update R.B.P.

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

JUL 6 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Reregistration of Amitraz: Product and Residue Chemistry Considerations

FROM: R.B. Perfetti, Ph.D., Chemist
Dietary Exposure Branch
Health Effects Division (H7509C) R B Perfetti

THRU: Richard D. Schmitt, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division (H7509C) R. Loranger for

TO: L. Rossi, Chief
Reregistration Branch
Special Review and Registration Division (H7508C)

and

R. Engler, Ph,D., Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Introduction

Amitraz (N'-(2,4-dimethylphenyl)-N-({2,4 dimethyl-phenylimino}methyl) -N- methylmethanimidamide is an insecticide-acaracide. Tolerances for the combined residues of parent and two metabolites have been established for milk, meat, pears, and apples (40 CFR 180.287). This memo will outline product and residue chemistry conclusions with respect to reregistration of amitraz.

Also, attached please find updated product and residue chemistry chapters for this chemical. These chapters were prepared by Dynamac Corporation under the supervision of the Dietary Exposure Branch, HED. They have undergone secondary review in DEB and have been revised to reflect Branch policies.

Please note our conclusions regarding remaining data deficiencies and pending actions in the Introduction and Conclusions at the beginning of each respective chapter. Updated data tables for both product and residue chemistry have also been provided.

Product Chemistry

As can be seen in the attached product chemistry update several deficiencies remain to be resolved for Nor-Am's 93% T (EPA Reg No. 45639-51). A complete product chemistry data set is required for a second Nor-Am 93% T (EPA Reg. No. 45639-129 transferred from EPA Reg No. 1023-58). Perhaps this second product is to be voluntarily canceled. In any event these data are required.

Provided that the Registrant(s) submits the data required above and either certificates that the suppliers of beginning materials and manufacturing process for the two amitraz technicals and any MUP's have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, DEB has no objections to the reregistration of amitraz with respect to product chemistry data requirements.

Residue Chemistry

As can be seen in the attached residue chemistry update the remaining data requirement for amitraz involves the need for dermal metabolism studies in cattle and swine. The requirement for cold dermal experiments (Magnitude of the Residue in Meat and Milk) is reserved until the metabolism questions are satisfactorily resolved. It should be noted that there are pending tolerance/registration actions involving cottonseed and citrus along with concomitant dietary meat, milk, poultry and egg residue questions (See Residue Chemistry Update Introduction.).

A pending dermal use registration on goats and sheep has received a favorable recommendation from DEB. The Branch is not objecting to the granting of this registration at this time in light of the minimal additional dietary risk involved for goat and sheep meat products vs beef and pork. At such time as the cattle and swine meat and milk tolerance questions are resolved the Branch will make a final conclusion regarding the minor use of amitraz on goats and sheep.

Tolerance Reassessment

The present tolerances for amitraz residues are as follows;

(180.287) Amitraz tolerances for residues.

Tolerances are established for residues of the insecticide amitraz (N'[2,4-dimethylphenyl] -N-[[(2,4-dimethylphenyl)imino]

methyl]]-N-methylmethanimidamide) and its metabolites N-(2,4-dimethylphenyl)-N-methyl formamide and N-(2,4-dimethylphenyl)-N-methylmethanimidamide (both calculated as the parent) in or on the following raw agricultural commodities (RAC) at the following levels:

Commodity	Parts per million
Apples	0
Cattle, fat	0.1
Cattle, mbyp	0.3
Cattle, meat	0.05
Goats, fat	0
Goats, mbyp	0
Goats, meat	0
Hogs, fat	0.1
Hogs, kidney	0.2
Hogs, liver	0.2
Hogs, mbyp	0.3
Hogs, meat	0.05
Horses, fat	0
Horses, mbyp	0
Horses, meat	0
Milk	0.03
Milk, fat	0.3
Pears	3
Sheep, fat	0
Sheep, mbyp	0
Sheep, meat	0

The Branch has evaluated the tolerances above and has determined that:

1) The zero tolerance for apples should be revoked since there are no uses for this R.A.C.

2) The 3 ppm tolerance for residues of amitraz and its 2 metabolites on pears is acceptable. No modifications are needed.

3) At such time as the required cattle and swine dermal metabolism studies (and possibly dermal magnitude of the residue in meat and milk studies) are submitted and found to be acceptable, a final conclusion regarding appropriate tolerance regulations and levels for milk and meat, fat, and meat by products in cattle, swine, goats, and sheep as a result of the dermal use of amitraz will be made.

4) Pending registration actions regarding amitraz residues in citrus and cottonseed as well as secondary residues in meat, milk, poultry, and eggs as a result of dietary exposure to

residues of amitraz and their effect on total residues to be expected on animal commodities as a result of both pathways of exposure will be addressed by DEB in a future update on amitraz reregistration.

Minor Uses

There are no minor use concerns for amitraz at present.

Codex

Codex MRL's are established for residues of amitraz and one of its two metabolites (dimethyphenyl-N'- methylformamidine) on the following commodities:

Commodity	Limit (mg/kg)
Cattle Meat	0.05
Pig Meat	0.05
Edible offal of cattle, Pigs, and Sheep	0.2
Sheep Meat	0.1
Milk	0.01

In light of the uncertainty regarding both the dermal metabolism of amitraz in animals and the levels to be expected in animal commodities as a result of dermal and dietary exposure, no conclusion regarding the compatibility of U.S. tolerances and Codex MRL's can be made at this time.

There are no Canadians or Mexican limits for residues of amitraz.

If you have any questions please advise.

Attachment 1: Product Chemistry Reregistration Update for Amitraz.

Attachment 2: Residue Chemistry Reregistration Update for Amitraz.

cc: (With Attachments 1 and 2) : R.B.P., Amitraz Reregistration Standard File, Amitraz Subject File, E. Saito (TOX), J. Burrell (PIB/FOD), C. Furlow (PIB/FOD), Dynamac, Addressees.

cc: (Without Attachments): Circ (7), RF, R.D. Schmitt (DEB), P. Fenner-Crisp (HED), M. Hawkins (HED), W. Boodee (DEB).

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H7509C:DEB:R.B.P.:sc:Rm810:X77324:CM#2:07//02/90

DYNAMAC
CORPORATION

Final Report

AMITRAZ
Task 4: List A - Product Chemistry Registration Standard Update

January 10, 1990

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

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AMITRAZ

LIST A REGISTRATION STANDARD UPDATE

PRODUCT CHEMISTRY

Task - 4

INTRODUCTION

The 8/6/85 update of the Index of Pesticide Chemicals identifies two registered 93% technical (T) products (EPA Reg. Nos. 45639-129 and 45639-51) for amitraz.

The Amitraz Guidance Document dated 10/87 identifies outstanding data gaps for several product chemistry topics. Nor-Am Chemical Company has submitted data for the 93% technical product (EPA Reg. No. 45639-51) in response to these requirements (1987; MRIDs 40650701, 40650702, 40650703, 40650704, 40650705, 40650706, and 40650707); the data are the subject of an Agency memorandum by H. Fonouni (DEB No. 3975, dated 7/21/88).

