk using standards in the matrix were 67%/68% while the recoveries were 66% using standards in the solvent. Recoveries from muscle using standards in the matrix were 81%-83% and were 83%-85% using standards in the solvent. The recoveries from liver using standards in the matrix were 78%-80% using standards in liver and were 75%-77% using standards in the solvent. While recoveries were less in 3 out of 4 matrices using standards in the solvent then in using standards in the matrix these differences are not statistically significant. The petitioner has provided adequate bridging data to show that the initial recovery data though it used a control sample did, in this instance, provide adequate method validation data.

In summary, the petitioner has generated extensive method validation data for imidacloprid and its olefin guanidine, hydroxy, and 6-CNA metabolites in bovine liver, fat, muscle, and kidney, and in milk. In bovine tissues the method validation were at the LOQ, around or at the proposed tolerances and above tolerances. In poultry tissues (liver, muscle, and fat) and in eggs the petitioner has provided imidacloprid and its olefin, guanidine, and 6-CNA recovery data at the LOQ, at or near the proposed tolerances, and above the proposed tolerances. These recovery data are sufficient to show that the proposed enforcement method for animal tissues, Bayer method number 00191, is suitable to gather the magnitude of the residue data and can enforce the proposed tolerances. Deficiencies 15, 16, and 17 are resolved. No additional petitioner generated method validation data for Bayer method number 00191 are needed for this petition, PP# 3F4169, and for the co-pending petition, PP# 3F4231.

STORAGE STABILITY

Deficiency

7b. While the frozen storage stability data show no decline in total imidacloprid residues in potatoes, apples and apple processed commodities, cottonseed processed commodities, and in wheat processed commodities at 3 months, CBTS defers judgement on these data to support the magnitude of the residue crop field trials residue data in this petition until the petitioner has completed the study and submitted the final report. In the interim the petitioner is encouraged to submit an additional interim report that includes storage stability data for 6, 12, and possibly 18 months.

Petitioner's response

The petitioner submitted the results of 3 storage stability studies. One study was titled "Imidacloprid and Metabolites - Freezer Storage Stability Study in Crops (Wheat Matrices, Cottonseed, Tomato, Cauliflower, and Lettuce) Addendum 2" by C.A. Lenz dated March 16, 1994, coded Miles study number N3131601 and Miles report number 103949-2 (MRID # 431972-01). This study reports the results of the 12 and 18 month storage intervals. As part of PP# 3F4231 the petitioner presented the results of the 6 months frozen lettuce storage in a document titled " Imidacloprid and Metabolites - Freezer Storage Stability Study in Crops (Wheat matrices, Cottonseed, Tomato, Cauliflower, and Lettuce) (Addendum 1)" by C.A. Lenz dated April 2. 1993, and coded report number 103949-1 (MRID # 428103-13). This 6 month interim report will now be reviewed as an amendment to PP# 3F4169, not part of PP# 3F4231. The 6 month storage interval for wheat matrices, cottonseed, tomato, and cauliflower were submitted in a study titled "Imidacloprid and Metabolites - Freezer storage Stability Study in Crops (Wheat matrices, Cottonseed, Tomato, Cauliflower, and Lettuce)" by C.A. Lenz dated December 31, 1992, and coded Miles report number 103949 (MRID# 428103-12). This interim report will now be reviewed as part of PP# 3F4169, not part of PP# 3F4231.

Another report was titled "Storage Stability of NTN 33893 (imidacloprid) and its Five Metabolites in Corn, Lemon, and Lettuce" by N. Morishima dated March 11, 1994, and coded Miles report number 103820-01 (MRID # 431972-02). This study report only the results of the 12 and 24 month intervals.

