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TO: Dennis Edwards Mario Fiol
Product Manager PM 19 and SRRD
Registration Division

FROM: Paul J. Mastradone, Ph.D., Section Chief
Environmental Chemistry Review Section #1
Environmental Fate & Ground Water Branch/EFED (H7507C)

THRU: Henry Jacoby, Branch Chief
Environmental Fate & Ground Water Branch/EFED (H7507C)

Attached, please find the EFGWB review of...

Reg./File #: 106201/045639-RUA Ovasyn

Common Name: Amitraz

Product Name: OVASYN

Company Name: NOR-AM

Purpose: Review of environmental fate assessment on amitraz and its degradates, hydrolysis studies, aquatic metabolism study, field dissipation study, and field crop rotation study to support a conditional registration to use amitraz on cotton.

Type Product: Insecticide Action Code: 180/660 EFGWB #(s): 91-0025/92-0349 Review Time: 20.0 days

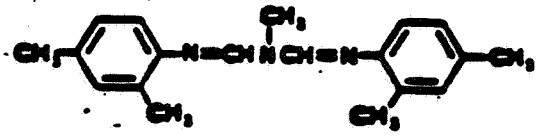
EFGWB Guideline/MRID/Status Summary Table: The review in this package contains...

161-1	Hydrolysis-BTS 27271 BTS 27919	Y	162-4	Addendum to MRID 41444205 Aquatic Metabolism Study	Y	164-4			166-1		
161-2			163-1			164-5			166-2		
161-3			163-2			165-1			166-3		
161-4			163-3			165-2	MRID 41637302	Y	167-1		
162-1			164-1	MRID 41637301	Y	165-3			167-2		
162-2			164-2			165-4	Addendum to MRID 41444206	N	201-1		
162-3			164-3			165-5			202-1		

Y = Acceptable (Study satisfied the Guideline)/Concur P = Partial (Study partially satisfied the Guideline, but additional information is still needed)
S = Supplemental (Study provided useful information, but Guideline was not satisfied) N = Unacceptable (Study was rejected)/Non-Concur

1.0 CHEMICAL:

chemical name: N,N'-[(Methylimino)-dimethylidyne]-di-2,4-xyline
common name: Amitraz
trade name: Ovasyn, Mitac, Taktic, Triatox
structure:
CAS #:
Shaughnessy #:106201



2.0 TEST MATERIAL: discussed in DER

3.0 STUDY/ACTION TYPE: Review of environmental fate assessment on amitraz and its degradates, hydrolysis studies, aerobic aquatic metabolism study, field dissipation study, and field crop rotation study to support a conditional registration to use amitraz on cotton.

4.0 STUDY IDENTIFICATION:

Allen, R. 1991. W105 2nd Edition- Addendum 1: The Fate of [^{14}C]-Amitraz Following Repeated Application in a Sediment/Water 'Microcosm'. Performed by Schering Agrochemicals Ltd., Essex, England. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Addendum to MRID 41444205.

Allen, R. 1991. W150: The Fate of [^{14}C]-Amitraz in Sediment/Water 'Microcosms'. Performed by Schering Agrochemicals Ltd., Essex, England. Submitted by Nor-Am Chemical Company, Wilimington, Delaware.

Barrett, K. L. 1991. W111-Addendum 1: Determination of the Accumulation and Elimination of [^{14}C]-Amitraz in Bluegill Sunfish (Lepomis machrochirus). Performed by Schering Agrochemicals Ltd., Essex, England. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Addendum to MRID 41444206.

Castro, L.E. 1990. Dissipation of Amitraz in the Following Applications of OVASYN to Cotton, U.S.A. 1988. Performed and submitted by Nor-Am Chemical Co. Pikesville, N.C. MRID 41637301.

Castro, L.E. 1990. Residues of Amitraz in Rotational Crops Following Treatment of OVASYN of Cotton, U.S.A. 1988/1989. Performed and and submitted by Nor-Am Chemical Co. Pikesville, N.C. MRID 41637302.

Fordham, L.R., A.S. McGibbon, and I. D. Kelley. 1984. W66 Amitraz: The Kinetics of Hydrolysis of BTS 27919 Under Acid, Neutral, and Basic Conditions. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Performed by Schering Agrochemicals Ltd., Essex, England.

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42124616

Fordham, L.R., A.S. McGibbon, and I. D. Kelley. 1984. W65 Amitraz: The Kinetics of Hydrolysis of BTS 27271 Under Acid, Neutral, and Basic Conditions. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Performed by Schering Agrochemicals Ltd., Essex, England.

Kelly, I. D., R. R. Stevens, J. J. Vuklich, and P. F. Paul. 1991. Amitraz: Summary and Discussion of the Environmental Fate and Ecological Impact Following Application of Ovasyn to Cotton. Performed and and submitted by Nor-Am Chemical Co. Pikesville, N.C.

Meyer, L.A. 1990. Residues of Amitraz in Rotational Crops Following Treatment of OVASYN of Cotton, U.S.A. 1988/1989. Submitted by Nor-Am Chemical Co. Pikesville, N.C. Performed by Analytical Bio-Chemistry Laboratories Columbia, MO. MRID 41637302.

Stalker, A. M. and J.C. Ward. 1991. BTS 27271 Product Chemistry Guideline Series 63. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Performed by Schering Agrochemicals Ltd., Essex, England. MRID 42124614.

Stalker, A. M. and J.C. Ward. 1991. BTS 27919 Product Chemistry Guideline Series 63. Submitted by Nor-Am Chemical Company, Wilimington, Delaware. Performed by Schering Agrochemicals Ltd., Essex, England. MRID 42124615.

Vukich, J. J., 1991. Request and Justification for a Conditional Registration for Use of OVASYN on Cotton and Expedited Review of this Request. Submitted by Nor-Am Chemical Company, Wilimington, Delaware.

5.0 REVIEWED BY:

James A. Hetrick, Ph.D.
Chemist, ECRS # 1
EFGWB/EFED/OPP

Signature: James A. Hetrick
Date:

6.0 APPROVED BY:

Paul Mastradone, Ph.D.
Section Chief, ECRS # 1
EFGWB/EFED/OPP

Signature: Paul J Mastradone
Date:

7.0 CONCLUSIONS:

7.1 Status of Data Requirements:

Data Requirements		Review Status
Hydrolysis	(161-1)	- Satisfied
Aqueous photolysis	(161-2)	- Partially[1]
Soil photolysis	(161-3)	- Partially[1]
Aerobic soil metabolism	(162-1)	- Satisfied
Anaerobic soil metabolism	(162-2)	- Satisfied
Aerobic aquatic metabolism	(162-4)	- Satisfied

Leaching/adsorption/desorption	(163-1)	- Satisfied
Laboratory volatility	(163-2)	- Satisfied
Field volatility	(163-3)	- Reserved
Terrestrial field dissipation	(164-1)	- Satisfied
Confine crop accumulation	(165-1)	- Not Satisfied
Field crop accumulation	(165-2)	- Satisfied
Fish accumulation	(165-4)	- Not Satisfied
Nontarget aquatic organism accumulation	(165-5)	- Reserved
Drop Spectrum	(201-1)	- Required[2]
Field Drift	(201-2)	- Required[2]

1- Partially satisfied indicates the data requirement has been fulfilled for parent amitraz;however, EFGWB has not reviewed environmental fate data for the primary amitraz degradates.

2- Spray drift studies are required for aerially applied insecticides with a Tox 1 or Tox 2 classification; or if the pesticide is deemed as posing an environment hazard.

7.2 The environmental fate data base for amitraz is nearly complete to support a conditional registration for amitraz use on cotton. The environmental fate data requirements for parent amitraz (except for the confined crop rotation (165-1), accumulation in fish (165-4), droplet spectrum (201-1), field drift (201-2)) have been satisfied. In addition, environmental fate data (including hydrolysis, aerobic soil metabolism, aerobic aquatic metabolism, and terrestrial field dissipation) have been submitted on the primary amitraz degradates 2,4-dimethylformanilide (BTS 27919) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271). (Please refer to Section 7.9 for environmental fate assessment on amitraz and its degradates.)

7.3 The hydrolysis studies for 2,4-dimethylformanilide (BTS 27919) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271) provide acceptable data. These hydrolysis studies, in addition to the hydrolysis study on parent amitraz (MRID 40780512), fulfill the 161-1 data requirement for amitraz and its degradates.

Based on acceptable data, parent amitraz hydrolyzes rapidly ($t_{1/2}$ < 26 hours) in pH 5, 7, 9 buffer solutions. The hydrolytic degradates of amitraz were identified as BTS 27919, BTS 27271, and 2,4-dimethylaniline (BTS 24868). BTS 27271 further hydrolyzes to form BTS 27919; the mean hydrolysis half-life for BTS 27271 was 2,280 days in pH 5.00 buffer solution, 14 days in pH 7.00 buffer solution, and 5.0 hours in pH 9.00 buffer solution. However, BTS 27919 was stable to abiotic hydrolysis.