The available data, up to November 27, 1989, have been reviewed by the Agency.

Corresponding to each of the Topical Discussions listed below are the Guideline Reference Numbers from "Pesticide Assessment Guidelines - Subdivision D - Product Chemistry", referred to in Title 40 of the Code of Federal Regulations (40 CFR), Part 158, "Data Requirements for Registration", Subpart C, "Product Chemistry Data Requirements". These regulations and guidelines explain the minimum data that the Agency needs to adequately assess the product chemistry of amitraz.

	Guidelines Reference No. from 40 CFR §158.155-190
Product Composition and Manufacture	61-(1-3)
Analysis and Certification of Product Ingredients	62-(1-3)
Physical and Chemical Characteristics	63-(2-20)

PRODUCT IDENTITY AND COMPOSITION

61-1. Product Composition
61-2. Starting Materials and Manufacturing Process
61-3. Discussion of the Formation of Impurities

The information/data provided in MRIDs 40650701, 40650702, and 40650703 for the 93% technical product (EPA Reg. No. 45639-51) satisfy the requirements for these topics (H. Fonouni; DEB No. 3975, dated 7/21/88).

No product chemistry data have been submitted for the Nor-Am 93% T (EPA Reg. No. 45639-129). Data gaps for the topics identified in the Guidance Document for this product remain outstanding.

ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

62-1. Preliminary Analysis
62-2. Certified Limits
62-3. Enforcement Analytical Methods

The information/data provided in MRIDs 40650703, 40650704, 40650705, and 40650706 for the 93% technical product (EPA Reg. No. 45639-51) satisfy the requirements for these topics (H. Fonouni; DEB No. 3975, dated 7/21/88).

No product chemistry data have been submitted for the Nor-Am 93% T (EPA Reg. No. 45639-129). Data gaps for these topics identified in the Guidance Document for this product remain outstanding.

PHYSICAL AND CHEMICAL CHARACTERISTICS

The information/data provided in MRID 40650707 for the 93% technical product (EPA Reg. No. 45639-51) satisfy the requirements for Guidelines Reference Nos. 63-2 through 63-7, 63-9, 63-11, and 63-12 (H. Fonouni; DEB No. 3975, dated 7/21/88). Additional data on solubility, dissociation constant, stability of the product, including thermal stability, sensitivity to sunlight, metals, and metal ions are required. No product chemistry data have been submitted for the Nor-Am 93% T (EPA Reg. No. 45639-129); thus, a full complement of data on physical chemical characteristics for this product is required.

DEFICIENCIES REMAINING TO BE RESOLVED - PRODUCT CHEMISTRY

1. The registrant must submit data on solubility, dissociation constant, stability of the product, including thermal stability, sensitivity to sunlight, metals, and metal ions for the Nor-Am Chemical Company 93% T (EPA Reg. No. 45639-51).

2. The registrant must submit data on beginning materials and manufacturing process, formation of impurities, preliminary analysis, certification of limits, enforcement analytical methods, and a full complement of physical chemical characteristics for the Nor-Am Chemical Co. 93% T product (EPA Reg. No. 45639-129 transferred from EPA Reg. No. 1023-58).

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Product Chemistry Citations (used):

40650701 Johnson, M. (1987) Amitraz Manufacturing Process and Discussion of Formation of Impurities; Description of Beginning Materials: Project ID: AD 49/87: AD 51/87. Unpublished study prepared by Schering Agrochemicals Ltd. 49 p.

40650702 Lal, S.; Brehm, M. (1987) Preliminary Analysis of Technical Amitraz Determination of N-Nitrosamines in Technical Amitraz: Project ID: AD 62/87; APC 57/86. Unpublished study prepared by Schering Agrochemicals Ltd. and Schering AG. 41 p.

40650703 Johnson, M. (1987) Amitraz Chemical Product Composition: Project ID: AD 56/87. Unpublished study prepared by Schering Agrochemicals Ltd. 6 p.

40650704 Leete, A. (1987) The Determination of Amitraz in Technical Material and Formulations by Gas Chromatography (GC): The Validation of the Analytical Method AM 1800/1/6 for the Determination of Amitraz in its Technical Material and Wettable Powder Formulation: Project ID; AM 1800/6/1 and AD/65/87. Unpublished study prepared by Schering Agrochemicals Ltd. 19 p.

40650705 Lal, S. (1987) The Determination of BTS 27919, BTS 27271, BTS 28037 and BTS 24868 Impurities in Amitraz Technical by Gas Chromatography: An Assessment of the Accuracy ... in Technical Amitraz by Gas Chromatography: Project ID: AM No. 1800/5/1; AD 68/87. Unpublished study prepared by Schering Agrochemicals Ltd. 33 p.

40650706 Lal, S. (1987) The Determination of (...) in Technical Amitraz by Gas Chromatography (GC): An Assessment of the Accuracy and Precision of the Analytical Method (AM 1800/6/1) for the Determination of (...) in Technical Amitraz by Gas Chromatography: Project ID: AM 1800/6/1; AD 69/87. Unpublished study prepared by Schering Agrochemicals Ltd. 13 p.

40650707 Johnson, M.; Leete, A.; Bright, A.; et al. (1987) Amitraz: Physical and Chemical Characteristics: Project No.: AD 52/87 CHEM/87/78. Unpublished study prepared by Schering Agrochemicals Ltd. 88 p.

TABLE A. GENERIC DATA REQUIREMENTS FOR THE AMITRAZ TECHNICAL GRADE OF THE ACTIVE INGREDIENT.[1]

Data Requirement	Test Substance[2]	Does EPA have data to satisfy this requirement?	Bibliographic Citation	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.155-190 Product Chemistry				
Product Composition[3]				
61-2. Beginning Materials and Production Process	TGAI	Partial	40650701	Yes[3]
61-3. Formation of Impurities	TGAI	Partial	40650701	Yes[3]
Analysis and Certification of Product Ingredients				
62-1. Preliminary Analysis	TGAI	Partial	40650702	Yes[3]
Physical and Chemical Characteristics				
63-2. Color	TGAI	Partial	40650707	Yes[4]
63-3. Physical State	TGAI	Partial	40650707	Yes[4]
63-4. Odor	TGAI	Partial	40650707	Yes[4]
63-5. Melting Point	TGAI	Partial	40650707	Yes[4]
63-6. Boiling Point	TGAI	Partial	40650707	Yes[4]
63-7. Density, Bulk Density, or Specific Gravity	TGAI	Partial	40650707	Yes[4]
63-8. Solubility	TGAI or PAI	No	N/A	Yes[4,5]
63-9. Vapor Pressure	TGAI or PAI	Partial	40650707	Yes[4]
63-10. Dissociation Constant	TGAI or PAI	No	N/A	Yes[4,6]

(Continued, footnotes follow)

TABLE A. (Continued).