The third report was titled "Imidacloprid and Metabolites - Freezer Storage Stability Study in Crops" by P. Noland and D. Chickering dated March 31, 1994, and coded Miles study number N3131602 and Miles report number 103237-2 (MRID # 431972-03). This study presented the results of the 12 and 18 month intervals. As part of PP# 3F4231 the petitioner submitted an interim report for the 6 month interval in a study titled "Imidacloprid and Metabolites - freezer Storage Stability Study in Crops (Interim Report)" by P. Noland dated February 17, 1993, and coded Miles study number N3131602 and Miles report number 103237-1 (MRID # 428103-11). This 6 month interim report will now be reviewed as an amendment to PP # 3F4169, not part of PP# 3F4231.

CBTS comments

The petitioner's report on the freezer stability of total ^{14}C-imidacloprid in corn, lemons, and lettuce is a continuation of the preliminary report initially reviewed in our September 21, 1993, review. The same ^{14}C-methylene labeled imidacloprid, guanidine, 5-hydroxy, nitrosimino, and 6-CNA were used; the same fortification

levels at 1 ppm, the same procedures and storage conditions, and the same analytical procedures were used.

In summary, lettuce stored for 12 and 24 months recoveries ranged from 99% for the guanidine to 108% for the olefin. CBTS concludes that imidacloprid and its major metabolites are stable under frozen conditions in lettuce for 24 months. While these data are supplementary to PP# 3F4169 they are germane to PP# 3F4231.

Corn forage stored at -20°C for 12 and 24 months had recoveries ranging from 96% for the guanidine to 113% for the olefin. In corn fodder stored 12 and 24 months recoveries ranged from 92% for the guanidine to 111% for the 5-hydroxy. Corn grain stored for 12 and 24 months at -20°C had recoveries ranging from 99% for 6-CNA to 122% for imidacloprid. CBTS concludes that imidacloprid and its major metabolites are stable under frozen conditions in corn grain, fodder, and forage for 24 months. These storage stability data are supplementary to PP#s 3F4169 and 3F4231.

In lemons there was a slight change in the 24 month chromatographic profile as would be expected under acidic conditions when the hydroxy and the nitrosimino can be converted to the olefin and guanidine. In lemons at 24 months there is essentially no change in values for imidacloprid, per se, and for the 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 concentrations with values above 125% of that in the initial fortification. While there has been a change in concentrations of the individual imidaclo-prid metabolites under the acidic 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 concludes that the total imidacloprid residues in lemons are stable for 2 years. These data are supplementary for PP#s 3F4169 and 3F4231.

For this storage stability study the petitioner has supplied sufficient supporting chromatographic data showing the initial TLC profile at the time of fortification and the TLC profile 24 months later. Daily temperature logs for the storage freezer were provided. The petitioner provided the raw DPM counting data for each matrix at the 12 and 24 month interval.

The petitioner's report on the stability of imidacloprid and its guanidine, olefin, hydroxy, and 6-CNA metabolites in apples and their processed commodities (apple pomace both wet and dried, apple juice), potatoes plus cottonseed processed commodities (cottonseed hulls, oil. and soapstock) and wheat processed commodities (wheat bran, flour, shorts, and wheat grain dust) is a continuation of the study initially reported for only a 3 month interval. In these combined reports the petitioner has presented total imidacloprid storage stability data in each of these commodities for 6, 12, and 18 months. The fortification procedures and storage conditions were unchanged throughout the study. The petitioner used the same residue analytical method in this study and has provided extensive method validation data at 0.1 ppm and concurrent validation data at 2.5 ppm from a combination of imidacloprid and its 4 metabolites.

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 the 115% of the initial fortification. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trials data reported for potatoes stored for up to 11 months from harvest to analysis. This part of deficiency 7b is resolved.

For whole apples the petitioner has presented frozen storage stability data that shows the total imidacloprid residues are stable in apples frozen for at least 19 months with recoveries running greater than 80% of the initial fortification at 6, 12, and 19 months. The large difference in recoveries noted at the 3 month interval was not observed in the data for the later sample intervals. In apple juice fortified with total imidacloprid (imidacloprid plus the guanidine, hydroxy, olefin, and 6-CNA), recoveries at 3, 6, 12, and 19 months frozen storage were all greater then 90%. Recoveries for total imidacloprid from wet apple pomace ranged from 80% to 100% of the initial fortification for all of the storage intervals during the 19 months. In dried apple pomace total imidacloprid recoveries ranged from 80% to 90% of the initial fortification for all of the sampling interval during the 19 months of frozen storage. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable in apples, apple juice, and apple pomace (wet an dried) for at least 19 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trials data that were reported for apples stored for up 9 months from harvest to analysis. This part of deficiency 7b is resolved.

