

4/22/1996

MEMORANDUM

SUBJECT: PP# 6F04765. Imidacloprid (Admire® and Provado®) on/in Safflower and the Cereal Grains and Legume Crop Groups. **Evaluation of Residue Data and Analytical Methods.** MRID# 440637-01. Chemical 129099. Barcodes D228500, D228459 & D228491. CBTS#s 17416, 17410 & 17415. Case 287982, 014226 & 030770.

FROM: G.F. Kramer, Ph.D., Chemist
Tolerance Petition Team I
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

THRU: E.T. Haeberer, Acting Branch Chief
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TO: C. Eiden/D. McCall
Registration Section, RCAB
Health Effects Division (7509C)

Bayer has proposed permanent tolerances for inadvertent or indirect residues of the insecticide imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine) and its metabolites, expressed as imidacloprid, in or on the following raw agricultural commodities (RACs):

Cereal Grains	--	0.05 ppm		Corn Fodder (Straw)	--	3.0
Corn Forage	--	2.0 ppm		Safflower seed	--	0.05
Legume seed	--	0.3 ppm		Soybean hay	--	2.5
Soybean forage	--	0.6 ppm				

CBTS has recommended for tolerances of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety on mangoes at 0.2 ppm (see PP# 3F4285); apples at 0.5 ppm, cottonseed at 6 ppm, and potatoes at 0.3 ppm, and their processed commodities, plus meat at 0.3 ppm, milk at 0.1 ppm, poultry at 0.05 ppm, and eggs at 0.02 ppm (see PP# 3F4169); lettuce at 3.5 ppm, grapes at 1 ppm, fruiting vegetables at 1 ppm and Brassica (cole) leafy vegetables at 3.5 ppm (see PP# 3F4231); hops at 6 ppm (see PP# 5E4425); and leafy vegetables crop leafy greens subgroup at 3.5 ppm. CBTS has also recommended for time-limited tolerances on sorghum grain at 0.05 ppm, and sorghum forage and fodder at 0.1 ppm (see PP# 4F4415); and canola seed and its processed commodities following seed treatment (see PP# 5F4534). There are co-pending petitions for total imidacloprid residues in/on barley, wheat, and sugarbeets and their processed commodities following seed treatment (see PP# 4F4337), pecans and citrus

fruits crop group and their processed commodities (see PP# 5F4480), and pome fruits (see PP# 5F4600). These petitions are in reject status.

The data supporting this petition were generated in accordance with a protocol approved by CBTS (Memo, F. Griffith 2/8/96; CBTS# 16508). The petitioner proposed to set crop group tolerances for rotational crops (inadvertent residues) based on the previously submitted limited rotational crop field trials (three representative crops planted at three sites) and a limited number of additional trials. The protocol did not propose the same number of crop field trials mentioned in our proposed Guideline OPPTS 860. 1900; i.e., the full number of trials needed for rotational crop tolerances is normally the same as for target crops. However, the protocol was deemed acceptable as i) imidacloprid apparently poses very low dietary risk, ii) the nature of the residue is well defined, including the nature of the residue from ^{14}C -imidacloprid confined rotational studies, iii) the proposals are based on field accumulation studies or complete data bases from representative crops for a number of crop groups, and iv) there are residue analytical methods, both common moiety and compound specific, that have passed an Agency PMV and can measure the residues well below the proposed rotational crop tolerances. However, if unacceptable dietary risks result from rotational crop tolerances obtained in this manner, then the full data set normally required for such tolerances will be needed.

Executive Summary of Chemistry Deficiencies

- Need soybean processing study.
- Need corn processing study.
- Need safflower processing study.
- Revised Section F.

CONCLUSIONS

1. CBTS concludes that after reviewing the CSF for the TGAI the impurities present in the TGAI imidacloprid are not expected to be a residue problem in the subject crops when Admire® or Provado® is used as directed.

