

MEMORANDUM

Subject: PP# 3F4169/3H5655 - Imidacloprid (Admire®) on apples, potatoes, cottonseed, meat, milk, poultry, and eggs.
Review of the August 9, and Sept. 1 and 15, 1994, Amendments. (MRID # 433372-01)[CBTS #s 13905, 14212, 14359, 14360, and 14391][DP Barcodes D204485, D206584, D207353, D207356, and D207599]

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and

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Thru: Richard A. Loranger, Ph.D., Acting Chief
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9/22/94

Background

Miles, Inc., Agricultural Division, submitted these amendments consisting of cover letters dated August 8 and September 1 and 15, 1994, signed by J.S. Thornton, a revised Section B (new directions for use and revised rotational crop restrictions) and a supplementary Section D (additional method validation data). These amendments were submitted in response to deficiencies outlined and summarized in our August 8, 1994, review by F. Griffith. The deficiencies are listed and repeated in the body of this review as they appeared in our August 8, 1994, review followed by the petitioner's responses, then CBTS comments. Our conclusions and recommendations follow.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- None -

CONCLUSIONS

1. CBTS Conclusions on Directions for Use

a. The petitioner has proposed adequate rotational crop directions for use of imidacloprid either as the flowable or the granular formulation. Only cotton and potatoes have immediate plant-back; ie, the crops listed on the label while all other crops have a 12 month plant-back interval. Deficiency 1d is resolved.

b. With the proposed 12 month plant-back interval on both labels deficiency 1e relating to rotational crop tolerances becomes moot, thus resolved.

2. CBTS conclusions on Residue Analytical Methods

a. CBTS concludes that the petitioner has provided the necessary additional validation data for Bayer method 00200. The method is suitable to gather the magnitude of the residue data for all of the raw and processed commodities in the petition. Except for a rapid turn around time the method meets all of the EPA requirements for an enforcement method and has been adequately validated to enforce all of the proposed total imidacloprid tolerances on apples, cottonseed, and potatoes. Since the method has completed a successful TMV in EPA labs it has been forwarded to FDA's Technical Editing Group to be published in a future edition of PAM-II (see letter from F. Griffith to FDA dated September 20, 1994). Deficiencies 3a from our August 8, 1994, and 5k from our June 8, 1994, reviews are resolved.

b. The petitioner provided the EPA Repository ordering codes for imidacloprid (F1037), and its olefin (F1036), guanidine (F1034), and hydroxy (F1035) metabolites. With the four ordering codes furnished by the petitioner we know that the residue analytical standards can be obtained by Federal and State enforcement laboratories when they need to analyze samples for total imidacloprid residues. This deficiency is resolved.

RECOMMENDATIONS

TOX and EFGWB considerations permitting CBTS recommends for the requested tolerances of combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as imidacloprid in/on apples at 0.5 ppm, potatoes at 0.3 ppm, milk at 0.1 ppm, meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep at 0.3 ppm, eggs at 0.02 ppm, and meat, fat, meat by-products of poultry at 0.05 ppm.

CBTS also recommends for the requested food/feed additive tolerances of combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as imidacloprid on apple pomace (wet or dried) at 3 ppm, on potato chips at 0.4 ppm, and on potato waste at 0.9 ppm.

CBTS recommends for the requested tolerances of combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all expressed as imidacloprid on cottonseed at 6 ppm and a FAT on cottonseed meal at 9 ppm with a 2 year expiration date to allow the petitioner adequate time to complete the additional cotton crop field trials and present a final report to the Agency.

DETAILED CONSIDERATIONS

DIRECTIONS FOR USE

Deficiencies

1d. The petitioner will need to revise the rotational crop restrictions. CBTS concludes that detectable residues were noted at the 11 month interval; thus, the label needs to be modified to have a 12 month plant back interval for all crops that do not have tolerances and registered uses. Since detectable residues at the MDL were noted in the turnip roots at 11 months, an 8 month plant back interval is not supportable and needs to be removed from the label. CBTS considers the 30 days plant back for grain only without the grower being allowed use of the forage, vines, or straw to be impractical. It is not practical to restrict growers to using only part of their crop. We feel this is extremely difficult to enforce; thus, should be removed from the label.