The reported data indicate parent amitraz and BTS 27271 should not persist under most environmental conditions. However, BTS 27271 may be more persistant in acidic environments because it does not hydrolyze. Additionally, BTS 27919 does not hydrolyze and hence may persist in natural environments.

7.4 The aerobic aquatic metabolism study (MRID 41637307) is acceptable and together with aerobic metabolism study (MRID 41444205) fulfills the 162-4 data requirement.

It is important to note the microcosms studies were conducted under stratified redox conditions; the water column was aerated yet the sediment was anoxic. Similar conditions were observed in the aerobic aquatic metabolism study (MRID 41444205). Although non-uniform redox potentials may simulate natural aquatic environments, these conditions within a microcosm could affect certain degradation processes (eg, microbial mineralization) and hence alter pesticide degradation rates. In future studies, a uniform redox potential should exist within the microcosms.

Based on acceptable data, parent amitraz rapidly dissipates in aquatic environments. In the water column and whole microcosm, the 50% dissipation time (DT50) for parent amitraz was less than 6 hours. The primary amitraz degradates, BTS 27271 and BTS 27919, were more persistance than parent amitraz. The DT50 for BTS 27271 ranged from 3.3 to 7.0 days and 7.7 to 6.1 days in the water column and whole microcosm, respectively. The DT50 for BTS 27919 ranged 9 to 20 days and 10 to 21 days in the water column and whole microcosm, respectively. Additionally, small quantities of volatile degradates (including BTS 24868 (< 5% of applied) and CO_2 (< 14% of applied)) were formed.

The reported data indicate parent amitraz and its degradates dissipate rapidly in aerobic aquatic environments. The major routes of amitraz residue dissipation appear to be dependent on abiotic hydrolysis, biological mineralization to CO_2, and residue binding to sediment.

7.5 The field dissipation study (MRID 41637307) provides acceptable data and fulfills the 164-1 data requirement.

Based on acceptable field dissipation data, parent amitraz dissipates rapidly (< 1 day) to form BTS 27271 and BTS 27919. These degradates were more persistant than parent amitraz under typical use conditions. The mean dissipation half-lives for BTS 27271 and BTS 27919 were 50 days and 41 days, respectively. Amitraz and its primary degradates do not appear to dissipate through leaching.

The reported data indicate BTS 27271 and BTS 27919 are more persistant than parent amitraz under typical use conditions.

7.6 The field crop rotation study (MRID 41637302) is acceptable and partially fulfills the 165-2 data requirements. This study together with the field crop rotation study (MRID 40998509) fulfill the 165-2 data requirement.

Based on acceptable data, accumulation of amitraz residues was observed in corn stover and forage. The total amitraz residue concentration (including parent amitraz, BTS 27271, and BTS 27919)

in corn stover and forage ranged from 0.11 to 0.16 $\mu g\ g^{-1}$; otherwise, total amitraz residue concentration in rotated crops was < 0.05 $\mu g\ g^{-1}$. Similar accumulation data was reported in a companion field rotational crop study (MRID 40998509).

The reported data suggest amitraz residues (including parent amitraz, BTS 27919, and BTS 27271) do not accumulate in rotated crop plants.

7.7 The fish accumulation study (MRID 41444206) cannot be evaluated without TLC separation efficiencies. Currently, the registrant has not submitted any information on TLC separation efficiencies. This information is necessary to evaluate the analytical methods. (Please refer to Section 10.2.)

7.8 The aerobic aquatic study (MRID 41444205), in addition to the information on extraction efficienies and analytical detection limits, fulfill the 162-4 data requirement. (Please refer to Section 10.3.)

7.9 Environmental Fate Assessment:

General: The environmental fate data requirements for parent amitraz and its primary degradates are nearly complete except for confined crop accumulation, bioaccumulation in fish, and spray drift data. Although the field rotational crop data requirement has been fulfilled, it is important that confined crop accumulation studies be conducted. These studies are necessary to determine if pesticide residue accumulation will occur in rotated crops and what the nature of those residues might be. Spray drift studies are required to determine the potential movement of amitraz residues from the application site under typical use conditions.

Based on environmental fate data from the 1987 Amitraz Registration Standard to present, parent amitraz degradation is dependent on hydrolysis. The rate of hydrolysis was dependent upon solution pH; the hydrolysis rate was inversely related to the pH of the medium. Amitraz hydrolysis was faster in slightly acidic environments ($t_{1/2}$ = 2 hours) than in alkaline environments ($t_{1/2}$ = 25.5 hours). In aerobic mineral soil, parent amitraz had a half-life of less than one day. The amitraz degradates formed during aerobic soil metabolism were as follows: BTS 27271 (≈13%), BTS 27919 (≈35%), BTS 24868(≈13%), and CO_2 (≈35%). Similarly, parent amitraz had a field dissipation half-life of less than a day. Parent amitraz, therefore, appears to be extremely unstable in terrestrial and aquatic ecosystems.

Amitraz rapidly hydrolyzes ($t_{1/2}$ < 1 day) to form BTS 27271, BTS 27919, and possibily BTS 24868. These degradates are more persistant than parent amitraz in terrestrial and aquatic environments. In aerobic soil metabolism studies, the calculated first order half-lives for BTS 27271 and BTS 27919 were 75 days and 89 days, respectively. Similar half-lives were reported in California and Florida field dissipation studies.

(Reviewer Note: It is important to note that a first-order decay model did not adequately describe data in the aerobic soil metabolism study; the interpolated half-lives for BTS 27919 and BTS 27271 range from 6 to 10 days.) In aquatic metabolism studies, the calculated 50% dissipation time (DT50) for BTS 27271 and BTS 27919 ranged from 6 to 7 days and 10 to 20 days, respectively, in water columns and whole microcosms. Amitraz degradate dissipation appears to be dependent on abiotic hydrolysis, microbial mediated processes (mineralization to CO_2 with residue incorporation into nonlabile organic matter), and sediment binding.

The amitraz degradates appear to be relatively immobile in column leaching studies and field dissipation. In column leaching studies, aged amitraz residues were detected in soil below the application depth (< 1% applied) and leachate samples (< 5% of applied). The ^{14}C-residues in the soil column leachate samples were not identified as BTS 27271 or BTS 27919. Similarly, leaching did not appear to be a route of dissipation in field studies. Based on product chemistry data, BTS 27271 and BTS 27919 should act electrostatically bind to soil particles because they have a high proton dissociation constant (pKa=9.0) and hence should act as cations in most environmental conditions. Although the amitraz degradates have vapor pressures (10^{-5} to 10^{-1} mm Hg) and hence are expected to be volatile, BTS 24868 and CO_2 were identified as the only volatile degradates. The average BTS 24868 concentration in air was 2.29 $\mu g/m^3$ at soil amitraz application rates of 1.55 kg a.i./ha.

Amitraz and its primary degradates do not appear to accumulate in fish and rotated crops. The amitraz bioconcentration factors for viscera, flesh and carcess were 1821X, 588X, and 1838X, respectively. The bioconcentrated amitraz residues in fish tissues were eliminated over a 14 day depuration period. Additionally, amitraz and its primary degradates were not detected (< 0.05 $\mu g\ g^{-1}$) in rotated crops.

8.0 RECOMMENDATIONS: Please refer to Section 7.0
9.0 BACKGROUND:

10.0 DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

10.1 The fish accumulation study (MRID 41444206) was reviewed and deemed as supplemental data pending submission of additional information on TLC separation efficiencies and amitraz residue storage stability studies. EFGWB review and response comments are as follows:

A. TLC Separation Efficiencies

EFGWB Comment: EFGWB believes TLC chromatograms do not indicate a clear separation of the amitraz degradates BTS 24868 and BTS 27919. Therefore, a poor TLC separation prevents confirmatory identification of BTS 24868 and BTS 27919 by co-chromatographic techniques.

NOR-AM Response: The oily nature of the fish extracts prevented direct HPLC analysis. Therefore, TLC systems were used to identify and quantify metabolites. The combination of TLC systems did give a full separation of all metabolites in the fish extracts because there is a good correlation between the results from the different TLC separations. The separation efficiency of metabolites is not obvious because the TLC radioscans had considerable background noise from oil and polar residues.

EFGWB Response: EFGWB believes that TLC separation efficiency cannot be discounted because there is a good correlation between the various TLC separation systems. What criteria are being used to designate a "good correlation" between different TLC separation methods? (The reviewer does not see any statistic defining the TLC system separation efficiency. Therefore, it is impossible to evaluate the study without TLC separation efficiencies.