2. The nature of the imidacloprid residue in poultry, ruminants, apples, potatoes, tomatoes, eggplant, cottonseed, and in corn grain, forage, and fodder is adequately understood (Memo, F.

Griffith 6/8/95; PP#5F04480). The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as imidacloprid. We are translating these data to the subject crops.

3. All samples were analyzed by the plant residue analytical method, Bayer Method 00200, reviewed previously and which has successfully passed a petition method validation (PMV) in EPA labs (Memo, F. Griffith 8/9/94; PP#3F04169).

4. The RAC samples from the field residue studies were stored for a maximum of 22 months. Residues of imidacloprid have been shown to be stable in a variety of RACs for up to 24 months of storage (Memo, F. Griffith 6/8/95; PP#5F04480). Storage stability is thus not an issue for this petition.

5a. Field rotational crop trials were conducted in MS, KS and CA. Soil was treated with imidacloprid at a rate of 0.3 lbs. ai/A (1X). After 30 days, rotational crops (corn, soybeans, peas, beans and safflower) were planted. The maximum total imidacloprid residues were 0.11 ppm in corn forage, 0.26 ppm in corn fodder, 0.22 ppm in legume vegetables, and 2.33 ppm in the foliage of legume vegetables. Residues in corn grain and safflower seed were <0.05 ppm.

5b. Between the field rotational crop trials submitted with this petition and those submitted previously, the petitioner has provided the residue data specified in the protocol approved by CBTS (Memo, F. Griffith 2/8/96; CBTS# 16508). The maximum imidacloprid residues were 1.81 ppm in cereal grain forage, 0.26 ppm in cereal grain stover, 2.7 ppm in cereal grain straw, 0.22 ppm in legume vegetables, and 2.33 ppm in the foliage of legume vegetables. Residues in cereal grain, sweet corn K+CWHR and safflower seed were <0.05 ppm. These results support the following tolerances:

Cereal grain, grain	- 0.05 ppm	Cereal grain, forage	- 2.0 ppm
Cereal grain, stover	- 0.3 ppm	Cereal grain, hay	- 6.0 ppm
Cereal grain, straw	- 3.0 ppm	Corn, sweet (K+CWHR)	- 0.05 ppm
Legume Vegetables	- 0.3 ppm	Safflower seed	- 0.05 ppm
Foliage of legume vegetables	- 2.5 ppm		

A revised Section F, containing these tolerances, is thus required for this petition.

6a. No processing studies were submitted with this petition. The petitioner has previously conducted a wheat processing study (Memo, F. Griffith 5/16/93; PP#4F04337). The imidacloprid application rate to the soil was 0.75 lb ai/acre (2.5X). Total imidacloprid residues were 0.02 ppm in the RAC and concentrated

in bran (3.5X) and shorts (2X). As the residues in bran and shorts are less than the proposed grain tolerance (0.05 ppm) when adjusted for the degree of exaggeration, tolerances are not required on cereal grain shorts and bran.

6b. The petitioner has conducted a cotton processing study using cottonseed bearing detectable total imidacloprid residues following an exaggerated application (Memo, F. Griffith 9/20/93; PP#3F04169). The RAC contained 2.88 ppm total imidacloprid. When cottonseeds were processed into hulls, meal, crude oil, refined oil, and soapstock the total imidacloprid residues were 1.07 ppm (0.37X conc. factor) in hulls, <0.5 ppm (<0.17X) in crude oil, refined oil, and soapstock, and 4.21 (1.46X conc. factor) in cottonseed meal. Total imidacloprid residues were shown to concentrate only in cottonseed meal. CBTS is willing to consider these data in regards to determining the need for additional processing studies on other crops to support the subject petition.