Cottonseed hulls, soapstock, and oil were fortified with the mixture of 0.5 ppm each of imidacloprid, its guanidine, hydroxy, olefin, and 6-CNA metabolites and placed into frozen storage at -20°C. While the 0 day recoveries from hulls and cottonseed soapstock were low, subsequent recoveries from cottonseed hulls and soapstock were generally greater then 80% at the 3, 6, 12, and 20 month sampling intervals. Total imidacloprid recoveries from cottonseed oil stored frozen and sampled at 3, 6, 12, and 19 months had total imidacloprid recoveries greater then 80% of the initial fortification. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable in cottonseed hulls, soapstock, and oil for at least 19-20 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trial data that were reported for cottonseed stored for up to 8 months from harvest to analysis. This part of deficiency 7b is resolved.

Frozen storage stability data were presented for total imidaclo-prid residues spiked at 2.5 ppm into wheat grain dust, flour, wheat bran, and wheat shorts. While the initial 0 day recovery of total imidacloprid in wheat grain dust was low (67%), total imidacloprid recoveries after 3, 6, 12, and 20 months of storage were acceptable, running at 80% and above. Total imidacloprid recoveries from flour ranged from 2.2 ppm at 3 and 6 months to 1.8 ppm at 12 months and 2 ppm after 20 months. Total imidacloprid recoveries from wheat bran were more variable and ranged from 1.8 ppm at 3 months frozen storage to 2.5 ppm at 12 months storage. Recovery of total imidacloprid residues in wheat shorts ranged from 80% to over 100% of the initial fortification for the 19 months of frozen storage. The petitioner has provided adequate frozen storage stability data to show that total imidacloprid residues are stable during frozen storage in wheat processed commodities for at least 19/20 months. CBTS concludes that these storage stability data for wheat processed commodities are supplementary for PPs 3F4169 and 3F4231.

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 wheat grain, forage, and fodder; cotton seed, tomato, cauliflower, and lettuce. 25 gram individual homogenized samples of each commodity were weighed into glass jars and fortified with the mixture of imidacloprid and its metabolites. Additional 25 gram samples of unfortified samples were frozen and retained for control and concurrent recoveries. All samples were allowed to air dry for a few minutes then capped and put in a cardboard box and placed into a freezer maintained at -20°C. Sample aliquots of the fortified and unfortified matrices were removed at 3, 6, 12, and 18 months for analysis. The 0 time samples were fortified and analyzed immediately.

The same residue analytical method was used as has been reviewed above. Extensive method validation data were provided for each individual compound plus a mixture of the parent and guanidine metabolite; and has been reviewed. Concurrent recoveries were run at each sampling point using a mixture of imidacloprid and its guanidine metabolite each at 1.25 ppm. Concurrent total imidacloprid recoveries in wheat grain, forage, fodder ranged from 87% to 112%. Concurrent recoveries from cottonseed ranged from 79% to 91%. Current recoveries of total imidacloprid from tomato, cauliflower, and lettuce ranged from 94% to 118% with 6 of the 8 recoveries being at or above 100%.

Total imidacloprid recoveries from wheat grain ranged from 2.11 ppm to 2.72 ppm from the initial 2.5 ppm fortification. Only the 12 month sample showed a slight decline in total imidacloprid residue; however recoveries were still greater then 80%. Recoveries of total imidacloprid from wheat straw ranged from 1.98 ppm to 2.38 ppm over 18 months of frozen storage. When the recoveries from the 3, 6, 12, and 18 month samples were compared to the 0 time samples there is little, if any decline in residues due to storage. Total imidacloprid recoveries from wheat forage ranged from 1.93 ppm to 2.86 ppm over 18 months with only the 12 month sample having recoveries less than 80%. In general, the petitioner has presented adequate storage stability data to show that total imidacloprid residues in wheat grain, forage, and fodder are stable in frozen storage for at least 18 months. Since there are no proposed tolerances for wheat commodities and wheat processed commodities in this petition and in PP# 3F4231 CBTS considers these storage stability data are supplementary.