Data Requirement	Test Substance	Does EPA have data to satisfy this requirement?	Bibliographic Citation	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
63-11. Octanol/Water Partitioning Coefficient	PAI	Partial	40650707	Yes[4]
63-12. pH	TGAI	Partial	40650707	Yes[4]
63-13. Stability	TGAI	No	N/A	Yes[4,7]
Other Requirements:				
64-1. Submittal of Samples	N/A	N/A	N/A	No

1. Additional data requirements are listed in the following Table B, "Generic Data Requirements for Amitraz Manufacturing-Use Products", for registered technical products.

2. Test substance: PAI = purified active ingredient; TGAI = technical grade of the active ingredient; MP = manufacturing-use product.

3. The registrant must submit data on beginning materials and manufacturing process, formation of impurities, preliminary analysis, and a full complement of physical chemical characteristics for the Nor-Am Chemical Co. 93% T product (EPA Reg. No. 45639-129 transferred from EPA Reg. No. 1023-58).

4. As required by 40 CFR §158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, Guidelines Reference Nos. 63-2 through 63-13, data must be submitted on all physicochemical characteristics (color, physical state, odor, melting point, boiling point, specific gravity, solubility, vapor pressure, dissociation constant, octanol/water partition coefficient, pH, and stability) for the Nor-Am Chemical Co. (EPA Reg. No. 45639-129), and for solubility, dissociation constant, and stability of the product for the Nor-Am Chemical Co. (EPA Reg. No. 45639-51). There are additional data requirements listed in Table B pertaining to physicochemical characteristics of those technical products which are also manufacturing use products.

TABLE A. (Continued).

5. The registrant must submit data regarding solubility of the Nor-Am Chemical Company 93% T (EPA Reg. No. 45639-51).

6. The registrant must submit data regarding dissociation constant of the Nor-Am Chemical Company 93% T (EPA Reg. No. 45639-51).

7. The registrant must submit data regarding stability of the Nor-Am Chemical Company 93% T (EPA Reg. No. 45639-51), including thermal stability, sensitivity to sunlight, metals, and metal ions.

TABLE B. PRODUCT SPECIFIC DATA REQUIREMENTS FOR AMITRAZ MANUFACTURING-USE PRODUCTS.[1]

Data Requirement	Test Substance[2]	Does EPA have data to satisfy this requirement?	Bibliographic Citation	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.155-190 Product Chemistry				
Product Composition[3]				
61-1. Product Composition	MP			No
61-2. Beginning Materials & Production/Formulation Process	MP	Partial	40650701	Yes[3]
61-3. Formation of Impurities	MP	Partial	40650701	Yes[3]
Analysis and Certification of Product Ingredients				
62-1. Preliminary Analysis	MP	Partial	40650702	Yes[3]
62-2. Certified Limits	MP	Partial	40650703	Yes[3]
62-3. Enforcement Analytical Methods	MP	Partial	40650704 40650705 40650706	Yes[3]
Physical and Chemical Characteristics				
63-2. Color	MP	Partial	40650707	Yes[4]
63-3. Physical State	MP	Partial	40650707	Yes[4]
63-4. Odor	MP	Partial	40650707	Yes[4]
63-7. Density, Bulk Density, or Specific Gravity	MP	Partial	40650707	Yes[4]
63-12. pH	MP	Partial	40650707	Yes[4]
62-14. Oxidizing or Reducing Action	MP	Partial	40650707	Yes[4]

(Continued, footnotes follow)

TABLE B. (Continued).

Data Requirement	Test Substance	Does EPA have data to satisfy this requirement?	Bibliographic Citation	Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
62-15. Flammability	MP	Partial	40650707	Yes[4]
63-16. Explodability	MP	Partial	40650707	Yes[4]
63-17. Storage Stability	MP	Partial	40650707	Yes[4]
63-18. Viscosity	MP	Partial	40650707	Yes[4]
63-19. Miscibility	MP	Partial	40650707	Yes[4]
63-20. Corrosion Characteristics	MP	Partial	40650707	Yes[4]
Other Requirements:				
64-1. Submittal of Samples	N/A	N/A	N/A	No

1. Additional data requirements are listed in the preceding Table A, "Generic Data Requirements for the Amitraz Technical Grade of the Active Ingredient", for those manufacturing-use products which consist only of the TGAI.

2. Test substance: PAI = purified active ingredient; TGAI = technical grade of the active ingredient; MP = manufacturing-use product.

3. The registrant must submit data on beginning materials and manufacturing process, formation of impurities, preliminary analysis, certification of limits, enforcement analytical methods, and a full complement of physical chemical characteristics for the Nor-Am Chemical Co. 93% T product (EPA Reg. No. 45639-129 transferred from EPA Reg. No. 1023-58).

4. As required in 40 CFR §158.190 and more fully described in the Pesticide Assessment Guidelines, Subdivision D, Guidelines Reference Nos. 63-2 through 63-20, data must be submitted on all physicochemical

TABLE B. (Continued).

characteristics of the Nor-Am Chemical Co. (EPA Reg. No. 45639-129) manufacturing-use product (color, physical state, odor, specific gravity, pH, oxidizing or reducing action, flammability, explodability, storage stability, viscosity, miscibility, and corrosion characteristics). Additional data requirements regarding physicochemical properties of manufacturing-use products which contain only the technical grade of the active ingredient are listed in Table A, "Generic Data Requirements for the Amitraz Technical Grade of the Active Ingredient."

DYNAMAC
CORPORATION

Final Report

AMITRAZ
Task 4: List A - Residue Chemistry Registration Standard Update

January 10, 1990

Revised Final Report dated May 10, 1990

Contract No. 68-D8-0080

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

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AMITRAZ

REGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 4

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AMITRAZ

REGISTRATION STANDARD UPDATE

RESIDUE CHEMISTRY

Task - 4

INTRODUCTION

The 8/6/85 update of the Index of Pesticide Chemicals identifies pears as the single registered food-use site for the insecticide Amitraz. Amitraz formulations registered for dormant and foliar applications to pears are the 1.5 lb/gal emulsifiable concentrate (EC) and 50% wettable powder (WP). The 12.5% EC formulation (EPA Reg. No. 45639-70) of amitraz is also registered for direct application to dairy cattle, beef cattle, and swine as a spray or dip treatment.

The Amitraz Guidance Document dated 10/87 identifies outstanding data gaps for plant metabolism and storage stability. In response to these requirements, Nor-Am Chemical Company has submitted data on plant metabolism (1989; MRID 41206701). Nor-Am Chemical Company has also submitted data in support of registration depicting the recovery of amitraz and its metabolites BTS 27271 and BTS 27919 using FDA Multiresidue Protocols I and II published in Pesticide Analytical Manual (PAM), Vol. I (1988; MRIDS 40811311 and 40811312). The available data, up to November 27, 1989, have been reviewed by the Agency or are otherwise reviewed here for their adequacy in fulfilling the outstanding data requirements.