1e. If the petitioner wishes to have shorter than 12 month plant back intervals for grains, seeds, and/or root crops, then he may generate the necessary rotational crop magnitude of the residue data to support rotational crop tolerances. At this time the lowest level validated for a rotational crop tolerance using Bayer method 00200 would be 0.05 ppm.

Petitioner's response

In the September 1, 1994, amendment the petitioner submitted revised labels for Admire® 2.5 Granular and Admire® 2 Flowable Systemic Insecticide that contained revised rotational crop instructions. The September 15 amendment contained a revised label for Admire® 2 Flowable that contained revised directions for use on cotton plus revised rotational crop instructions and trickle irrigation instructions.

CBTS comments

Review of the revised label for Admire® 2.5 Granular formulation for use on potatoes and cotton at planting shows there are no significant changes from the use initially proposed. Comments from our previous reviews on the proposed use of the 2.5% granular formulation are now incorporated herein by reference. For the 2.5 Granular formulation the petitioner has added the following directions for rotational crops. For crops not listed on the Admire label, a 12 month plant-back interval is to be observed and cover crops used for soil building and/or erosion control may be planted at any time; however, they may not be grazed or harvested for food or feed. The only crops listed for immediate plant back are cotton and potatoes. This part of deficiency 1d is resolved.

The petitioner has proposed an adequate set of directions for use of Admire® 2.5 Granular for use on cotton and potatoes at planting.

Review of the revised label submitted on September 1 for use of Admire 2 Flowable on cotton did not incorporate the changes for use on cotton agreed to in our August 9, 1994,

review. The petitioner quickly corrected this error with a revised label on September 15 for Admire 2 Flowable. Review of the revised label for Admire® 2 Flow-able formulation for use on potatoes, apples, and cotton either at planting or as a foliar use shows there are no significant changes from the use initially proposed. Comments from our previous reviews on the proposed use of the 2 lbs/gal formulation are now incorporated herein by reference. For the 2 lbs/gal flowable formulation the petitioner has added the following directions for rotational crops. For crops not listed on the Admire label, a 12 month plant-back interval is to be observed and cover crops used for soil building and/or erosion control may be planted at any time; however, they may not be grazed or harvested for food or feed. The only crops listed for immediate plant back are cotton and potatoes. This part of deficiency 1d is resolved.

The petitioner has proposed an adequate set of directions for use of Admire® 2 Flowable containing 2 lbs/gal a.i. imidacloprid for use on cotton, apples, and potatoes either at planting or for use as a foliar spray.

With the proposed 12 month plant-back interval on both labels deficiency 1e relating to rotational crop tolerances becomes moot, thus resolved.

RESIDUE ANALYTICAL METHOD

Deficiencies

3a. In response to the June 20 amendment CBTS concludes there are an insufficient number of method validation and concurrent recovery data at and above the proposed tolerances to show the method will perform as expected, and as it will perform at and near the LOQ. Since the petitioner has in progress the generation of additional method validation data for imidacloprid and its metabolites from apples, potatoes, and cottonseeds, and their processed commodities at and above the proposed tolerances, we feel it is prudent to await the presentation of these data for review. These data should address our concerns on method validation for PP# 3F4169. Deficiency 5k remains outstanding, continues unresolved, and it is reiterated as follows from our June 8, 1994, review:

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.

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 method validation data, the petitioner should

4

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 that 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 imidacloprid.