Total imidacloprid recoveries from cottonseed ranged from 2.06/ 2.07 ppm at 3 and 18 months to 2.78 at 6 months frozen storage. The petitioner has provided adequate frozen storage stability data for total imidacloprid residues in cottonseed to show that residues are stable for at least 18 months. These data are sufficient to support the magnitude of the total imidacloprid residue crop field trial data that were reported for cottonseed stored for up to 8 months from harvest to analysis. This part of deficiency 7b is resolved.

Total imidacloprid residues recovered from stored lettuce ranged from 2.11 ppm after 6 months to 2.57 ppm after 18 months. The recovery of "cold" total imidacloprid from lettuce is consistent with the recoveries of ^{14}C-imidacloprid and its labeled metabolites from lettuce. The petitioner has provided adequate "cold" total imidacloprid frozen storage stability data in lettuce to show that total imidacloprid residues are stable for at least 18 months. While these data are supplementary to PP# 3F4169 they are germane to PP# 3F4231.

From tomatoes the petitioner has provided recovery data for total imidacloprid residues

that ranged from 2.35 ppm at 12 months to over 2.8 ppm at 3 and 18 months. In cauliflower the recovery of total imidacloprid range 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 for at least 18 months. While these frozen storage stability data are supplementary to PP# 3F4169 they are germane to pp# 3F4231.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Deficiency

8a. For the proposed use the petitioner needs to present additional cotton crop field trial data from the Texas/New Mexico/Oklahoma region to improve geographical representation.

Petitioner's response

The petitioner did not response in this amendment.

CBTS comments

In 2 telcons the petitioner has been informed that at least 3 additional cotton field trials for the 1994 crop year are necessary to have adequate geographical representation. Specifically, these trials need to be in west Texas/ New Mexico/ west Oklahoma. In the April 14 telcon from D. Griffith to J. Thornton the petitioner was reminded that he needs to have the 3 new trials, as well as a total of 12 cotton field trials all at the proposed 1X imidacloprid use rate. For the 3 new trials on cotton the petitioner needs to have imidacloprid applied at the proposed use rate; ie, treated seed plus soil drench plus 4 foliar applications all at the proposed 1X application rate. Deficiency 8a is not resolved and continues outstanding.

CBTS reiterates that the petitioner has presented an adequate amount of varietal and geographically representative crop field trial residue data for imidacloprid on apples to support a 0.05 ppm tolerance. CBTS reiterates that the petitioner has presented an adequate amount of varietal and geographically representative crop field trial residue data for imidacloprid on potatoes to support the proposed 0.3 ppm tolerance.

PROPOSED TOLERANCES

Deficiencies

8a. The petitioner's cotton crop field trial residue data do not support the proposed 6 ppm tolerance on cottonseeds as there are insufficient geographical representation of cotton field trials.

8e. Since the Agency sets tolerances no higher then necessary, the petitioner needs to submit a revised Section F proposing a lower total imidacloprid tolerance for apples at 0.5 ppm. The maximum residue was 0.74 ppm only on 1 sample from a 1.62X exaggerated use, thus when this is extrapolated to a 1X use the expected residue is under 0.5 ppm. This is supported by a majority of the field trial residue data as well as the average residues being at

the 0.1-0.2 ppm level.

8g. Since the Agency sets tolerances no higher then necessary, the petitioner needs to submit a revised Section F proposing a lower total imidacloprid tolerance for potatoes at 0.2 ppm. The maximum residues were 0.28 ppm from a 1.67X exaggerated use, thus when this is extrapolated to a 1X use the expected residue is under 0.2 ppm. This is supported by a majority of the field trial residue data as well as the average residues being at the 0.05 ppm level.