Since issuance of the 1987 Amitraz Guidance Document, use of amitraz as a direct animal treatment to beef and dairy cattle (PP#4F2968) and hogs (PP#4F3081) has been registered and tolerances for residues of amitraz in animal products have been established. In additional actions since issuance of the Guidance Document, the registrant has sought registration of amitraz on citrus and an experimental use permit (EUP) on cottonseed, and has petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-dimethylaniline metabolites (calculated as the parent) in or on these commodities. The data submitted in conjunction with these proposals have undergone Agency review. Several deficiencies remain outstanding for the proposed use and tolerance for residues in or on citrus [MRIDs 40811300, 40811301, 40811302, 40811303, 40811304, 40811305, 40811306, 40811307, 40811308, 40811309, 40811310, 40811311, and 40811312 (DEB Nos. 4374/4375, dated 1/10/89); MRIDs 40590601 and 40539001 (DEB Nos. 3515/3735, dated 5/4/88)]. With regard to the EUP on cotton, DEB has recommended for an extension of temporary tolerances for amitraz residues in eggs, and the meat, fat, and meat byproducts of goats, horses, sheep, and poultry, and the establishment of

temporary tolerances for amitraz residues in or on cottonseed and poultry meat by-products [MRIDs 40999501, 40999502, 40999503, 40999504, 40999505, 40999506, 40999507, and 40999508 (DEB Nos. 5008/5009/5020/5021, dated 5/31/89); MRID 40590801 (DEB No. 3737, dated 5/11/88); MRIDs 40259302 and 40259303 (DEB Nos. 3402/3403, dated 5/11/88)].

Tolerances for residues of amitraz in or on raw agricultural commodities and animal products are currently expressed in terms of residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent)(40 CFR 180.287).

SUMMARY

The following Amitraz Residue Chemistry data are required:

- Additional data pertaining to the qualitative nature of the residue in animals.

QUALITATIVE NATURE OF THE RESIDUE IN PLANTS

Conclusions:

The qualitative nature of the residue in pears is adequately understood. The available data (1989; MRID 41206701) indicate that 79.8 and 86.4% of the total ^{14}C-activity has been identified in pears following application at 1 and 10x the maximum registered rate, respectively. The metabolites identified in pears following treatment at 1x were amitraz (35.2%), BTS 27271 (16.3%), BTS 27919 (13.8%), BTS 28037 (1%), BTS 28369 (4.1%), BTS 39098 (2%), FBC 31158 (1.6%), and BTS 24868 (5.8%).

Additional metabolism studies on cotton and citrus submitted in conjunction with petitions for permanent and/or temporary tolerances for residues of amitraz in or on these commodities have undergone Agency review. Studies on cotton were reviewed by F.B. Suhre (MRID 40590801; DEB Nos. 3402 and 3403 dated 5/11/88) and M.T. Flood (MRID 40999502; DEB Nos. 5008, 5009, 5020, and 5021 dated 5/31/89); these reviews conclude that the nature of the residue in cottonseed is adequately understood for purposes of establishing the proposed (PP#9F3730) permanent tolerance and extending the established temporary (PP#9G3742) tolerance for residues of amitraz and its metabolites containing the 2,6-dimethylaniline moiety in or on cottonseed. A study on citrus (MRID 40590601) was reviewed by F.B. Suhre (DEB Nos. 3515 and 3735 dated 5/5/88); this review concludes that the nature of the residue in citrus is adequately understood for the purpose of establishment of the proposed (PP#2F2705/FAP#2H5353) tolerances for amitraz and its metabolites containing the 2,6-

dimethylaniline moiety in or on citrus and its processed products.

The molecular structures and chemical names of amitraz and its metabolites and conversion products are presented in Table 4 beginning on page 8.

References (used):

MRID(s): 40590601. 40590801. 40999502. 41206701.

Discussion of the data:

Nor-Am Chemical Company (1989; MRID 41206701) submitted data pertaining to the metabolism of [^{14}C]amitraz in pears. Thirty-three individual pears received three applications at 2- to 3-week intervals with a WP formulation of [^{14}C]amitraz (136 µCi/mg specific activity, radiochemical purity 97%) and unlabeled amitraz (final specific activity 20 µCi/mg) at 0.45 mg ai/ml/fruit/application (equivalent to 0.375 lb ai/100 gal/application or 1.5 lb ai/A/application based on a maximum of 400 gal finished spray; 1x the maximum registered single application rate). The formulation was applied by pipette as small droplets evenly over the surface of each fruit. An additional set of pears received 10 applications at 2- to 3-week intervals of the same formulation at 4.64 mg ai/ml/fruit/application (10x the maximum registered single application rate). Three samples of fruit from each treatment group were harvested at day 0. The remaining fruit were harvested 7 days following the last application (maturity). Two samples were analyzed immediately following treatment; the remaining samples were stored at -70 C in glass jars surrounded by anhydrous silica gel and sealed in plastic containers.

Total Radioactive Residues

Samples were analyzed for total radioactivity by combustion/liquid scintillation spectrometry (LSS). The limit of detection of the radioassay was not specified. The total radioactive residue (expressed as amitraz equivalents) in or on one sample each of pears treated at 1 and 10x was 0.5 and 6.62 ppm, respectively.

Extraction

Fruit was dipped in triethylamine:hexane (Et_3N:hexane; 5:95, v/v), rinsed, and peeled. The immersion solvent and rinsing were combined (peel wash). The fruit was peeled and separated into flesh and peel. The peel was extracted sequentially with Et_3N:hexane (5:95, v/v) and Et_3N:acetone (5:95, v/v) and the extracts analyzed for total radioactivity by LSS. Flesh from fruit receiving the 1x treatment was extracted sequentially with

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Et_3N:acetone (5:95, v/v) and water-saturated butanol at pH 7, 32, and 1. The combined extracts were analyzed for total radioactivity by LSS. Flesh from fruit receiving the 10x treatment was extracted as described for the 1x flesh except partitioning to water-saturated butanol was conducted at unchanged pH. Fibre from the peel and flesh was extracted with methanol:water (50:50, v/v) prior to combustion.

Hydrolysis of fibre

Fibre from the 1x treated fruit was refluxed for 15 hours with 6 M sodium hydroxide with a volatile trap (containing hexane and water) fitted to the reflux apparatus. The hexane in the volatile trap was partitioned from water and cleaned-up by partitioning to 0.1 M hydrochloric acid. The acidic solution was adjusted to pH 9-10 with 2 M sodium hydroxide, partitioned back to hexane, and subjected to Kuderna-Danish concentration.

The alkaline residue from hydrolysis was filtered and the filter disc was combusted to determine radioactivity in the solid residue. The filtrate was partitioned sequentially to ether, ethyl acetate at unchanged pH, ethyl acetate at neutral pH, and water-saturated butanol at pH 3. The four organic extracts were combined, concentrated, and applied to a CN-Bond Klut column eluting sequentially with methanol:water (1:1 and 3:1, v/v) and methanol. The methanol:water eluants (1:1 and 3:1) were concentrated and analyzed by TLC. The distribution of the TRR in pears is presented below in Table 1.