B. Storage Stability Study

EFGWB Comment: EFGWB requested that storage stability studies be provided to confirm chemical stability of amitraz and degradates in fish tissue matrices.

NOR-AM Response: The samples were not intermediately stored for chemical analysis of whole fish, fish tissues, or extracts; instead, samples were analyzed immediately after sampling or extraction. Therefore, it is inappropriate to provide storage stability data on amitraz residues.

EFGWB Comment: EFGWB requested storage stability data as supportive information. This information will be required if additional chemical analyses are needed.

10.2 The aerobic aquatic metabolism study (MRID 41444205) was reviewed and deemed as supplemental data pending additional information on extraction efficiencies and analytical detection limits. EFGWB review and response comments are as follows:

A. Analytical Detection Limits

EFGWB Comment: EFGWB requested that limit of detection (LOD) and limit of quantification (LOQ) for the analytical methods be submitted.

NOR-AM Response: The LOQ for the radio-HPLC on water samples was 0.26 ng ml^{-1} for amitraz and BTS 27919, 0.29 ng ml^{-1} for BTS 27271, and 0.21 ng ml^{-1} for BTS 24868. The LOD of the radio-HPLC was 40 dpm above background.

The LOQ of the radio-TLC in sediment samples was 1.1 ng ml^{-1} for amitraz, BTS 27919, 1.2 ng ml^{-1} for BTS 27271, and 0.87 ng ml^{-1} for BTS 24868. The LOD of the radio-TLC was 100

dpm above background.

EFGWB Response: EFGWB believes the detection limits for the radio-HPLC and radio-TLC methods are adequate (10% of applied) to assess the dissipation of amitraz and its degradates.

A. Extraction Efficiency

EFGWB Comment: EFGWB requested that the extraction efficiencies (or recovery studies) for the analytical methods be submitted.

NOR-AM Response: Water samples were not extracted; therefore, extraction (or recovery) efficiencies from water are inappropriate. Additionally, sediment samples were sequentially soxhlet extracted with dichloromethane (non-polar solvent) and acetonitrile-water (polar solvent). This extraction scheme should have removed all the extractable metabolites. In addition, exhaustive extraction of the labeled residue, in addition to a complete mass balance of labelled residue, eliminates the need for extraction efficienicies of individual components.

EFGWB Response: EFGWB believes that recovery studies (eg, extraction/separation efficiencies) are necessary to validate analytical methods. These studies are important when test matrices (eg water or sediment) contain interfering substances. Mass balance data does not convey all the analytical problems because it is simply an additive concentration of **total** pesticide residue (including extractable and nonextractable residues.) Because this study has a high material balance (>90% of applied) and hence a complete material balance, EFGWB believes that extraction efficiency are not needed. In future studies, it would be helpful to have recovery studies for sediment extraction procedures.

The aerobic aquatic metabolism study (MRID 41444205),in addition to the information on extraction efficienies and analytical detection limits, fulfills the 162-4 data requirement.

11.0 COMPLETION OF ONE-LINER:
12.0 CBI APPENDIX: N/A

DATA EVALUATION REVIEW

I. Study Type: Hydrolysis

II. Citation:-

42124616 Fordham, L.R., A.S. McGibbon, and I. D. Kelley. 1984. W65 Amitraz: The Kinetics of Hydrolysis of BTS 27271 Under Acid, Neutral, and Basic Conditions. Submitted by Nor-Am Chemical Company, Wilimington Delaware. Performed by Schering Agrochemicals Ltd., Essex, England.

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist James A. Hetrick
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

IV. Approved by:

Name: Paul J. Mastradone, Ph.D., Chief Paul J. Mastradone
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

V. Conclusions:

This study provides acceptable data on the hydrolysis of N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271). This study, in addition to the hydrolysis studies on parent amitraz (MRID 40780512) and 2,4-dimethylformanilide (BTS 27919), fulfill the hydrolysis (161-1) data requirement for parent amitraz and its primary degradates.

Based on acceptable data, parent amitraz hydrolyzes rapidly (t1/2 < 26 hours) to form BTS 27919 and BTS 27271. BTS 27271 further hydrolyzes to form BTS 27919; the mean hydrolysis half-life of BTS 27919 was 2,280 days at pH 5.00 buffer solution, 14 days at pH 7.00 buffer solution, and 5.0 hours at pH 9.00 buffer solution.

The reported data indicate BTS 27271 hydrolyzes (or degrade) in neutral and alkaline environments. However, BTS 27271 does not hydrolyze in acidic environments and hence may be persistant.

Materials and Methods:

A subsample (45.5 ml) of sterile buffer solution (pH 5, acetate; pH 7, phosphate; and pH 9, borate) was placed into sterile 100 ml flasks. Each flask was amended with BTS 27919 stock solution (analytical grade BTS 27271 (99% purity), SA 50 mg a.i. ml^{-1}), to produce a final BTS 27271 concentration of 0.50 mg a.i. ml^{-1}. (Note: The BTS 27919 solubility in D*D H2O is 1.559 mg ml^{-1}.) The buffer solution was incubated in the dark using the following temperature regimes: pH 5.00 solutions were incubated at 59°C and 80°C; pH 7.04 solutions were incubated at 22°C and 59°C; and pH

9.19 solutions were incubated at 22°C. (Note: The temperature regimes were altered so that hydrolysis rates could be adjusted for temperature.) Solution samples were taken at time zero and 4 other sampling times to bracket either the half-life of BTS 27919 or until a minimum of 30 days.

Analytical

Prior to chemical analysis, a solution subsample (1 ml) was diluted with 0.2% heptane sulphonic acid in 1.0 M pH 4 acetate buffer solution.

Soluble residues were separated using an HPLC equipped with an Spherisorb 5-phenyl column (25 cm x 4.6 mm particle size) column and an acetonitrile:water:acetic acid (70:30:6) eluant with 1% heptane sulfonic acid (0.001M); and a UV detector set at 254 nm wavelength. Separated residues were identified using co-chromatography with standard compounds. The concentration of BTS 27271 was determined using a standard HPLC calibration curve.

The hydrolytic half-life was estimated using a first-order kinetic model. The activation energy of the BTS 27271 hydrolysis reaction was calculated from the Arrhenius equation.

VII. Study Author's Results and/or Conclusions:

A. The hydrolysis rate of BTS 27271 was dependent on pH; where the hydrolysis rate was directly proportional to solution pH. At 22°C, the mean hydrolysis half-life was 2,801.3 days at pH 5.00 buffer solution, 14.00 days at pH 7.00 buffer solution, and 5 hours at pH 9.00 buffer solution.

VIII. Reviewer Comments:

A. The reviewer agrees with the study author's results and conclusions.

DATA EVALUATION REVIEW

I. Study Type: Hydrolysis

II. Citation:

Fordham, L.R., A.S. McGibbon, and I. D. Kelley. 1984. W66 Amitraz: The Kinetics of Hydrolysis of BTS 27919 Under Acid, Neutral, and Basic Conditions. Submitted by NOR-AM Chemical Company, Wilimington Delaware. Performed by Schering Agrochemicals Ltd., Essex, England.

42124617

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

IV. Approved by:

Name: Paul J. Mastradone, Ph.D., Chief
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

V. Conclusions:

This study provides acceptable data on the hydrolysis of 2,4-dimethylformanilide (BTS 27919). This study, in addition to the hydrolysis studies on parent amitraz (MRID 40780512) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271), fulfill the hydrolysis (161-1) data requirement for parent amitraz and its primary degradates.

Based on acceptable data, parent amitraz hydrolyzes rapidly (t1/2 < 26 hours) to form BTS 27919 and BTS 27271. BTS 27271 further hydrolyzes to form BTS 27919. The mean extrapolated hydrolysis half-life for BTS 27919 was 2,280 days in pH 5.00 buffer solution, 14,500 days in pH 7.00 buffer solution, and 496 days in pH 9.00 buffer solution. 2,4-dimethylaniline (BTS 24868) was identified as the only hydrolytic degradate.

The reported data indicate BTS 27919 does not hydrolyze and hence may persist in natural environments.

Materials and Methods:

A subsample (99.0 ml) of sterile buffer solution (pH 5, acetate; pH 7, phosphate; and pH 9, borate) was placed into sterile 100 ml flasks. Each flask was amended with BTS 27919 stock solution (analytical grade BTS 27919 (99.7% purity), SA 25 mg a.i. ml^{-1}), to produce a final BTS 27919 concentration of 0.250 mg a.i. ml^{-1}. (Note: The BTS 27919 solubility in D*D H_2O is 0.540 mg ml^{-1}.) The buffer solution was incubated in the dark at temperatures of 22°C,

59°C, and 80°C. Solution samples were taken at time zero and 4 other sampling times to bracket either the half-life of BTS 27919 or until a minimum of 30 days.