9a. While an imidacloprid FAT is required for cottonseed meal, judgement is deferred on the proposed FAT as there are insufficient geographically representative crop field trial data available from the proposed imidacloprid use to determine the proper imidacloprid tolerance on cottonseed, and thus the FAT for cottonseed meal.

9b. While an imidacloprid FAT is required for wet and dry apple pomace, CBTS prefers the petitioner propose one total imidacloprid tolerance for apple pomace (wet and dried) using a 6X concentration factor, thus avoiding a proliferation of tolerances. The petitioner needs to propose in a revised Section F a total imidacloprid tolerance for apple pomace (wet and dried) at 3 ppm.

9c. Imidacloprid residues concentrated at 1.3X in potato chips and 2.9X in dry potato peels. While an imidacloprid FAT is required for dry potato peels and potato chips, the Agency sets tolerances no higher then necessary. We prefer the petitioner propose one total imidacloprid tolerance for processed potato waste, not dry potato peels, to avoid a proliferation of tolerances and use a 3X concentration factor for potato wastes. The petitioner needs to propose in a revised Section F a total imidacloprid tolerance for processed potato waste at 0.6 ppm and for potato chips at 0.25 ppm.

10a. Based on the results of the imidacloprid bovine feeding study CBTS concludes that finite residues will actually occur in milk and 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 in meat and milk. However, judgement is deferred on the study supporting the proposed 0.05 ppm tolerance in milk and the 0.2 ppm in meat, fat, and meat by-products until the petitioner has supplied additional cottonseed crop field trial residue data and the additional information to allow CBTS to complete its review of the bovine feeding study.

10c. Based on the results of the imidacloprid poultry feeding study CBTS concludes 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 in eggs and poultry. However, judgement is deferred on the study supporting the proposed 0.02 ppm tolerance in eggs and in poultry meat, fat, and meat by-products until the petitioner has supplied the following information to allow CBTS to complete its review of the poultry feeding study, and additional crop field trial data for cottonseed.

Petitioner's response

The petitioner has submitted the following tolerances in a revised Section F for imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

Apples	0.5 ppm
Cottonseed	6.0 ppm
Potatoes	0.3 ppm
Milk	<0.02 ppm
Eggs	<0.02 ppm
Meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep	<0.02 ppm
Meat, fat, and meat by-products of poultry	<0.02 ppm
Apple pomace (wet and dried)	3.0 ppm
Potato chips	0.4 ppm
Potato waste	0.9 ppm
Cottonseed meal	9.0 ppm

CBTS comments

The petitioner will need to modify the proposed tolerance expression in a revised Section F to reflect what is actually measured by the residue analytical enforcement method. The expression should read "tolerances of combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as imidacloprid on the following commodities:"

CBTS reiterates that at this time the petitioner's cotton crop field trial residue data do not support the proposed 6 ppm tolerance on cottonseeds as there are insufficient geographical representation of cotton field trials. The results from the additional crop field trials are necessary before a decision can be made on the adequacy of the proposed 6 ppm tolerance. This part of deficiency 8a remains unresolved and continues outstanding.

CBTS reiterates that while an imidacloprid FAT is required for cottonseed meal, judgement is deferred on the proposed FAT as there are insufficient geographically representative crop field trial data available from the proposed imidacloprid use to determine the proper imidacloprid tolerance on cottonseed, and thus the FAT for cottonseed meal. Deficiency 9a is not resolved and continues outstanding.

The petitioner has proposed a 0.5 ppm total imidacloprid tolerance on apples as suggested by CBTS. The petitioner has presented sufficient varietal and geographically representative magnitude of the residue crop field trial residue data to show that when Admire® is used as directed residues are not expected to exceed the proposed 0.5 ppm tolerance on apples. Deficiency 8e is resolved.