Table 1. Distribution of the TRR in pears following application with [^{14}C]amitraz at 1 and 10x.

Substrate	Fraction	% TRR 1x	% TRR 10x
Peel	Surface Wash	39.4	74.2
	Et_3N:Hexane	15.8	5.3
	Et_3N:Acetone	15.3	7.4
	Methanol:Water	2.8	1.2
	Fibre	17.5	7.4
Flesh	Et_3N:Acetone	6.1	3.0
	Methanol:Water	0.8	0.4
	Fibre	2.3	1.2
	Total	100.0	100.0

Characterization

Soluble residues were analyzed by one-dimensional TLC using one of five solvent systems: (i) hexane:triethylamine (17:3, v/v); (ii) cyclohexane:ethylacetate:triethylamine (5:3:2, v/v); (iii) ethylacetate:isopropanol:water (65:23:12, v/v); (iv) chloroform:methanol:acetic acid (10:0.75:0.1); and (v) methanol:water:acetic acid (78:20:2, v/v). Radioactive zones were located by autoradiography, identified by cochromatography with known standards, and radioassayed by LSS. The standard compounds used in this study were amitraz (BTS 27419; N-methylbis(2,4-xylyliminomethyl)amine); BTS 27271 (N-methyl-N'-(2,4-xylyl) formamidine); BTS 27919 (Form-2',4'-xylidide); BTS 28037 [N, N'-bis(2,4-xylyl)formamidine]; BTS 24868 (2,4-dimethylaniline); BTS 28369 (4-amino-m-toluic acid); BTS 39098 (4-formamido-m-toluic acid); and FBC 31158 (4-acetomido-m-toluic acid).

In summary, the qualitative nature of the residue in pears is adequately understood. The registrant has adequately characterized 79.8 and 86.4%, respectively, of the total in pears following application of at 1 and 10x. The metabolites identified in pears following treatment at 1x were (35.2%), BTS 27271 (16.3%), BTS 27919 (13.8%), BTS 28037 (1%), BTS 28369 (4.1%), BTS 39098 (2%), FBC 31158 (1.6%), and BTS 24868 (5.8%).

Enforcement Method

Samples of pears treated with for the metabolism study were also analyzed by the GLC residue method titled "Method of Analysis for Residues of Amitraz and All Metabolites Hydrolyzing to 2,4-DMA in Miscellaneous Crops" (R.C. Longland; April 1987). The GLC method quantified 70.3% and 86.0% of the total ^{14}C-residues determined by LSS analysis, and 97.5% and 107.9% of the ^{14}C-residues determined by chromatography to contain the 2,4-DMA moiety. This GLC method is similar to the PAM Vol. II enforcement procedure (Method II, Reg. Sec. 180.287). The PAM method prescribes the conversion of residues of to 2,4-DMA by base hydrolysis and partitioning to iso-octane, whereas the subject method utilizes acid hydrolysis and distillation into hexane. Both methods prescribe derivatization with heptafluorobutyric anhydride, and quantitation of the derivative by electron capture gas-liquid chromatography.

Table 2. Characterization of soluble amitraz metabolites in pears following application at 1x.

Metabolite or Fraction	Percent of total ^{14}C-residues					
	Wash	Et_3N Hexane	Et_3N Acetone	Me:OH Water	Fibre	Total
<u>Peel</u>						
Amitraz	34.3	0.8	--	--	--	35.1
BTS 27271	3.8	12.2	0.1	--	--	16.1
BTS 27919	1.3	1.7	9.6	--	--	12.6
BTS 28037	0.4	0.2	--	--	--	0.6
BTS 28369	--	--	0.9	--	1.5	2.4
BTS 39098	--	--	1.2	--	0.7	1.9
FBC 31158	--	--	0.9	--	0.4	1.3
BTS 24868	--	--	--	--	5.8[b]	5.8
Remainder	--	0.9[a]	2.6[a]	2.8[c]	5.7[a]	12.0
Fibre	--	--	--	--	3.4	3.4
<u>Flesh</u>						
Amitraz	--	--	0.1	--	--	0.1
BTS 27271	--	--	0.2	--	--	0.2
BTS 27919	--	--	1.2	--	--	1.2
BTS 28037	--	--	0.4	--	--	0.4
BTS 28369	--	--	1.7	--	--	1.7
BTS 39098	--	--	0.1	--	--	0.1
FBC 31158	--	--	0.3	--	--	0.3
BTS 24868	--	--	--	--	--	--
Remainder	--	--	2.1[a]	0.8[c]	--	2.9
Fibre	--	--	--	--	2.3	2.3
Total	39.8	15.8	21.4	3.6	19.8	100.4

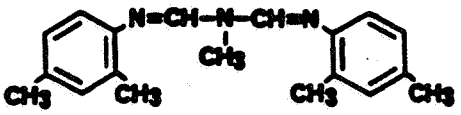
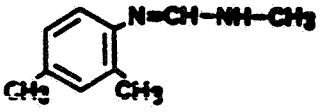
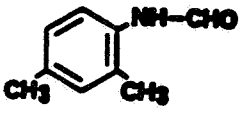
[a]The registrant indicates that no single unidentifiable component represents >1% of total ^{14}C-activity.
[b]Observed only following 6 M sodium hydroxide hydrolysis.
[c]Not analyzed.

Table 3. Characterization of soluble amitraz metabolites in pears following application at 10x.

Metabolite	Percent of total ^{14}C-residues					
	Wash	Et_3N Hexane	Et_3N Acetone	Me:OH Water	Fibre	Total
Peel						
Amitraz	66.9	0.3	0.2	--	--	67.4
BTS 27271	3.7	4.4	0.9	--	--	9.0
BTS 27919	2.9	0.5	2.2	--	--	5.6
BTS 28037	0.9	0.1	0.2	--	--	1.2
BTS 28369	--	--	0.5	--	--	0.5
BTS 39098	--	--	0.3	--	--	0.3
FBC 31158	--	--	0.6	--	--	0.6
Remainder	--	--	2.5[a]	1.2[b]	--	3.7
Fibre	--	--	--	--	7.4	7.4
Flesh						
Amitraz	--	--	--	--	--	--
BTS 27271	--	--	0.1	--	--	0.1
BTS 27919	--	--	0.6	--	--	0.6
BTS 28037	--	--	0.1	--	--	0.1
BTS 28369	--	--	0.7	--	--	0.7
BTS 39098	--	--	0.1	--	--	0.1
FBC 31158	--	--	0.2	--	--	0.2
Remainder	--	--	1.2[a]	0.4[b]	--	1.6
Fibre	--	--	--	--	1.2	1.2
Total	74.4	5.3	10.4	1.6	8.6	100.3

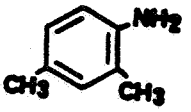
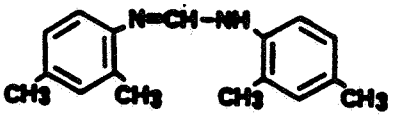
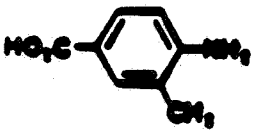
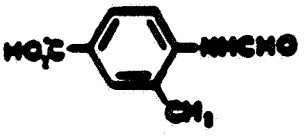
[a]The registrant indicates that no single unidentifiable component represents >1% of total ^{14}C-activity.
[b]Not analyzed.