Analytical

Prior to chemical analysis, each solution sample (10 ml) was twice partitioned with dichloromethane. The dichloromethane extracts were combined, passed through an anhydrous sodium sulphate column, and the extract was diluted with dichloromethane/2,4-dichlorobenzamide (2,4-DCBA) ethanol solution.

Soluble residues were separated using an HPLC equipped with an Ultrasphere Si (25 cm x 4.6 mm particle size) column and an acetonitrile:1 chlorobutane (20:80 v:v) eluant. Separated residues were identified using co-chromatography with standard compounds. The concentration of BTS 27919 was determined using a standard HPLC calibration curve.

The hydrolytic half-life was estimated using a first-order kinetic model. The activation energy of the BTS 27919 hydrolysis reaction was calculated from the Arrhenius equation.

VII. Study Author's Results and/or Conclusions:

A. The hydrolysis rate of BTS 27919 was temperature dependent. At 22°C, the mean hydrolysis half-life was 2,280 days at pH 5.00 buffer solution, 14,500 days at pH 7.00 buffer solution, and 496 days at pH 9.00 buffer solution. At 59°C, the hydrolysis half-life was 159.4 days at pH 5.00 buffer solution, 41.4 days at pH 7.00 buffer solution, and 11.6 days at pH 9.00 buffer solution. At 80°C, the hydrolysis half-life was 45 days at pH 5.00 buffer solution, 2.5 days at pH 7.00 buffer solution, and 2.0 days at pH 9.00 buffer solution.

B. BTS 24868 was identified as the only hydrolytic degradate.

VIII2. Reviewer Comments:

A. The reviewer agrees with the study author's results and conclusions.

DATA EVALUATION REVIEW

I. Study Type: Aerobic Aquatic Study

II. Citation:

Allen, R. 1991. W150: The Fate of [^{14}C]-Amitraz in Sediment/Water 'Microcosms'. Performed by Schering Agrochemicals Ltd., Essex, England. Submitted by Nor-Am Chemical Company, Wilimington, Delaware.

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist James A. Hetrick
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

IV. Approved by:

Name: Paul J. Mastradone, Ph.D., Chief Paul J. Mastradone
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

V. Conclusions:

This study is acceptable and fulfills the aerobic aquatic metabolism (162-4) data requirement for parent amitraz and BTS 27271.

It is important to note the microcosms studies were conducted under stratified redox conditions; the water column was aerated yet the sediment was anoxic. Similar conditions were observed in the aerobic aquatic metabolism study (MRID 41444205). Although non-uniform redox potentials may simulate natural aquatic environments, these conditions within a microcosm could affect certain degradation processes (eg, microbial mineralization) and hence alter pesticide degradation rates. In future studies, a uniform redox potential should exist within the microcosms.

Based on partially acceptable data, parent amitraz rapidly dissipates in the aquatic environments. The 50% dissipation time (DT50) of amitraz was < 6 hours in the microcosm water columns and whole microcosms (water column and anaerobic sediment). The primary amitraz degradates, 2,4-dimethylformanilide (BTS 27919) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271), were more persistance than parent amitraz. The DT50 for BTS 27271 in the water column and whole microcosm was 3.3 to 7 days and 6.1 to 7 days, respectively. The DT50 for BTS 27919 ranged from 9 to 21 days in water and whole microcosms. Additionally, small quantities of volatile degradates (including 2,4-dimethylaniline (BTS 24868) (< 5% of applied) and CO_2 (< 14% of applied)) were formed.

The reported data indicate parent amitraz and degradates dissipate rapidly in aerobic aquatic environments. The major route of amitraz and BTS 27271 dissipation appears to dependent on hydrolysis , soil binding, and mineralization to CO_2.

Materials and Methods:

Three sediments (River Granta, Rampton Ditch, and Wokefield) were used in the sediment/water microcosm studies. Physicochemical properties of the sediments are shown in Table 1.

Each sediment (sediment mass was not reported) was placed into each of eight 477.12 ml glass clyinders (30 cm X 4.5 cm i.d.) and covered with 7 mls of water (Figure 1). (Note: The water chemistry was not described in the study.)

The microcosms containing River Granta and Rampton Ditch sediments were amended with 251 μg ^{14}C-amitraz (formulated as MITAC 20 EC, radiopurity of 96.9%, and a SA of 138 $\mu Ci\ mg^{-1}$), to produce an equivalent application rate of 1.14 lbs a.i./A. The water column in each microcosm was aerated with CO_2-free air, and the effluent air was passed through solution gas traps. The microcosms were incubated in the dark at a temperature of 25°C or 8°C.

The microcosms containing Wokefield sediment were amended with 257 μg ^{14}C-amitraz (formulated as MITAC 20 EC, radiopurity of 97%, and a SA of 231 $\mu Ci\ mg^{-1}$), to produce an equivalent application rate of 1.14 lbs a.i./A. Air was passed over the water colum, and then the effluent air was passed through solution gas traps. The microcosms were incubated in the dark at a temperature of 25°C.

The microcosms were sampled at specific time intervals over a 91 posttreatment period (Table 2). At each sampling interval, water samples were decanted and filtered through Whatman #1 filter paper; and the suspended sediments were collected on filter paper.

Four microcosms containing Rampton Ditch and Wokefield sediments were prepared for sediment redox and water pH monitoring. Sediment redox potentials were measured using a single junction Pt electrode.

Analytical

Each sediment was sequentially soxhlet extracted with dichloromethane and acetonitrile/water (80:20 v:v). Subsamples (50 to 100 ml) of the dichloromethane extracts were further concentrated for chemical analysis. Subsamples (50 to 100 ml) of the acetonitrile/water (80:20 v:v) extracts were concentrated and diluted with water. The aqueous portion of the extract was passed through a C-8 Elut column and collected for chemical analysis.

Soluble residues in sediment extracts and water samples were separated using a HPLC equipped with Dynamac C18 column (10 mm X 250 mm particle size); and an UV detector. The HPLC separations

were conducted in solvent systems with different ratios of acetonitrile and phosphate buffer. Soluble residues also were separated using 1-D TLC with toluene/triethylamine (9:1 v:v) and cyclohexane/ethyl acetate/triethylamine (5:3:2 v:v:v) solvent systems. The separated residues were identified by co-chromatography with known standard compounds. The [^{14}C]-residue content in sediment extracts and water samples was determined by LSC. The total [^{14}C]-residue content in sediments was determined by combustion-LSC.

VII. Study Author's Results and/or Conclusions:

A. The mass balance of [^{14}C]-residues accounted for > 86.8% of the applied amitraz (Tables 4 to 8). The [^{14}C]-residues were distributed in the water column (8 to 47% of applied), sediment extracts (3 to 13% of applied), unextractable sediment bound (6 to 62% of applied), ethanediol gas trap (< 5.3% of applied), and ethanolamine gas trap (< 14% of applied).

B. Parent amitraz dissipation was dependent on hydrolysis and sediment binding. The water column amitraz concentration ranged from 65 to 75% (of applied) immediately posttreatment, 4 to 14% (of applied) at 1 day posttreatment, and not detectable at 7 to 14 days posttreatment. The sediment amitraz concentration was < 5.4% (of applied) immediately posttreatment, 5.6 to 12% (of applied) at 7 to 10 days posttreatment, and < 0.5% (of applied) at 91 days posttreatment. The DT50 for parent amitraz ranged form 1.7 to 3.4 hours and 3.4 to 6 hours in the water column and whole microcosm, respectively.

C. Amitraz degradation led to the formation of BTS 27919 and BTS 27271.

BTS 27919: The BTS 27919 concentration in water column ranged from < 5% (of applied) immediately posttreatment, 35 to 56.3% (of applied) at 3 to 14 days posttreatment, and <0.4% at 91 days posttreatment. The BTS 27919 concentration in sediment ranged from 2.8 to 11.4% (of applied) immediately posttreatment, 4.1 to 6.0% (of applied) at 7 to 14 days posttreatment, and < 1.7% (of applied) at 91 days posttreatment. The DT50 for BTS 27919 was 9 to 20 days and 10 to 21 days in water and whole microcosm, respectively.

BTS 27271: In neutral and alkaline microcosms, the BTS 27271 water column concentration was <3.2% (of applied) immediately posttreatment, <2.2% (of applied) at 7 to 15 days posttreatment, and not detectable at 91 days posttreatment. The sediment amitraz concentration was < 3.1% (of applied) immediately posttreatment, 5% (of applied) at 7 to 10 days posttreatment, and <1.7% (of applied) at 91 days posttreatment. The DT50 for BTS 27271 was 3.3 to 5.8 days and 7.7 to 6.1 days in water column and whole microcosm, respectively.