6c. In corn grain, total imidacloprid residues were <LOD (≈ 0.01 ppm). The results of the cottonseed study show that concentration would be likely only in corn meal. As the maximum concentration factor for corn meal is approximately 17X (*CRC Handbook of Processing and Utilization in Agriculture, Vol II*), residues in corn meal in excess of the tolerance proposed for corn grain (0.05 ppm) are possible. A corn processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to perform the requisite corn processing study. If this option is chosen, then a time-limited tolerance of 0.2 ppm should be proposed for residues of imidacloprid and its metabolites in corn meal.

6d. In soybean seed, total imidacloprid residues were a maximum of 0.2 ppm. As the theoretical maximum concentration factor for soybean meal is 2.2X, residues in soybean meal in excess of the tolerance proposed for legume vegetables (0.3 ppm) are possible. A soybean processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to perform the requisite soybean processing study. If this option is chosen, then a time-limited tolerance of 0.5 ppm should be proposed for residues of imidacloprid and its metabolites in soybean meal.

6e. In safflower seed, total imidacloprid residues were <0.05 ppm, but residues above the LOD were observed (estimated to be up to 0.03 ppm). As the theoretical maximum concentration factor for safflower meal is 9.1X, residues in safflower meal in excess of the tolerance proposed for safflower (0.05 ppm) are possible. A safflower processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to

perform the requisite safflower processing study. If this option is chosen, then a time-limited tolerance of 0.5 ppm should be proposed for residues of imidacloprid and its metabolites in safflower meal.

7. The worst-case ruminant dietary burdens associated with pending and approved uses of imidacloprid are 6.3 ppm for beef cattle and 9.0 ppm for dairy cattle. The petitioner has conducted a ruminant feeding study (Memo, F. Griffith 9/20/93; PP#3F04169). At a 15 ppm feeding level, the maximum total imidacloprid residues were 0.055 ppm in milk, 0.033 in muscle, 0.106 in kidney, 0.168 in liver and not detectable in fat. As these values are all less than the existing meat and milk tolerances (0.1 ppm for milk and 0.3 ppm for meat, fat and meat byproducts), CBTS concludes that the existing meat and milk tolerances are adequate to support the proposed new uses of imidacloprid.

8. The worst-case poultry dietary burden associated with pending and approved uses of imidacloprid is 2.2 ppm. The petitioner has conducted a poultry feeding study (Memo, F. Griffith 9/20/93; PP#3F04169). At a 2 ppm feeding level, the maximum total imidacloprid residues were 0.042 in liver and residues were not detectable in fat, eggs and muscle. As these values are all less than the existing meat and egg tolerances (0.02 ppm for eggs and 0.05 ppm for meat, fat and meat byproducts), CBTS concludes that the existing poultry meat and egg tolerances are adequate to support the proposed new uses of imidacloprid.

9. HED notes that the Food Quality Protection Act of 1996 has amended and strengthened the standard for establishing tolerances under the FFDCA. OPP is still assessing the full impact of this change in the law on the tolerance-setting process and plans to issue guidelines concerning the establishment of tolerances under the amended statute. All tolerance petitions have to meet the requirements of the FFDCA as amended by the FQPA and OPP may require additional data to determine if the terms of the amended statute are met.

10. There is neither a Codex proposal, nor Canadian or Mexican limits for residues of imidacloprid in/on safflower and the cereal grains and legume crop groups. Therefore, a compatibility issue is not relevant to the proposed tolerance. A copy of the IRLS sheet is attached to this memorandum.

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for imidacloprid and its metabolites for reasons detailed in conclusions 5b, 6c, 6d, 6e, and 9.

A DRES run may be initiated at this time using the following

tolerances:

Cereal grains	-	0.05 ppm
Legume Vegetables	-	0.3 ppm
Safflower seed	-	0.05 ppm

DETAILED CONSIDERATIONS

Product Chemistry

CBTS concludes that after reviewing the CSF for the TGAI the impurities present in the TGAI imidacloprid are not expected to be a residue problem in the subject crops when Admire® or Provado® is used as directed.