Table 4. Amitraz and its metabolites and conversion products.

Code	Chemical name Structure	Substrate	MRID Common name
I.	N'-(2,4-dimethylphenyl)-N-[[(2,4-dimethylphenyl)imino]methyl]-N-methylmethanimidamide		
		Poultry fat	40999503
		Lemon fruit	None[a]
		Apple fruit	00055718
		Apple leaves	00028666
		Pear fruit	41206701
			Amitraz
		(BTS-27419; RD-27419; and U-36,059)	
II.	N'-(2,4-dimethylphenyl)-N-methylmethanimidamide		
		Lemon fruit	None[a]
		Apple fruit	00055718
		Apple leaves	00028666
		Cow milk	40811305
		Poultry fat	40999503
		Pear fruit	41206701
			BTS-27271 and U-40481
III.	N-(2,4-dimethylphenyl)formamide		
		Lemon fruit	None[a]
		Apple fruit	00055718
		Apple leaves	00028666
		Cow liver	40811305
		Cow milk	40811305
		Egg yolk	40999503
		Poultry fat	40999503
		Pear fruit	41206701
			BTS-27919 and U-36893

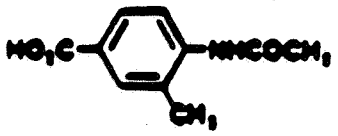
(Continued)

Table 4. Amitraz its metabolites (continued).

Code	Chemical name Structure	Substrate	MRID Common name
IV.	2,4-dimethylbenzenamine		
		Lemon fruit	None[a]
		Cow kidney	40811305
		Cow liver	40811305
		Pear fruit	41206701
			BTS-24868
V.	N,N'-bis(2,4-dimethylphenyl) methanimidamide		
		Lemon fruit	None[a]
		Pear fruit	41206701
			BTS-28037
VI.	4-amino-m-toluic acid		
		Cow liver	40811305
		Cow milk	40811305
		Egg white and yolk	40999503
		Poultry muscle	40999503
		Poultry liver	40999503
		Pear fruit	41206701
			BTS-28369
VII.	4-formamido-m-toluic acid		
		Cow milk	40811305
		Cow liver	40811305
		Pear fruit	41206701
			BTS-39098

(Continued)

Table 4. Amitraz its metabolites (continued).

Code	Chemical name Structure	Substrate Common name	MRID
VIII.	4-acetomido-m-toluic acid		
		Pear fruit	41206701
		Cow milk	40811305
		Cow liver	40811305
		Poultry liver	40999503
		Poultry muscle	40999503
			FBC-31158

[a]McGibbon, A.S., and I.D. Kelly. 1984. The metabolism of [^{14}C]amitraz in lemons under glasshouse conditions (an interim report). [Unpublished study submitted by FBC Limited, Saffron Walden, Essex England under PP#2F2705/2H5353(253132).]

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QUALITATIVE NATURE OF THE RESIDUE IN ANIMALS

Conclusions:

The Amitraz Guidance Document dated 10/87 concludes that data are not required for this topic because the registered uses and established tolerances cover crops (apples and pears) that do not involve feed items. Since issuance of the Guidance Document, use of amitraz as a direct animal treatment to beef and dairy cattle (PP#4F2968) and hogs (PP#4F3081) has been registered and tolerances for residues of amitraz in animal products have been established. Data reflecting dermal application of radiolabeled amitraz to beef and dairy cattle were provided by the registrant in conjunction with proposals for use of amitraz on apples and pears (Agency memorandum by W.S. Cox, dated 2/7/75, and located in the correspondence file for PP#5G1558). These data from studies completed in 1970 and 1972, do not meet the requirements of the 1982 Guidelines and recent Agency acceptance criteria for metabolism studies that depict dermal application to livestock because animals were not sacrificed within 24 hours of the final treatment and ^{14}C-activity present in milk and tissues was not characterized. The following additional data are required:

- Metabolism studies in which cattle and swine receive direct dermal application of ring-labeled [^{14}C]amitraz. Animals must be treated at a concentration that will result in sufficient residues in the tissues for characterization. Animals must be sacrificed 24 hours following three consecutive applications and residues characterized in muscle, fat, kidney, liver, and milk (cattle only). Treated animals should be maintained to minimize oral exposure due to grooming.

In addition to the actions described above, the registrant has sought registration of amitraz on citrus and an experimental use permit (EUP) on cottonseed, and has petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-dimethylaniline (2,4-DMA) metabolites in or on these commodities. Data on the qualitative nature of the residue in animals submitted in conjunction with these proposals have undergone Agency review.

A poultry metabolism study (MRID 40999503) was reviewed by M.T. Flood (EPA Memoranda DEB Nos. 5008, 5009, 5020, and 5021 dated 5/31/89) who concludes that the nature of the residue in poultry is adequately understood for purposes of establishing the proposed (PP#9F3730) permanent tolerances for residues of amitraz and its metabolites containing the 2,6-dimethylaniline moiety in eggs, poultry fat, meat, and meat by-products, and extending the established temporary (PP#9G3742) tolerances for the same residues in poultry meat by-products. The principal residue is

BTS 28369, BTS 28369, and FBC 31158 for poultry muscle and liver; parent amitraz, BTS 27271 and BTS 27919 for fat; BTS 28369 for egg white; and BTS 27919 and BTS 28369 for egg yolk.

A dairy cow metabolism study reflecting oral ingestion of amitraz (MRID 40811305) was reviewed by M.F. Kovacs (EPA Memoranda DEB Nos. 4374 and 4375 dated 1/10/89) who concludes that the nature of the residue in ruminants is adequately understood pending judgement on the toxicological significance of the acidic metabolites [R. Landolt, Toxicology Branch II (Agency memorandum dated 2/13/89) concludes that the metabolite BTS 28369 is not of toxicological concern]. The major DMA components of amitraz in cattle liver are BTS 24868 and BTS 27919; BTS 27271 and BTS 27919 comprise the major DMA components in milk. The acidic metabolites BTS 28369, BTS 39098, and FBC 31158 comprise a significant portion of the total terminal residue in liver and milk.

References (used):

MRID(s): 40811305. 40999503.

Discussion of the data:

N/A.

RESIDUE ANALYTICAL METHODS

Conclusions:

The Amitraz Guidance Document dated 10/87 concludes that residue analytical methods are adequate for determination of amitraz in or on plant commodities and reserves the requirement for methodology on animal commodities because the registered uses and established tolerances (apples and pears) do not cover crops involving feed items. Since issuance of the Guidance Document, the registrant has sought registration of amitraz on citrus and an experimental use permit (EUP) on cottonseed, and has petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-DMA metabolites in or on these commodities. Residue analytical methods for determination of amitraz residues in animal commodities submitted in conjunction with those proposals have undergone Agency review.