In acidic microcosms,the BTS 27271 concentration in water column was 0.4% (of applied) immediately posttreatment, 27% (of applied)

at 3 days posttreatment, 6.0% at 7 to 15 days posttreatment. The BTS 27271 concentration in sediment was <0.4% (of applied) immediately post- treatment, <1.3% (of applied) at 3 days posttreatment, and <0.3% (of applied) at 15 days posttreatment. The DT50 for BTS 27271 was 7 days in water and whole microcosm.

D. BTS 24868 was found in the ethandiol gas traps. The BTS 24868 concentration in the ethandiol gas trap was < 5% (of applied) over the 91 day experiment.

E. Amitraz and its degradates also were mineralized to CO_2 (14% of the applied).

G. Unidentified degradates were also found in water column and sediment samples. The concentration of unidentified degradates was < 10.6% (of applied) in water column and sediment samples.

H. Sediment redox potentials ranged from -235 to -450 mV and -100 to -340 mV for Rampton and Wakefield sediments, respectively (Table 3). (Reviewer Note: It is important to note the microcosms had a stratified redox potential; the water columns were aerated yet the sediments were anoxic.)

VIII. Reviewer Comments:

A. The extraction efficiency of amitraz and its degradates from sediment was not presented. Because the mass balance of 14C-residues was > 86%, EFGWB believes that sediment extraction efficiency is not required for this study. In future studies, sediment extraction efficiencies would be helpful in assessing analytical methods.

B. The microcosms had stratified redox potentials; the water columns were aerated yet the sediments were anaerobic. Similar conditions were observed in a previously reviewed aerobic aquatic metabolism study (MRID 41444205). It is important to note that CO_2-free air was bubbled into the microcosm water column, or air was passed over the surface of the water column to aerate the microcosm. These aeration methods may create redox stratifcation because of poor oxygen diffusion or indirect pH effects on redox potential (that is as pH increases the pe will decrease). Redox stratification may confound the interpretation of results because vastly different redox dependent degradation processes (ie, microbial mineralization, etc.) may exist within a given microcosm. EFGWB appreciates the effort to report sediment redox conditions regardless of redox stratification problems. Redox measurements are rarely, if ever, reported in aquatic metabolism studies.

DATA EVALUATION REVIEW

I. Study Type: Field Dissipation Study

II. Citation:

Castro, L.E. 1990. Dissipation of Amitraz in the Following Applications of OVASYN to Cotton, U.S.A. 1988. Performed and submitted by NOR-AM Chemical Co. Pikesville, N.C. MRID 41637301.

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist James A. Hetrick
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

IV. Approved by:

Name: Paul J. Mastradone, Ph.D., Chief Paul J. Mastradone
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

V. Conclusions:

The study provides acceptable data and fulfills the terrestrial field dissipation (164-1) data requirement.

Based on acceptable field dissipation data, parent amitraz hydrolyzes rapidly (< 1 day) to form 2,4-dimethylformanilide (BTS 27919) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271). These degradates were more persistant than parent amitraz under typical use conditions. In a California study, the dissipation half-life was 30 days (R^2=0.96) and 17 days (R^2=0.88) for BTS 27271 and BTS 27919, respectively. In a Florida study, the dissipation half-life was 70 days (R^2=0.90) and 65 days (R^2=0.26) for BTS 27271 and BTS 27919, respectively. Although some amitraz residues were detected at low concentrations (<0.03 $\mu g\ g^{-1}$) in subsurface soil samples (below 7.62 cm), these residue detections appear to be false positives because specific concentrations of amitraz and its degradates were greater than the total amitraz residue concentration.

The reported data indicate BTS 27271 and BTS 27919 are more persistant than parent amitraz under typical use conditions.

VI. Materials and Methods:

Field dissipation studies were conducted on sites in Cantonment, FL and Fresno, CA. Site descriptions and study designs were as follows:

Fresno, CA - The site was described as being level (0 % slope) with a Hanford fine sandy, silty substratum soil (Typic Xerorthent) (Table 1). The depth to the permanent water table was 50 feet.

The site was used for pesticide trials on wheat and barley in 1986. Cantonment, FL - The site was described as nearly-level (0 to 2% slope) with a Tifton soil (Plinthic Paleudults) (Table 1). The depth to the permanent water table was between 55 to 60 feet. The site was planted in oat cover crops in 1985, and then was fallow during 1986 and 1987.

Both the amitraz and control treatments consisted of a square plot (Fresno, CA-1625 ft^2 and Cantonment, FL - 4560 ft^2) with 64 sampling plots. The study plots were planted with cotton Gossypium hirsutum (var. Acala GC-510 in Fresno CA; and DES-119 in Cantonment, FL) on 2/5/88 and 6/23/88 in Fresno, CA and Cantonment, FL respectively. Prior to or during the study, the plots were irrigated with water (furrow or sprinkler) to supplement rainfall, and fertilized with N. Additionally, the sites were treated with appropriate herbicides and fungicides: the Fresno,CA site was amended with trifluralin, prometryn, sethoxydim, Agridex, EPTC, ancymidol, DEF 6; and the Cantonment, FL site was amended with azinphos-methyl, malathion, merphos 6E, ethephon 6E.

Amitraz was applied 1 to 1.5 months post planting. The amitraz, formulated as OVASYN (emulsifiable concentrate with 19.5 to 20.5% a.i.), was boom sprayed twice (over a 7 day interval) at a rate 0.5 lbs a.i./A. Therefore, the amitraz treated plots received a total of 1.0 lbs a.i./A.

The field plots were sampled at 7 days pretreatment, immediately after each amitraz treatment (1A and 2A),+1,+3,+7,+14-16,+28,+60-+62,+91-92,+119-122,+178-184,+365,+428-445,+490-496, and+541-549 days of 2A. At each sampling interval, three randomized areas within the field plots were selected for sampling. Each selected plot area was sampled using a 1 inch soil probe with a 6 inch zero comtamination sleeve; 5 - 1 inch soil cores (0-6 and 7-36 inches) were taken from each sampling area. After each sampling interval, the samples were frozen within 3 hours post-sampling, transferred to a laboratory freezer, and then stored at -20°C. Prior to or after freezing, the 5 soil cores (representing a sampling area within a sampling period) were subdivided and composited according to soil depth (0-3, 3-6, 6-12, 12-24, and 24-36 inches). Therefore, each soil sample represents a composite of 5 soil samples. (Reviewer Note: Due to a misunderstanding in protocol, soil samples were composited between the sample blocks for the 1A, 2A,+1,+3,+7, 16 days 2A sampling dates at the Cantonment, FL site. These sampling points are representive of a single composite sample.)

Analytical

It was reported that analytical interfences were observed during chemical analysis of parent amitraz, BTS 27271, and BTS 27919. To alleviate this analytical problem, each compound was separately extracted from soil and the operating condition for the gas chromatograph was taylored for each chemical analysis. The following is a description of methods used to extract and detect

the soil amitraz residues.

Amitraz: Parent amitraz was extracted from soil using acetone. This extract was further dried by rotary evaporation, redissolve in ethyl acetate, and diluted to volume with toluene. Parent amitraz in the soil extract was separated using a gas chromatograph equipped with either a HP-1, 10 meter x 0.54 mm column (2.65 μm film) at oven temperatures of 225, 195, 215°C or DB-1, 15 meter x 0.54 mm (3.0 μm film) at an oven temperature of 215°C with a helium carrier; and a nitrogen-phosphorus detector. Amitraz was identified by co-chromatograhy with a known standard. The extraction efficiency was 93% ± 12 % (CV 12.9%) (Table 8). The level of quantification (LOQ) was 0.02 μg g^{-1}.

BTS 27271: BTS 27271 was extracted from soil using toluene and alkaline water. This extract was acidified, basified, and reextracted with toluene. BTS 27271 in the soil extract was separated using a gas chromatograph equipped with either a HP-1, 10 meter x 0.54 mm column (2.65 μm film) at oven temperatures of 105, 100, 125°C or DB-1, 15 meter x 0.54 mm column (3.0 μm film) at an oven temperature of 130 and 140°C with a helium carrier; and a nitrogen-phosphorus detector. BTS 27271 was identified by co-chromatograhy with a known standard. The extraction efficiency was 88% ± 28% (CV 31.8%) (Table 8). The level of quantification (LOQ) was 0.02 μg g^{-1}.