The petitioner has proposed a 3 ppm tolerance on apple pomace (wet and dried) which

helps avoid proliferation of tolerances as suggested by CBTS. CBTS reiterates that the petitioner has conducted an apple processing study using apples bearing detectable total imida-cloprid residues following an exaggerated imidacloprid application. The results of the study show a 6X concentration factor for apple pomace; thus a feed additive tolerance of 3 ppm for apple pomace (wet and dried) is necessary. Deficiency 9b is resolved.

The petitioner proposes a 0.3 ppm total imidacloprid tolerance for potatoes. In the cover letter the petitioner points out that a majority of the imidacloprid residue in potatoes is from the soil application, not the foliar applications, and that the highest residue is due to mainly soil application. The petitioner feels that 0.3 ppm is a more appropriate tolerance. After reconsideration CBTS agrees. The petitioner has presented an adequate amount of varietal and geographically representative magnitude of the residue crop field trial residue data that shows when Admire® is used as directed total residues of imidacloprid are not expected to exceed the 0.3 ppm tolerance. Deficiency 8g is resolved.

In the revised Section F the petitioner has proposed new tolerances for potato chips and potato waste based on the new tolerance proposed for the rac potatoes. CBTS reiterates that the petitioner has conducted an adequate potato processing study using potatoes bearing detectable residue from an exaggerated application. Total imidacloprid residues were shown to concentrate in potato chips at a 1.3X concentration factor requiring a revised FAT of 0.4 ppm and to concentrate in dry potato peels at 2.9X requiring a revised FAT of 0.9 ppm for potato waste. Deficiency 9c is resolved.

CBTS reiterates that based on the results of the imidacloprid bovine feeding study CBTS concludes that finite residues will actually occur in milk and 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 imida-cloprid tolerances are required in meat and milk. In the revised Section F the petitioner proposed total imidacloprid tolerances in milk, fat, meat, and meat by-products of cattle, goats, hogs, horses, and sheep at <0.02 ppm. The proposed limit of detection secondary tolerances are not acceptable. CBTS suggests the petitioner propose in a new Section F revised milk and meat tolerances at the levels submitted with PP# 3F4231; that is 0.1 ppm in milk and at 0.3 ppm in the meat, fat, meat by-products of cattle, goats, hogs, horse, and sheep. These levels include all livestock feed items reviewed in this petition and in the co-pending petition currently under review. Deficiency 10a is not resolved and continues outstanding.

CBTS reiterates that based on the results of the imidacloprid poultry feeding study we conclude 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 in eggs and poultry. In the revised Section F the petitioner has proposed total imidacloprid tolerances in eggs and poultry meat, fat, and meat by-products at <0.02 ppm. These proposed limit of detection secondary tolerances in poultry are not acceptable. CBTS suggests that the petitioner propose in a new Section F revised total imidacloprid tolerances in eggs at 0.02 ppm and at 0.05 ppm (assuming the cottonseed tolerance will not be significantly different as a result of the new field trials residue data) for poultry meat, fat, and meat by-products. These levels include all poultry feed items reviewed in this petition and in the co-pending petition currently under review. Deficiency 10c is not

resolved and continues outstanding.

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

Deficiencies

10b. CBTS reiterates that since the feeding study was conducted at Bayer's Research Center in Monheim, Germany the petitioner needs to more completely define normal housing practices so we can compare these to dairy housing practices in the USA. The type of hay needs to be defined as well as what is a high energy dairy concentrate. The petitioner needs to provide a sample label for the concentrate (in English), and the label should list the amount of protein, fat, and fiber, and major ingredients that are in the feed. And finally we were unable to locate any data showing the feeds were free from other potentially interfering heavy metals, aflatoxins, and other pesticides. The petitioner needs to provide these data.

10d. CBTS reiterates that the petitioner needs to provide a sample label for the poultry feed (in English), and the label should list the amount of protein, fat, and fiber, and major ingredients that are in the feed. And finally we were unable to locate any data showing the feeds were free from other potentially interfering heavy metals, aflatoxins, and other pesticides. The petitioner needs to provide these data.

10e. The petitioner needs to further identify the poultry breed used in the feeding study so that we may ascertain whether this is a commercially accepted breed.