Nor-Am Chemical Co. (MRID 40811310) submitted a GLC-EC method for determination of amitraz and its 2,4-DMA metabolites in animal tissues, milk, and eggs in conjunction with the proposed use of amitraz on citrus (PP#2F2705/FAP#2H5353). This method is the subject of an agency review by M.F. Kovacs (EPA Memoranda DEB Nos. 4374 and 4375 dated 1/10/89) who concludes that this method is similar to Method I in PAM Vol. II and therefore adequate for

determination of amitraz and its metabolites containing the 2,4-DMA moiety in animal commodities and for enforcement purposes.

The submitted multiresidue test data (1988; MRIDS 40811311 and 40811312) were discussed in an Agency memorandum by M.F. Kovacs (EPA Memoranda DEB Nos. 4374 and 4375, dated 1/10/89). Amitraz and its 2,4-DMA metabolites, BTS 27271 and BTS 27919 were tested using multiresidue method (MRM) Protocols II and III. BTS 27919 was the only compound of the three tested which was analyzed by either MRM protocol. The report was submitted to the Food and Drug Administration (FDA) for review.

References (used):

MRID(s): 40811310. 40811311. 40811312.

Discussion of the data:

N/A.

STORAGE STABILITY DATA

Conclusions:

Nor-Am Chemical Company (MRID 40999508) submitted additional data regarding storage stability of amitraz in cottonseed in conjunction with PP#9G3742 and PP#9F3730 for proposed use of amitraz on cottonseed. Storage stability data pertaining to citrus (1988; MRID 40811309) and animal products (MRID 40811308) were also submitted in conjunction with PP#2F2705/FAP#2H5353 for proposed use of amitraz on citrus. These data have undergone Agency reviews (M.F. Kovacs, EPA Memoranda DEB Nos. 4374 and 4375, dated 1/10/89; M.T. Flood, EPA Memoranda DEB Nos. 5008, 5009, 5020, 5021, dated 5/31/89) which conclude that: (i) the 2-CPA metabolites (BTS 27271 and BTS 27919) are stable in citrus stored at -20 C for up to 18 months; (ii) amitraz and its 2-CPA metabolites (BTS 27271 and BTS 27919) are stable in cow tissue and milk at -20 C for 12-15 months; and (iii) amitraz residues are stable in cottonseed for over one year under frozen storage. These data satisfy the additional requirements on this topic outlined in Amitraz Guidance Document.

References (used):

MRID(s): 40811308. 40811309. 40999508.

Discussion of the data:

N/A.

MAGNITUDE OF THE RESIDUE IN PLANTS

Conclusions:

Since the issuance of the Guidance Document, the registrant has sought registration of amitraz on citrus and an experimental use permit (EUP) on cottonseed, and has petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-dimethylaniline metabolites in or on these commodities. The data submitted in conjunction with these proposals have undergone Agency review; refer to DEB memoranda by M.F. Kovacs (DEB Nos. 4374 and 4375 dated 1/10/89) and M.T. Flood (DEB Nos. 5008, 5009, 5020, 5021 dated 5/31/89) for conclusions pertaining to these reviews.

Pome Fruits Group

Apples

Tolerance(s):

A tolerance of "0 ppm" has been established for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in or on apples [40 CFR §180.287].

Conclusions:

The Amitraz Guidance Document dated 10/87 does not require additional data to support the established "0 ppm" tolerance for resides of amitraz in or on apples. Since the use site apples does not appear on any amitraz product label, the entry "Apples" should be deleted from 40 CFR §180.287.

References (used):

MRID(s): N/A.

Discussion of the data:

N/A.

Pears

Tolerance(s):

A tolerance of 3 ppm has been established for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in or on pears [40 CFR §180.287].

Conclusions:

The Amitraz Guidance Document dated 10/87 concludes that the available data on pears support the established 3 ppm tolerance for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in or on pears. No additional data are required for this topic.

References (used):

MRID(s): N/A.

Discussion of the data:

N/A.

MAGNITUDE OF THE RESIDUE IN MEAT, MILK, POULTRY, AND EGGS

Milk (and Milk Fat) and Meat, Fat, and Meat By-products of Cattle, Goats, Hogs, Horses, and Sheep

Tolerance(s):

Tolerances have been established for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in the fat (0.1 ppm), meat (0.05 ppm), and meat by-products (0.3 ppm) of cattle and hogs. Tolerances of 0.2 ppm have been established for the same residues in the kidney and liver of hogs (40 CFR §180.287).

Tolerances of 0.03 and 0.3 ppm have been established for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in milk and milk fat, respectively (40 CFR §180.287).

Tolerances of "0-ppm" have been established for the same residues in the fat, meat, and meat by-products of goats, horses, and sheep (40 CFR §180.287).

Tolerances have been proposed for residues of amitraz and its metabolites BTS 27271 and BTS 27919 (both calculated as the parent) in the liver and kidney of sheep and goats at 0.3 ppm and in the fat of sheep and goats at 0.5 ppm (PP#9F3772).

Use directions and limitations:

The 12.5% EC formulation is registered for direct application to beef and dairy cattle as either a spray applied until runoff (0.025%; 760 ml product/100 gal of water) or a spray dip (0.05%; 1520 ml product/100 gal of water). Animals may be retreated 7-10

days following the initial application. There is no established posttreatment slaughter interval for beef and dairy cattle and no withholding period for milk following application to lactating dairy cattle. The 12.5% EC may also be applied to swine (and premises, walls, floor, and fittings in the pens) as a spray to run-off (760 ml product/50 gal of water). The treatment to swine and premises may be repeated 7-10 days after the application. Additional treatments for maintenance include application to sows before and after transfer to farrowing pens and application to boars every 2 or 3 months. A 1-day preslaughter interval has been established. Use on horses is not permitted. These use directions were obtained from the product label (EPA Reg. No. 45639-70 accepted 11/12/87.

Use of the 12.5% EC formulation as a direct treatment to sheep and goats has been proposed. The spray is to be applied as a 0.025% or 0.05% spray solution (380 ml product/50 gal of water or 760 ml product/100 gal of water) until penetration of sheared wool and runoff is achieved. The treatment may be repeated 7- to 10-days after the first for control of mange and 10- to 14-days after the first for control of lice. These proposed use directions were obtained from DEB Memorandum No. 5459 by R.W. Cook, dated 1/17/90 (PP#9F3772).

Conclusions:

The Amitraz Amitraz Guidance Document dated 10/87 concludes that data are not required for this topic because the registered uses and established tolerances (apples and pears) do not cover crops involving livestock feed items. Since issuance of the Guidance Document, use of amitraz as a direct animal treatment to beef and dairy cattle (PP#4F2968) and hogs (PP#4F3081) has been registered and tolerances for residues of amitraz in animal products have been established. In additional actions since issuance of the Guidance Document, the registrant has: (i) sought registration of amitraz as a direct treatment to sheep and goats (PP#9F3772); (ii) sought registration of amitraz on citrus (PP#2F2705/FAP#2H5353) and cotton (PP#9F3730 and PP#9G3730); and (iii) petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-dimethylaniline metabolites in or on these commodities.