BTS 27919: BTS 27919 was soxhlet extracted from soil using distilled toluene. This extract was concentrated using rotary evaporator, and then the concentrate was purified by a silica gel cartridge. BTS 27919 in the soil extract was separated using a gas chromatograph equipped with either a HP-1, 10 meter x 0.54 mm column (2.65 μm film) at oven temperatures of 90, 95, 100, 115, 125°C or DB-1, 15 meter x 0.54 mm column (3.0 μm film) at an oven temperature of 100 and 130°C with a helium carrier; and a nitrogen-phosphorus detector. BTS 27919 was identified by co-chromatograhy with a known standard. This extraction efficiency was 92% ± 22% (CV 23.9%), (Table 8). The level of quantification (LOQ) was 0.02 μg g^{-1}.

Total Amitraz Residues: The total soil amitraz residue content (including parent amitraz, BTS 27271, and BTS 27919) was determined using base hydrolysis. Amitraz and its degradates were hydrolyzed to 2,4-dimethylaniline (DMA). This degradate was used as an indicator of the total amitraz residue content. The DMA in the soil base extract was further extracted in the hexane, derivatized with heptafluorobutyric anhydride, and purified through silica gel. Total amitraz residues in the soil extract was separated using a gas chromatograph equipped with DB-17, 30 meter x 0.25 mm column (0.25 μm film) at an oven temperature of 145°C with a helium carrier; and a Ni-63 electron-capture detector. Amitraz residues were identified by co-chromatograhy with a known DMA standard. The extraction efficiency was 93% ± 26% (CV 27.9%) (Table 8).

Storage Stability: A separate storage stability study was conducted

concurrently with the field dissipation study. (Reviewer notes: The description of the storage stability study was incomplete.)

The stability studies indicate that parent amitraz is unstable during freezer storage; however, the hydrolytic degradates, BTS 27271 and BTS 27919, were stable during 317 days of freezer storage. After the 317 day stability study, BTS 27271 and BTS 27919 accounted for 88 and 79% (of applied), respectively. (Reviewer Note: The percent stability was not corrected for extraction efficiency.)

VII. Study Author's Results and/or Conclusions:

A. In the surface soil samples (0-3 inch) the concentration of amitraz residues was consistently below the LOQ of 0.02 $\mu g\ g^{-1}$ (Table 13). These data indicate that parent amitraz hydrolyzes rapidly to form BTS 27271 and BTS 27919.

B. The hydrolytic degradates, BTS 27271 and BTS 27919, were more persistant than parent amitraz under typical use conditions.

In the California study the calculated dissipation half-lives for BTS 27271 and BTS 27919 were 30 days (R^2= 0.96) and 17 days (R^2=0.88), respectively (Table 17; Figures 1 and 2). In surface soil, the concentration of BTS 27271 was 0.18 $\mu g\ g^{-1}$ immediately after the second amitraz application, 0.10 $\mu g\ g^{-1}$ at 14 days posttreatment, and 0.01 $\mu g\ g^{-1}$ at 365 days posttreatment. The concentration of BTS 27919 was 0.12 $\mu g\ g^{-1}$ at immediately after the second amitraz application, 0.04 $\mu g\ g^{-1}$ at 14 days posttreatment, and < 0.01 $\mu g\ g^{-1}$ at 365 days posttreatment.

In the Florida study, the calculated dissipation half-lives for BTS 27271 and BTS 27919 was 70 days (R^2=.90) and 65 days (R^2=0.26), respectively (Table 17; Figures 3 and 4). In surface soil, the concentration of BTS 27271 was 0.27 $\mu g\ g^{-1}$ immediately after the second amitraz application, 0.17 $\mu g\ gm^{-1}$ at 16 days posttreatment, and 0.04 $\mu g\ g^{-1}$ at 365 days posttreatment. The concentration of BTS 27919 in soil was 0.15 $\mu g\ g^{-1}$ immediately after the second amitraz application, 0.02 $\mu g\ g^{-1}$ at 16 days posttreatment, and < 0.01 $\mu g\ g^{-1}$ at 365 days posttreatment.

C. Amitraz residues were predominately found in the 0-3 inch soil layer. Although amitraz residues were detected below the surface layer in very low concentrations (<0.03 $\mu g\ g^{-1}$), the residue detections appear to be false positives because specific soil residue concentrations of amitraz and its degradates were consistently greater than total amitraz residue concentrations (<0.01 $\mu g\ g^{-1}$)(Table 16).

VIII. Reviewer Comments:

A. The reviewer agrees with the study author's results and/or conclusions.

DATA EVALUATION REVIEW

I. Study Type: Field Crop Rotation Study

II. Citation:

Castro, L.E. 1990. Residues of Amitraz in Rotational Crops Following Treatment of OVASYN of Cotton, U.S.A. 1988/1989. Submitted by NOR-AM Chemical Co. Pikesville, N.C. Performed and and submitted by NOR-AM Chemical Co. Pikesville, N.C. MRID 41637302.

Meyer, L.A. 1990. Residues of Amitraz in Rotational Crops Following Treatment of OVASYN of Cotton, U.S.A. 1988/1989. Submitted by NOR-AM Chemical Co. Pikesville, N.C. Performed by Analytical Bio-Chemistry Laboratories Columbia, MO. MRID 41637302.

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist James A. Hetrick
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

IV. Approved by:

Name: Paul J. Mastradone, Ph.D., Chief Paul J. Mastradone
Title: Environmental Chemistry Review Section #1
Organization: EFGWB/EFED/OPP

V. Conclusions:

This study is acceptable and partially fulfills the 165-2 data requirement. This study together with the field crop rotation study (MRID 40998509) fulfills the 165-2 data requirement.

It is important to note the study has the following Subdivision N guideline deficiency:

- The analytical method for detecting amitraz residues was not specific; total residue analysis was used as the analytical method. Because total amitraz residues (including parent amitraz, 2,4-dimethylformanilide (BTS 27919) and N-2,4-dimethylphenyl-N-methylformamidine (BTS 27271)) were not detected ($<0.05\ \mu g\ g^{-1}$) in rotated crop plants, EFGWB believes the analytical method is acceptable for this study.

Based on acceptable data, accumulation of amitraz residues was observed in corn stover and forage. The total amitraz residue concentration (including parent amitraz, BTS 27271, and BTS 27919) in corn stover and forage ranged from 0.11 to 0.16 $\mu g\ g^{-1}$; otherwise, the total amitraz residue concentration in rotated crops was less than 0.05 $\mu g\ g^{-1}$. (Note: No residue tolerance for amitraz has been established for cotton.) Similar accumulation data were

reported in a companion field rotational crop study(MRID 40998509).

The reported data suggest that amitraz residues (including parent amitraz, BTS 27919, and BTS 27271) do not accumulate in rotated crops plants.

VI. Materials and Methods:

Field crop rotation studies for typical cotton rotation schemes were conducted at Elko, SC; Donaldsonville, GA; Prattville, AL; and Cantonment, FL. The study design and site information for each field rotational crop study was as follows:

Elko, SC: The site had a soil (soil classification unknown) with a loamy sand texture, slightly-acid pH (pH 5.5), and an organic matter content of 1.6%. Cotton (var. Delta Pine 90) was planted on May 5, 1990 according to regional agricultural practices. Four months after planting the site was amended with Amitraz, formulated as OVASYN (20.4% w:w a.i.), in four applications of 0.25 lbs a.i/A. Therefore, the cumulative amitraz application rate was 1 lb a.i./A. The cotton crop was harvested 5 months post-planting.

The site was then tilled and planted to the following crops: field corn (var. Pioneer 3165) was planted in April 1989; and soybeans (var. Centennial), milo (NK 2660), and peanuts (var. Florunner) were planted in May 1989. The crops were sampled at specific time intervals during the growing season (Table 5). Soil samples also were taken immediately post amitraz treatment (PTR), + 202,+238, +355,+365,+379, and +424 days PTR (Table 6)[1]. Crop and soil samples were frozen (-20°C) prior to sample preparation and chemical analysis.

Donaldsonville, GA: The site had a soil (soil classification unknown) with a sandy loam texture, slightly-acid pH (pH 5.8), and an organic matter content of 1.2%. Cotton (var. McNair 220) was planted on May 5, 1988 according to regional agricultural practices. Four months after planting the site was amended with Amitraz, formulated as OVASYN (20.4% w:w a.i.), in four applications of 0.25 lbs a.i/A. Therefore, the cumulative amitraz application rate was 1 lb a.i./A. The cotton was harvested 5 months post planting.

The site was then tilled and planted to the following crops: field winter wheat was planted November 1988; corn (var. GK750), milo (NK 8333), soybeans (var. Braxton) were planted March 1989; and soybeans (var. Braxton) and peanuts (var. Florunner) was planted May 1989. The crops were sampled at specific time intervals during the growing season (Table 5). Soil samples also were taken immediately post amitraz treatment (PTR), + 60,+180,+196,+236,

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[1] Each field plot was sampled by taking 15 12 inch soil cores. These soil cores was divided (0 to 6 and 7 to 12 inches) and composited according to soil depth.