Proposed Use

The maximum use rate for most crops is 0.3 lbs. ai/A. This use rate was specified in the protocol approved by CBTS. The petitioner has submitted revised rotational crop restrictions for Admire 2 Flowable (EPA Reg. No. 3125-422) and Provado 1.6 Flowable (EPA Reg. No. 3125-457) in which the plantback intervals for cereals, legumes and safflower have been lowered from 12 months to 30 days.

Rotational Crop Studies

The petitioner has presented adequate limited field rotational crop studies from 3 sites (Memo, F. Griffith 8/9/94; PP#3F04169). These limited field crop rotational studies with the 3 crop groups support an overall 12 month plant back restriction. For shorter plant-back intervals on crops for which use of imidacloprid is not registered, rotational crop magnitude of the residue data is required to support rotational crop tolerances.

Nature of Residue

The nature of the imidacloprid residue in poultry, ruminants, apples, potatoes, tomatoes, eggplant, cottonseed, and in corn grain, forage, and fodder is adequately understood (Memo, F. Griffith 6/8/95; PP#5F04480). The residues of concern are combined residues of imidacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as imidacloprid.

We are translating these data to the subject crops.

Analytical Methodology- Plants

All samples were analyzed by the plant residue analytical method, Bayer method 00200, reviewed previously and which has successfully passed a petition method validation (PMV) in EPA labs (Memo, F. Griffith 8/9/94; PP#3F04169).

Storage Stability Studies

The RAC samples from the field residue studies were stored for a maximum of 22 months. Residues of imidacloprid have been shown to be stable in a variety of RACs for up to 24 months of storage (Memo, F. Griffith 6/8/95; PP#5F04480). Storage stability is thus not an issue for this petition.

Magnitude of Residue- Plants

Submitted with this petition:

Admire 2F - Magnitude of the Residue in Rotational Crops.
MRID# 440637-01.

Field rotational crop trials were conducted in MS, KS and CA. Soil was treated with imidacloprid at a rate of 0.3 lbs. ai/A. A cover crop was planted. After 30 days, the cover crop was disced under and rotational crops (corn, soybeans, peas, beans and safflower) were planted. The samples were sampled at maturity, frozen and shipped to Bayer (KS) for analysis. The enforcement method was validated over a range of 0.05-2.5 ppm. The average concurrent recovery was $92.3 \pm 12.1\%$ (n=17). Analyses of the treated samples showed that the maximum total imidacloprid residues were 0.11 ppm in corn forage, 0.26 ppm in corn fodder, 0.22 ppm in legume vegetables, and 2.33 ppm in the foliage of legume vegetables. Residues in corn grain and safflower were <0.05 ppm.

Table 1- Imidacloprid residues in rotational crops at a 1-month plant-back interval.

Crop Group	Crop	RAC	Location	PHI (Days)	Total Residues (ppm)
15 (Cereal Grains)	Sweet Corn	K+CWHR	MS	91	<0.05
			CA	103	<0.05
			KS	95	<0.05
	Corn	Grain	MS	150	<0.05
			CA	141	<0.05
16 (Forage, Fodder and Straw of Cereal Grains)	Corn	Forage	MS	91	<0.05
			CA	93	0.11
			KS	95	<0.05
	Corn	Fodder	MS	150	<0.05
			CA	141	0.26
			KS	157	<0.05
6 (Legume Vegetables)	Soybean	Seed	MS	150	<0.05
			CA	125	0.20
			KS	147	<0.05
	Bean	Whole Pod	MS	59	0.10
			CA	91	0.10
			KS	67	<0.05
		Succulent Seed	MS	59	0.18
			CA	91	0.08
			KS	67	<0.05
		Dry Seed	MS	91	0.12
			CA	126	0.07
			KS	131	<0.05
	Pea	Whole Pod	MS	53	0.06
			CA	63	0.09
			KS	50	<0.05
		Succulent Seed	CA	63	0.08
			CA	86	0.22
		Dry Seed	KS	73	<0.05
7 (Foliage of Legume Vegetables)	Soybean	Forage	MS	95	<0.05
			CA	86	0.53
			KS	82	0.08
	Soybean	Hay	MS	95	0.18
			CA	86	2.33
			KS	82	0.27