Petitioner's response

The petitioner provided additional data for the bovine feeding study in a document titled "NTN 33893 - Cattle Feeding Study Additional Information Addendum 1" by J. Murphy dated February 25, 1994, and coded Miles report number 103833-1 (MRID # 432432-06).

The petitioner has provided additional information for the poultry feeding study in a document titled "NTN 33893 - Poultry
Feeding Study Additional Information Addendum 1" by J. Murphy dated February 25, 1994, and coded Miles report number 103832-1 (MRID # 431432-07).

CBTS Comments

Ruminant

In the cover letter the petitioner provided the ages of the cows in the feeding study. The ages ranged from >2 years to >4 years. The cows were obtained from "Cattle and Meat Company" in Varel Germany. These cows would have been in their prime lactation. This part of deficiency 10b is resolved.

The petitioner has provided a description of the housing practices as used in Germany for conducting the bovine feeding study. The cows were all housed indoors, in individual stands that were over 6 feet X nearly 4 feet. Climatic data for temperature, humidity, lighting period were recorded and reported. The daily housing practices are similar in Germany to the

USA. This part of deficiency 10b is resolved.

The petitioner provided an English translation of the label for the feed used in the bovine feeding study. The "concentrate" is a supplementary feed which contains 16% protein, 3.2% fat, 9% fiber, and 10% ash; plus vitamin A and D supplements. This part of deficiency 10b is resolved.

The type of hay used was from a grass meadow which had no history of any chemical treatment. This part of deficiency 10b is resolved.

While the petitioner does not have the results of specific tests showing the absence of significant levels of heavy metals, other pesticides, and mycotoxin in the cow feed he does have the quality assurance data from the German feed producing plant, daily health report for each cow from the attending veterinarian, plus a weekly intensive examination for each cow. The health report noted all cows ate and drank normally during the study, there were no changes in health during the study, and no differences were reported at autopsy between the control and test groups. These are sufficient data for CBTS to conclude the cow feed was free from significant contamination from other pesticides, mycotoxin, and heavy metals. This part of deficiency 10b is resolved.

In conclusion, CBTS reiterates that the petitioner has conducted an adequate imidacloprid bovine feeding study and based on the results of this feeding study CBTS concludes that finite residues will actually occur in milk and meat, fat, and meat by-products of cattle, goats, hogs, horse, and sheep 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 imida-cloprid tolerances are required in milk and meat as described above. No further data are necessary for the bovine feeding study in this petition and the co-pending petition PP# 3F4231.

Poultry

The petitioner provided an English translation of the label for the feed used in the poultry feeding study. The poultry feed is a complete laying hen diet. It contains 16.5% protein, 3.5% fat, 6% fiber, and 12% ash; plus vitamins A, D, and E fortifications. This part of deficiency 10d is resolved.

While the petitioner does not have the results of specific tests showing the absence of significant levels of heavy metals, other pesticides, and mycotoxin in the poultry feed he does have the quality assurance data from the German feed producing plant and daily health report for each hen from the attending veterinarian. The health report noted all hens ate and drank normally during the study, there were no changes in health during the study, and no differences were reported at autopsy between the control and test groups. These are sufficient data for CBTS to conclude the poultry feed was free from significant contamination from other pesticides, mycotoxin, and heavy metals. This part of deficiency 10d is resolved.

The breed used in the poultry feeding study was Lohmann Single Comb White Leghorn. This is a commercial poultry breed. Deficiency 10e is resolved.

In conclusion, CBTS reiterates that the petitioner has conducted an adequate imidacloprid poultry feeding study and based on the results of this feeding study we conclude that finite residues will actually occur in eggs and poultry meat, fat, and meat by-products 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 in eggs and poultry as described above. No further data are necessary for the poultry feeding study in this petition and the co-pending petition PP# 3F4231.

cc:R.F.,Circ.,Reviewer(FDG),PP#3F4169.
7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:5/6/94:edit:fdg:6/1/94.
RDI:SecHd:RSQuick:6/1/94:BrSrSci:RALoringer:6/6/94.