+243,+314,+319,+383, and +405 days PTR (Table 6). Crop and soil samples were frozen (-20°C) prior to sample preparation and chemical analysis.

Prattville, AL: The site had a soil (soil classification unknown) with a sandy loam texture, a nearly neutral pH (pH-6.7), and an organic matter content of 0.8%. Cotton (var. DPL-90) was planted on April 25, 1988 according to regional agricultural practices. The site was amended with Amitraz, formulated as OVASYN (20.4% w:w a.i.), in two intervals at a rate of 0.50 lbs a.i/A. Therefore, the cumulative amitraz application rate was 1 lb a.i./A. The cotton was harvested 5 months post planting..

The site was then tilled and planted to the following crops: winter wheat was planted on December 1988; corn (var. Pioneer 3320) was planted on May 1989; and milo (var. DK-28), soybeans (var. DPL-105), and peanuts (var. Spanish) were planted on May 1989. The crops were sampled during the growing season (Table 5). Soil samples also were taken immediately post amitraz treatment (PTR), +105,+252,+276,+299,+326,+355, and + 417 days PTR (Table 6). Crop and soil samples were frozen (-20°C) prior to sample preparation and chemical analysis.

Cantonment, FL: The site had a soil (soil classification unknown) with a sandy loam texture, a nearly neutral pH (pH-6.1), and an organic matter content of 2%. Cotton (var. DES 119) was planted on May 19, 1988 into two independent field crop rotation studies. The two studies are described below:

> Study 1 (NOR-AM # 188USO01FO11): The site was amended with Amitraz, formulated as OVASYN (20.4% w:w a.i.), in eight intervals at a rate of 0.125 lbs a.i/A. Therefore, the cumulative application rate was 1.0 lbs a.i/A. The cotton was harvested on September 21, 1988. The site was tilled and planted to field winter wheat (var. Caldwell) on December 2, 1989; and planted corn (var. Pioneer 3320) on May 28, 1989 and milo (var. DK -28), soybeans (var. DPL-105) and peanuts (var. Spanish) on May 5, 1989 (PH).
>
> Study 2 (NOR-AM # 188USO01FO11): The site was amended with amitraz, formulated as OVASYN (20.4% a.i.) with a tank mixture cypermethrin, in eight intervals at rate of 0.25 lbs a.i/A. Therefore, the cumulative amitraz application rate was 1 lb a.i./A. The cotton was harvested on September 21, 1988. The site was then tilled and planted to winter wheat on December 6, 1988.

The crops in both studies (NOR-AM# 188USO01FO11) were sampled during the growing season (Table 5). Soil samples were taken during the immediately post amitraz treatment (PTR), + 60 (Study 2),+105,+ 241 (Study 2),+ 252, +276,+299,+326,+355, and +417 days PTR (Table 6). Crop and soil samples were frozen (-20°C) prior to sample preparation and chemical analysis.

Analysis

The amitraz residue content (including parent amitraz, BTS 27271, and BTS 27919) in crop plants was determined using an acid hydrolysis method. The crop residues were refluxed in 2M HCl, basified with NaOH, and then liquid-liquid extracted with hexane. In contrast, the total soil amitraz residue content was determined using base hydrolysis and then liquid-liquid extracted with hexane.

The hexane extract was derivatized with heptafluorobutyric anhydride and purified through silica gel. Total amitraz residues in the soil extract was separated using a gas liquid chromatograph equipped with DB-5, 30 meter x 0.25 mm column at an oven temperature of 350°C with a helium carrier; and an electron-capture detector. Amitraz residues were identified by co-chromatograhy with a known standard. The extraction efficiency was 99% ± 12% and 96% ± 12% in crop and soil matrices, respectively. (Note: It is important to note that low recovery efficiencies (≈50% of applied) were observed during extraction of BTS 27271 fortified crop samples. These low recoveries were apparently caused by precipitation of BTS 27271. The problem was resolved by dissolving BTS 27271 in methanol.)

Storage Stability: A separate storage stability study was conducted concurrently with the field dissipation study. (Reviewer Notes: The description of the storage stability study was incomplete.) The stability studies indicate that the amitraz residues were stable over a 301 days of freezer storage period; total amitraz residues in fortified soil accounted for 84% of applied amitraz residues.

VII. Study Author's Results and/or Conclusions:

A. There total amitraz crop residue concentration ranged from 0.11 to 0.16 $\mu g\ g^{-1}$ in corn stover and corn forage; otherwise, the amitraz residue concentration in rotated crops (including peanuts, soybeans, milo, wheat) was below the analytical detection limit of 0.05 $\mu g\ g^{-1}$ (Table 10). (Note: The registrant believes that amitraz crop accumulation in corn stover and forage was attributed to high background concentrations of extractable amitraz-type residues. The total amitraz residue background concentration ranged from 0.022 to 0.096 $\mu g\ g^{-1}$ (Mean=0.068 SD=.040)(Table 9).

B. The total soil amitraz residue concentration at all sites ranged from 0.07 to 0.28 $\mu g\ g^{-1}$ immediately post pesticide application, and 0.6 $\mu g\ g^{-1}$ at the last harvest of rotational crops (Table 11). Additionally, there was no evidence that amitraz residues leached into the soil.

VIII. Reviewer Comments:

A. The analytical method for detecting amitraz residues was not specific; total residue analysis was used as the analytical

method. EFGWB believes the analytical method is acceptable for this study because total amitraz residues (including parent amitraz, BTS 27271, and BTS 27919) were not detected (<0.05 $\mu g\ g^{-1}$) in rotated crop plants.

B. EFGWB believes the registrant should have completed confined rotational crop studies before starting field rotational crop studies.

DATA EVALUATION REVIEW

I. Study Type: Environmental Fate Assessment for Amitraz and Its Degradates

II. Citation:

MRID 42124620

Kelly, I. D., R. R. Stevens, J. J. Vuklich, and P. F. Paul. 1991. Amitraz: Summary and Discussion of the Environmental Fate and Ecological Impact Following Application of Ovasyn to Cotton. Performed and and submitted by Nor-Am Chemical Co. Pikesville, N.C.

III. Reviewer:

Name: James A. Hetrick, Ph.D., Chemist James A. Hetrick
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Name: Paul J. Mastradone, Ph.D., Chief Paul J. Mastradone
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Organization: EFGWB/EFED/OPP

V. Conclusions:

General: Nor-Am submitted additional environmental fate information to support a conditional registration for amitraz use on cotton. This additional information was requested by EFGWB and EEB to further assess the environmental fate of the amitraz degradates (including BTS 27919, BTS 27271, and BTS 24868) in terrestrial and aquatic ecosystems. This DER presents a review of the registrant's environmental fate assessment for amitraz and its degradates.

EFGWB believes the environmental fate assessment on the amitraz degradates, BTS 27271, BTS 27919, BTS 24868, provides the following information:

Amitraz rapidly hydrolyzes ($t_{1/2}$ < 1 day) to form BTS 27271, BTS 27919, and possibily BTS 24868. These degradates are more persistant than parent amitraz in terrestrial and aquatic environments. In aerobic soil metabolism studies, the calculated first order half-life for BTS 27271 and BTS 27919 was 75 days and 89 days, respectively. Similar half-lives were reported in California and Florida field dissipation studies. (Reviewer Note: It is important to note a first-order decay model did not adequately describe data in the aerobic soil metabolism study; the interpolated half-lives for BTS 27919 and BTS 27271 range from 6 to 10 days.) In aquatic metabolism studies, the calculated 50% dissipation time (DT50) for BTS 27271 and BTS 27919 ranged from 6 to 7 days and 10 to 20 days, respectively, in water columns and whole microcosms.

Amitraz degradate dissipation appears to be dependent on abiotic hydrolysis, microbial mediated processes (mineralization to CO_2 with residue incorporation into nonlabile organic matter), and sediment binding. Parent amitraz hydrolyzes rapidly to form BTS 27919 and BTS 27271. BTS 27271 further hydrolyzes in neutral and alkaline environments ($t_{1/2}$ = 14 days and 5.1 hours, respectively) to form BTS 27919. In acidic environments, however, BTS 27271 was stable to abiotic hydrolytic degradation. Similarly, BTS 27919 was stable to abiotic hydrolysis. The route of BTS 27271 and BTS 27919 dissipation also appears to be dependent on microbial mediated processes (mineralization to CO_2 with residue incorporation into nonlabile organic matter) as well as sediment binding.