-	Safflower	Seed	MS	100	<0.05
			CA	126	<0.05
			KS	97	<0.05

Conclusions: Between the field rotational crop trials submitted with this petition and those submitted previously, the petitioner has provided the residue data specified in the protocol approved by CBTS (Memo, F. Griffith 2/8/96; CBTS# 16508). The maximum imidacloprid residues were 1.81 ppm in cereal grain forage, 0.26 ppm in cereal grain stover, 2.7 ppm in cereal grain straw, 0.22 ppm in legume vegetables, and 2.33 ppm in the foliage of legume vegetables. Residues in cereal grain, sweet corn K+CWHR and safflower seed were <0.05 ppm. Residue data were not provided for cereal grain hay. However, as hay was not included in Table II at the time these trials were initiated, CBTS is willing to recommend for a hay tolerance based on the forage tolerance and a dry-down factor of 3. These results thus support the following tolerances:

Cereal grain, grain - 0.05 ppm	Cereal grain, forage - 2.0 ppm
Cereal grain, stover - 0.3 ppm	Cereal grain, hay - 6.0 ppm
Cereal grain, straw - 3.0 ppm	Corn, sweet (K+CWHR) - 0.05 ppm
Legume Vegetables - 0.3 ppm	Safflower seed - 0.05 ppm
Foliage of legume vegetables - 2.5 ppm	

A revised Section F, containing these tolerances, is thus required for this petition.

Magnitude of the Residue- Processed Fractions

No processing studies were submitted with this petition.

The petitioner has conducted a wheat processing study (Memo, F. Griffith 5/16/93; PP#4F04337). The imidacloprid application rate to the soil was 0.75 lb ai/acre (2.5X). Total imidacloprid residues on the RAC were 0.02 ppm. Imidacloprid was detected in the flour and middlings at 0.01 ppm, thus no concentration is indicated. Total imidacloprid residues were detected in bran at 0.07 ppm (a 3.5X conc. factor) and shorts at 0.04 ppm (a 2X conc. factor). As the residues in bran and shorts are less than the proposed grain tolerance (0.05 ppm) when adjusted for the degree of exaggeration, tolerances are not required on cereal grain shorts and bran.

The petitioner has previously conducted a cotton processing study

using cottonseed bearing detectable total imidacloprid residues following an exaggerated rate application (Memo, F. Griffith 9/20/93; PP#3F04169). The RAC cottonseed contained 2.88 ppm total imidacloprid. When cottonseeds were processed into hulls, meal, crude oil, refined oil, and soapstock the total imidacloprid residues were 1.07 ppm (0.37X conc. factor) in hulls, <0.5 ppm (<0.17X) in crude oil, refined oil, and soapstock, and 4.21 (1.46X conc. factor) in cottonseed meal. Total imidacloprid residues were shown to concentrate only in cottonseed meal. CBTS is willing to consider these data in regards to determining the need for additional processing studies on other crops to support the subject petition.

In corn grain, total imidacloprid residues were <LOD (≈ 0.01 ppm). The results of the cottonseed study show that concentration would be likely only in corn meal. As the maximum concentration factor for corn meal is approximately 17X (*CRC Handbook of Processing and Utilization in Agriculture, Vol II*), residues in corn meal in excess of the tolerance proposed for corn grain (0.05 ppm) are possible. A corn processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to perform the requisite corn processing study. If this option is chosen, then a time-limited tolerance of 0.2 ppm should be proposed for residues of imidacloprid and its metabolites in corn meal.