Petitioner' response

(MRID # 433372-01)

The petitioner presented the additional method validation data to show that the total imidacloprid common moiety method, Bayer method 00200, is capable of enforcing tolerances in a study titled "Additional Validation Data to Support Imidacloprid Analytical Method 102624-R1" by P. Noland, et. al., dated August 3, 1994, and coded ABC Laboratories Project ID Number 41669 and Miles report number 106781.

CBTS comments

The petitioner had ABC Laboratories in Columbia, Missouri conduct an additional series of method validations using the total imidacloprid common moiety method, Bayer method 00200. This method has been previously reviewed and has completed a tolerance method validation (TMV) in EPA labs (see ACB/BEAD memorandum dated April 11, 1994). The method was validated as written without additional modifications. The determination step used a Hewlett-Packard 5890 A Series II gas chromatograph connected to HP 5971A MSD with data acquisition by a HP Vectra 486 computer. The GC column was a 12 m x 0.2 mm (id), HP Ultra 1. The petitioner has provided extensive chromatographic data with a photocopy of each chromatogram for independent verification of results. The raw data sheets from ABC labs were presented which show the peak areas for each fortified sample and each control sample. Our review of the raw data sheets confirm that the LOQ of Bayer method 00200 is 0.05 ppm and the MDL is 0.01 ppm. Duplicate control samples were analyzed with each recovery sample set.

Raw apples were fortified separately with imidacloprid, the guanidine, and 6-CNA metabolites at 0.5 ppm and at 2.5 ppm, duplicate fortifications at each recovery level. Recoveries of imidacloprid and 6-CNA from whole apples ranged from 87% to 99% (n = 8) while the guanidine recoveries ranged from 68% to 72% (n = 4). Wet apple pomace was fortified separately with imidacloprid, the guanidine, and the olefin metabolites at 3 and 15 ppm with duplicate fortifications at each recovery level. Recoveries of imidacloprid and its olefin metabolite from wet apple pomace ranged from 88% to 100% (n = 8) and recoveries of the guanidine metabolite ranged from 67% to 86%.

Cottonseeds were fortified separately with imidacloprid, the guanidine, and the 6-CNA metabolites at 6 and 30 ppm, duplicate fortifications at each recovery level. Recoveries ranged from 71% (1 sample with recovery below 80%) to 104% (1 sample with recovery above 100%). Cottonseed meal was fortified separately with imidacloprid, the guanidine,

and the olefin metabolites at 9 and 45 ppm, duplicate fortifications at each recovery level. Recoveries ranged from 70% (2 samples) to 106% (5 samples above 100%).

Potato tubers were fortified separately with imidacloprid, the guanidine, and the olefin metabolites at 0.3 and 1.5 ppm, duplicate fortifications at each recovery level. Recoveries ranged from 83% to 99% (n = 12). Potato chips were fortified separately with imidacloprid, the guanidine, and the hydroxy metabolites at 0.4 and 2 ppm, duplicate fortifications at each recovery level. Recoveries ranged from 90% to 104% (n = 12). Potato waste was fortified separately with imidacloprid, the guanidine, and the 6-CNA metabolites at 0.9 and 4.5 ppm, duplicate fortifications at each recovery level. Recoveries ranged from 79% to 100% (n = 12).

CBTS concludes that the petitioner has provided the necessary additional validation data for Bayer method 00200. The method is suitable to gather the magnitude of the residue data for all of the raw and processed commodities in the petition. Except for a rapid turn around time Bayer method 00200 meets all of the EPA requirements for an enforcement method and has been adequately validated to enforce all of the proposed total imidacloprid tolerances on apples, cottonseed, and potatoes. Since the method has completed a successful TMV in EPA labs it has been forwarded to FDA's Technical Editing Group to be published in a future edition of PAM-II (see letter from F. Griffith to FDA dated September 20, 1994). Deficiencies 3a from our August 8, 1994, and 5k from our June 8, 1994, reviews are resolved.

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cc:R.F.,Circu.,Reviewer(FDG),PP#3F4169.
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6