The amitraz degradates appear to be relatively immobile in column leaching studies and field dissipation. In column leaching studies, aged amitraz residues were detected in soil below the application depth (< 1% applied) and leachate samples (< 5% of applied). The [^{14}C]-residues in the leachate samples were not identified as BTS 27271 or BTS 27919. In field studies, leaching did not appear to be route of dissipation. Because BTS 27271 and BTS 27919 are amines with a dissociation constant (pKa= 9) and hence should act as cations in most environmental conditions, they should bind to soil particles by electrostatic attraction.

VII. Study Author's Results and/or Conclusions:

Hydrolysis

Nor-Am Statement: BTS 27271 and BTS 27919 degradation appear to be dependent on abiotic hydrolysis and other unspecified processes. The abiotic hydrolysis half-lives for BTS 27271 were 2800 days in pH 5 buffer solution, 14 days in pH 7 buffer solution, and 5.1 hours in pH 9 buffer solution. The abiotic hydrolysis half-lives for BTS 27919 were 2,280 days in pH 5 buffer solution, 14,500 days in pH 7 buffer solution, and 496 days in pH 9 buffer solution.

Based on reported hydrolysis rates and the patterns of degradate dissipation, parent amitraz hydrolyzes rapidly to form BTS 27271 and BTS 27919. The BTS 27271 further hydrolyzes to form BTS 27919. Nor-Am believes the hydrolysis rates for BTS 27271 under acid conditions and BTS 27919 are too slow to account for the formation of BTS 24868; therefore, parent amitraz must degrade directly (mechanism unspecified) into BTS 24868.

EFGWB Response: Based on the hydrolysis rates of BTS 27271 and BTS 27919, EFGWB believes BTS 27271 should be a transient degradate in neutral and alkaline environments, and possibly a persistant degradate in acidic environments. Conversely, BTS 27919 should be persistant (based solely on abiotic hydrolysis) in most environmental conditions.

Aerobic Soil Metabolism

Nor-Am Statement: In aerobic mineral soil, the first order half-life for BTS 27271 and BTS 27919 was 75 days (R^2=0.535 to 0.802) and 89 days (R^2= 0.681 to 0.591), respectively. The aerobic soil metabolism half-life for BTS 24868 was not reported.

Nor-Am believes the degradation of BTS 27271 and BTS 27919 may be a biphasic process; biphasic degradation is characterized by an initial rapid degradation followed by a slower degradation rate. Therefore, the actual degradation rate for the amitraz degradates may be faster than predicted by a monophasic first order decay model.

The concentration of BTS 27271 in soil was 13% (of applied amitraz) immediately post amitraz application, 7% (of applied amitraz) at 1 day post amitraz application, and < 1% (of applied amitraz) at 30 days post amitraz application. The concentration of BTS 27919 in soil was 35% (of applied amitraz) at 1 day post amitraz application, and was 5% (of applied amitraz) at 60 days post amitraz application. The concentration of BTS 24868 in soil was 13% (of applied amitraz) on the day of amitraz application, 6% (of applied amitraz) at 1 day post amitraz application, and <1% (of applied amitraz) at 30 days post amitraz treatment.

EFGWB Response: EFGWB agrees the degradation of BTS 27271 and BTS 27919 was not described by first-order decay kinetics. In fact, the interpolated half-life for BTS 27271 and BTS 27919 in aerobic soil metabolism studies was less than 10 days (Appendix II and III). Therefore, the interpolated half-lives for BTS 27271 and BTS 27919 may represent the actual degradation time. (Reviewer Note: It is interesting that the dissipation/degradation rate for amitraz degradates in field studies and aerobic soil metabolism studies are similar. These data suggest the amitraz degradates are moderately persistant ($t_{1/2}$ 40 to 80 days). Based on field and laboratory studies, the amitraz degradates are more persistant than parent amitraz in terrestrial environments. And the actual persistance of the degradates may be less than predicted by first-order decay kinetics.

Aquatic Metabolism Studies

Nor-Am Statement: In aquatic microcosm studies, the 50% dissipation times (DT50) for BTS 27271 and BTS 27919 ranged from 6.0 to 7.7 days and 10 to 21 days, respectively. BTS 27271 was a minor metabolite (< 10% applied) in neutral or alkaline microcosms, and a major degradate (27% of applied at 3 days posttreatment) in acidic microcosms. BTS 27919 was a major degradate (56% applied at 3 days posttreatment) in acidic, neutral, and slightly-alkaline microcosms. Additionally, BTS 24868 was a minor volatile degradate (< 10% of applied) in the microcosm studies.

EFGWB Response: EFGWB believes it is important to note the microcosms studies were conducted under stratified redox

conditions; the water column was aerated yet the sediment was anoxic. Similar conditions were observed in the aerobic aquatic metabolism study (MRID 41444205). Although non-uniform redox potentials may simulate natural aquatic environments, these conditions within a microcosm could affect certain degradation processes (eg, microbial mineralization) and hence alter pesticide degradation rates. It is expected the metabolism rate of amitraz and its degradates would be faster in an aerobic aquatic condition because of enhanced mineralization. Hence, the dissipation times for amitraz and it degradates as presented in the microcosm studies probably represents a worst-case situation.

Terrestrial Field Dissipation

Nor-Am Statement: The field dissipation pattern of amitraz and its degradates was similar to that reported in the aerobic soil metabolism study. The mean dissipation half-lives for BTS 27271 and BTS 27919 were 50 days and 40 days, respectively. The maximum concentration of BTS 27919 and BTS 27271 was 0.3 $\mu g\ g^{-1}$ (30% of applied) immediately post amitraz application.

EFGWB Response: The calculated dissipation half-lives of BTS 27271 and BTS 27919 were similar in field (40 to 50 days) and laboratory (75 to 80 days) studies. EFGWB is surprised the degradates appear to be more persistant in field studies when compared to laboratory studies. The field and laboratory studies indicate the amitraz degradates are more persistant than parent amitraz in terrestrial environments. And the actual persistance of the degradates may be less than predicted by first-order decay kinetics.

Mobility and Bioaccumulation in Fish

General: Nor-Am believes the mobility and bioaccumulation of BTS 27271 and BTS 27919 can be addressed using product chemistry data and environmental fate data. Product chemistry data for BTS 27271 and BTS 27919 are shown below:

	Amitraz	BTS 27271[1]	BTS 27919	Reports
Water Solubility	0.09% mg/l	99.2 g/l	680 mg/l	C142 (2nd ed), C278, C262
octanol/water distribution coefficient (K_{ow})	3×10^5	0.1472	43.1	C141 (2nd ed), C279, C265
log (K_{ow})	5.5	-.0.83	1.63	C141 (2nd ed), C279, C265
pKa	6.2	9.3	14.1	C182, C280, C261

Mobility

Nor-Am Statement: BTS 27919 and BTS 27271 have low Kow's (1.63) and hence should not readily bind to soil. However, these degradates are secondary amines and hence have high proton dissociation constants pK_a (9.3 to 14.1). A high pK_a indicates the compound will be protonated, or act as a cation, under most environmental conditions. Therefore, Nor-Am believes the amitraz degradates (BTS 27271 and BTS 27919) should bind to soil.

Aged soil column leaching studies indicate BTS 27271 and BTS 27919 have limited mobility; less than 1% (of applied) aged amitraz residue leached below the 15 cm application site; and < 5% (of applied) of the aged residues were detected in leachate samples. Nor-Am believes the polar residues in leachate samples may be [^{14}C]-carbonate ions. Therefore, the column leaching data suggest amitraz degradates are not mobile in soil.

EFGWB Response: Based on product chemistry data, EFGWB agrees the degradates may electrostatically bind to soil through a cation exchange process. It is unfortunate that batch equilibrium data for the degradates are not available to confirm this retention hypothesis.

EFGWB agrees that [^{14}C]-carbonate/bicarbonate ions may be leaching as observed in the soil column leaching studies. The soils used in the column leaching studies had free calcuim carbonate and hence could support carbonate equilibria. The mobile residues, however, should have been characterized to confirm the carbonate/bicarbonate leaching hypothesis.

Bioaccumulation in Fish

Nor-Am Statement: The bioaccumulation factor for BTS 27919 and BTS 27271 was estimated using the following regression equation: log BCF = 0.76*log K_{ow} - 0.23. The predicted bioaccumulation factors for BTS 27919 and BTS 27271 were 0.14 and 10.2, respectively. In addition, fish bioaccumulation studies indicate that amitraz residues are eliminated over a 14 day depuration period. Therefore, amitraz and its degradates should not bioaccumulate in fish tissues.

EFGWB Response: EFGWB agrees that amitraz and its degradates do not appear to bioaccumulate in fish tissues.