In soybean seed, total imidacloprid residues were a maximum of 0.2 ppm. As the theoretical maximum concentration factor for soybean meal is 2.2X, residues in soybean meal in excess of the tolerance proposed for legume vegetables (0.3 ppm) are possible. A soybean processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to perform the requisite soybean processing study. If this option is chosen, then a time-limited tolerance of 0.5 ppm should be proposed for residues of imidacloprid and its metabolites in soybean meal.

In safflower seed, total imidacloprid residues were <0.05 ppm, but residues above the LOD were observed (estimated to be up to 0.03 ppm). As the theoretical maximum concentration factor for safflower meal is 9.1X, residues in safflower meal in excess of the tolerance proposed for safflower (0.05 ppm) are possible. A safflower processing study is thus required. However, CBTS is willing to recommend in favor of time-limited tolerances and a conditional registration provided the petitioner agrees to perform the requisite safflower processing study. If this option is chosen, then a time-limited tolerance of 0.5 ppm should be proposed for residues of imidacloprid and its metabolites in safflower meal.

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Magnitude of the Residue- Ruminants

Dietary Burden: The maximum dietary burden in dairy cows results from diet comprised of wheat forage and pea vines:

Feed Item	% Diet	proposed Tolerance	% DM	ppm in Diet
Wheat Forage	50	2.0 ppm	25	4.0
Pea Vines	50	2.5 ppm	25	5.0
Total	100			9.0

The maximum dietary burden in beef cows results from diet comprised of legume and cereal grain RACs and cottonseed:

Feed Item	% Diet	proposed Tolerance	% DM	ppm in Diet
Wheat Forage	25	2.0 ppm	25	2.0
Pea Vines	25	2.5 ppm	25	2.5
Cottonseed	25	6.0 ppm	88	1.7
Corn Stover	25	0.3 ppm	83	0.1
Total	100			6.3

Conclusions: The worst-case ruminant dietary burdens associated with pending and approved uses of imidacloprid are 6.3 ppm for beef cattle and 9.0 ppm for dairy cattle. The petitioner has conducted a ruminant feeding study (Memo, F. Griffith 9/20/93; PP#3F04169). At a 15 ppm feeding level, the maximum total imidacloprid residues were 0.055 ppm in milk, 0.033 in muscle, 0.106 in kidney, 0.168 in liver and not detectable in fat. As these values are all less than the existing meat and milk tolerances (0.1 ppm for milk and 0.3 ppm for meat, fat and meat byproducts), CBTS concludes that the existing meat and milk tolerances are adequate to support the proposed new uses of imidacloprid.

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Magnitude of the Residue- Poultry

Dietary Burden: The maximum dietary burden results from a poultry diet comprised of legume, cereal grain and cottonseed RACs and processed fractions:

Feed Item	% Diet	Tolerance	ppm in Diet
Cottonseed Meal	20	9.0 ppm	1.8
Soybean Meal	40	0.5 ppm	0.2
Safflower Meal	25	0.5 ppm	0.12
Pea Seed	15	0.3 ppm	0.04
Total	100		2.2

*Existing, recommended or proposed

Conclusions: The worst-case poultry dietary burden associated with pending and approved uses of imidacloprid is 2.2 ppm. The petitioner has conducted a poultry feeding study (Memo, F. Griffith 9/20/93; PP#3F04169). At a 2 ppm feeding level, the maximum total imidacloprid residues were 0.042 in liver and residues were not detectable in fat, eggs and muscle. As these values are all less than the existing meat and egg tolerances (0.02 ppm for eggs and 0.05 ppm for meat, fat and meat byproducts), CBTS concludes that the existing poultry meat and egg tolerances are adequate to support the proposed new uses of imidacloprid.

Attachment 1- IRLS Sheet

cc: D. Edwards/P. Jenkins (RD, 7505C), PP#6F04765, Kramer, R.F., Circ.
RDI: TPT1 (9/19/96), E. Haeberer (9/20/96), R.A. Loranger (9/20/96)
G.F. Kramer:804V:CM#2:(703)305-5079:7509C