Shering Agrochemicals Ltd. (MRIDs 40811306 and 40811307) submitted a dairy cow feeding study which was reviewed by DEB (M.F. Kovacs, EPA Memoranda DEB Nos. 4374 and 4375 dated 1/10/89). This review concludes that the current tolerances for residues of amitraz and its 2,4-DMA metabolites in cattle fat (0.1 ppm), meat (0.05 ppm), meat by-products (0.3 ppm), and milk (0.03 ppm) will cover residues in these animals for the proposed use on citrus. With regard to the proposed use of amitraz on cotton (PP#9F3730), DEB (M.T. Flood, EPA Memoranda DEB Nos. 5008,

5009, 5020, and 5021 5/31/89) has required a revised Section F, proposing tolerances of 0.01 ppm for fat and meat of goats, horses, and sheep and a tolerance of 0.05 ppm for the meat by-products of these animals.

Nor-Am Chemicals (MRID 41127401) submitted data pertaining to residues of amitraz in sheep tissues following dermal application which is reviewed by R.W. Cook (EPA Memorandum DEB No. 5459 dated 1/17/90) who concludes that the available data support the proposed tolerances of 0.3 ppm in the meat and meat byproducts of sheep and goats and 0.5 ppm in the fate of sheep and goats. In addition, DEB suggests that the registrant propose tolerance levels of 0.2 ppm for amitraz residues in the liver and kidney of sheep and goats.

Presently, the nature of the residue in animals (cattle and swine) from dermal application is not adequately understood. Upon receipt of the requested animal metabolism data, the expected dietary intake for cattle (beef and dairy) and swine will be calculated and the need for additional residue studies will be reevaluated. It should be noted that the established tolerances for residues of amitraz in animal commodities are based on data from dermal application studies. If residues are found in feed items (processed products from citrus and cottonseed), tolerances must be set high enough to cover both dermal and oral routes of exposure. For this purpose, it is generally assumed that residues from oral ingestion and dermal treatments are additive.

References (used):

MRID(s): 40811306. 40811307.

Discussion of the data:

N/A.

Eggs and the Meat, Fat, and Meat By-products of Poultry

Tolerance(s):

No tolerances have been established for residues of amitraz in poultry tissues or eggs. Nor-Am Chemical Co. has proposed (1989; PP#9F3730) tolerances for residues of amitraz and its metabolites containing the 2,4-DMA metabolites (calculated as parent) in eggs (0.01 ppm), poultry fat and meat (0.01 ppm), and poultry meat by-products (0.05 ppm).

The Amitraz Guidance Document dated 10/87 concludes that data are not required for this topic because the registered uses and

established tolerances (apples and pears) do not cover crops involving feed items. Since issuance of the Guidance Document, the registrant has sought registration of amitraz on citrus and an experimental use permit (EUP) on cottonseed, and has petitioned the Agency for permanent and/or temporary tolerances for residues of amitraz and its 2,4-dimethylaniline metabolites in or on these commodities and in eggs, poultry fat, meat, and meat by-products.

Shering Agrochemicals Ltd. (MRIDs 40999504 and 40999505) submitted a poultry feeding study which has been reviewed by M.T. Flood (DEB Nos. 5008, 5009, 5020, 5021, dated 5/31/89). This review concludes that the available data are not adequate to support the proposed tolerances for residues in poultry by-products; chromatograms of extracts for controls, spiked controls, and kidney and liver from all dose levels must be submitted.

References (used):

MRID(s): 40999504. 40555505.

MASTER RECORD IDENTIFICATION NUMBERS

The following references were obtained from a Guideline Sequence Number search conducted on November 27, 1989 for amitraz.

References (used):

40259302 Nor-Am Chemical Co. (1987) R231-Total Residues of Amitraz and Metabolites in Cottonseed following Early and Mid-season Application of Mitac EC in Trials Run in the USA in 1985 and 1986: Laboratory Project ID: 12005. Unpublished study prepared by Nor-Am Chemical Co. 35 p.

40259303 Castro, L. (1987) R232-Total Residues of Amitraz and Metabolites in Cottonseed following Late-season Application of Mitac EC in Trials Run in the 1985 and 1986: Laboratory Project ID: 12007. Unpublished study prepared by Nor-Am Chemical Co. 31 p.

40539001 Nor-Am Chemical Company (1988) Amitraz: Summary of Citrus Residue Data. Unpublished study. 18 p.

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TABLE A. GENERIC DATA REQUIREMENTS FOR AMITRAZ.

Data Requirement	Test Substance[1]	Does EPA have data to satisfy this requirement?	Bibliographic Citation[2]		Must additional data be submitted under FIFRA Sec. 3(c)(2)(B)?
40 CFR §158.240 Residue Chemistry					
171-2. Chemical Identity[3]					
171-3. Directions for Use		(See Index)[4]			
171-4. Nature of the Residue (Metabolism) - Plants	PAIRA & plant metabolites	Yes	40590601. 40999502.	40590801. 41206701.	No
171-4. Nature of the Residue (Metabolism) - Livestock	PAIRA & plant metabolites	Partially	40811305.	40999503.	Yes[5]
171-4. Residue Analytical Methods	TGAI & metabolites	Yes	40811310. 40811312.	40811311	No
171-4. Storage Stability	TEP & metabolites	Yes	40811308. 40999508.	40811309.	No
171-4. Magnitude of Residue in Plants					
Pome Fruits - Pears	TEP	Yes	N/A		No
171-4. Magnitude of residue in Meat/Milk/Poultry/Eggs	TGAI or plant metabolites	Partially	40811306. 40999504.	40811307. 40999505.	Reserved[6]

1. Test substance: PAI = purified active ingredient; TGAI = technical grade of the active ingredient; MP = manufacturing-use product.

TABLE A. (Continued).

2. These references were submitted in response to the Amitraz Guidance Document dated 10/87. Underlining denotes documents that have been reviewed in this update document.

3. The same chemical identity data are required as under 40 CFR §158.150-190, with emphasis on impurities that could constitute residue problems. Refer to Product Chemistry Data Requirements tables.

4. The 8/6/85 update of the index of uses for amitraz was used in preparing this update.

5. Metabolism studies in which cattle and swine receive direct dermal application of ring-labeled [^{14}C]amitraz. Animals must be treated at a concentration that will result in sufficient residues in the tissues for characterization. Animals must be sacrificed 24 hours following three consecutive applications and residues characterized in muscle, fat, kidney, liver, and milk (cattle only). Treated animals should be maintained to minimize oral exposure due to grooming.

6. The nature of the residue in livestock following dermal application is not understood. On receipt of the requested ruminant metabolism data, the need for additional residue studies will be reevaluated.