

12-15-92

File

DP Barcode : D182987
PC Code No : 129099
EEB Out : 12/15/92

DEC 15 1992

To: Dennis Edwards Jr.
Product Manager 19
Registration Division (H7505C)

From: Douglas J. Urban, Acting Chief
Ecological Effects Branch/EFED (H7507C)

Attached, please find the EEB review of...

Reg./File # : 3125-URU
Chemical Name : Imidacloprid
Type Product : Insecticide
Product Name : NTN 33893
Company Name : Miles Inc.
Purpose : Review studies

Action Code : 116 Date Due : 1/26/93
Reviewer : Dana Lateulere

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT
71-1(A)			72-2(A)			72-7(A)		
71-1(B)			72-2(B)			72-7(B)		
71-2(A)			72-3(A)			122-1(A)		
71-2(B)			72-3(B)			122-1(B)		
71-3			72-3(C)			122-2		
71-4(A)			72-3(D)			123-1(A)		
71-4(B)	424805-02	Y*	72-3(E)			123-1(B)		
71-5(A)			72-3(F)			123-2		
71-5(B)			72-4(A)	424805-01	S	124-1		
72-1(A)			72-4(B)			124-2		
72-1(B)			72-5			141-1		
72-1(C)			72-6			141-2	424805-03	S
72-1(D)						141-5		

Y=Acceptable (Study satisfied Guideline)/Concur
P=Partial (Study partially fulfilled Guideline but additional information is needed)
S=Supplemental (Study provided useful information but Guideline was not satisfied)
N=Unacceptable (Study was rejected)/Nonconcur

* - a NOEC not established but new study not necessary



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

MEMORANDUM

SUBJECT: NTN 33893 Data Submissions for Pending Registration, DP Barcode #D182987.

FROM: Anthony Maciorowski, Chief *Anthony Maciorowski*
Ecological Effects Branch
Environmental Fate and Effects Division H7507C

TO: Dennis Edwards, PM 19
Registration Division H7505C

EEB has reviewed the data submitted by Miles Inc. for their pending Sec. 3 registration of NTN 33893 technical and it's formulations. The following is a summary of the reviews:

1. Gagliano, G.G. 1992. Raw Data and Statistical Analysis Supplement for Early Life Stage Toxicity of NTN 33893 Technical to Rainbow Trout (*Oncorhynchus mykiss*). Report No. 101214-1. Study conducted by Analytical Bio-Chemistry Laboratories, Inc., Columbia, Missouri. Submitted by Miles Inc., Agricultural Chemicals Division, Kansas City, Missouri. Original report - EPA MRID No. 420553-20 - Supplemental Raw Data Submission - EPA MRID No. 424805-01).

Review of the raw data submission concluded that a NOEC was not determined. Effects were noted at 1.2 ppm, the lowest concentration tested, for fry survival, percent swim-up and weight. This study will be classified as supplemental; however, the study does not have to be repeated unless the registrant chooses to refute the presumption of chronic risk that will be assumed from these results.

2. Mayer, D.F., J.D. Lunden and M.R. Husfloen. 1991. Integrated Pest and Pollinator Investigations 1991 (Including Honey Bee Toxicity to NTN 33893). Report No. 103815. Conducted by Department of Entomology, Irrigated Agriculture Research and Extension Center, Washington State University, Rt. 2, Box 2953-A, Prosser, WA 99350-9687. Submitted by Miles Inc., Kansas City, MO. EPA MRID No. 424805-03.

This study does not fulfill any guideline requirements; the data will be used as supplemental and added to NTN 33893's toxicity database. A Foliar Residue Study is still required at this time. EEB acknowledges the letter sent to Miles Inc. from Wildlife International explaining the weather difficulties in performing



this test and thus it's delay.

3. Stafford, T.R. 1992. "Technical NTN 33893: A One Generation Reproduction Study with Mallard Ducks". Prepared by Miles Incorporated, Agricultural Division, Kansas City, KS. Laboratory Study No. N3740802. Laboratory Report No. 103813. Submitted by Miles Incorporated, Kansas City, MO. EPA MRID No. 424805-02.

This study is scientifically sound but does not entirely fulfill the guideline requirements for an Avian Reproduction Study with the Mallard duck. Based on eggshell thickness, the NOEC was determined to be less than 61 ppm, the lowest concentration tested. Female body weight gain and eggshell strength were effected at levels of 241 ppm. Other observable effects (neck droop) were apparent at 128 ppm. A NOEC was not established for eggshell thickness, a lower concentration should have been tested. Guidelines suggest multiple levels of five, multiples of two were tested. The study does not have to be repeated; this submission in conjunction with the original (MRID No. 420553-13) will provide adequate information for a risk assessment.

Questions regarding these reviews, contact Dana Lateulere at 308-2856.

ADDENDUM
DATA EVALUATION RECORD

1. **CHEMICAL:** NTN 33893.
Shaughnessey No. 129059.
2. **TEST MATERIAL:** Bay NTN 33893 Technical; Batch No. 9030211;
Formula PF8543; 95% active ingredient; a beige powder.
3. **STUDY TYPE:** Freshwater Fish Early Life-Stage Test.
Species Tested: Rainbow Trout (*Oncorhynchus mykiss*).
4. **CITATION:** Cohle, P. and J. Bucksath. 1991. Early Life
Stage Toxicity of NTN 33893 Technical to Rainbow Trout
(*Oncorhynchus mykiss*) in a Flow-Through System. Report No.
101214. Study conducted by Analytical Bio-Chemistry
Laboratories, Inc., Columbia, Missouri. Submitted by Mobay
Corporation, Agricultural Chemicals Division, Kansas City,
Missouri. Original report - EPA MRID No. 420553-20 -
Supplemental Raw Data Submission - EPA MRID No. 424805-01).

5. **REVIEWED BY:**
Dana Lateulere, Biologist
Ecological Effects Branch
Environmental Fate and
Effects Division

Signature: *Dana Lateulere*

Date: 12/14/92

6. **APPROVED BY:**
Ann Stavola, Section Head, #5
Ecological Effects Branch
Environmental Fate and
Effects Division

Signature: *Ann Stavola*

Date: 12/14/92

7. **CONCLUSIONS:** The raw length and weight data received for
the Fish Early Life Stage study with NTN 33893 was
statistically analyzed using Bonferroni's Test. The controls
were determined to be significantly different via a t-test;
therefore, only the solvent control data was used for
analysis. The weight data showed significant effects at
1.2, 4.9, 9.8, and 19 mg a.i./L. The length data showed
effects at ≥ 2.5 mg a.i./L.

Effects occurred at the following levels in the respective
parameters:

Fry Survival - 1.2, 4.9, 19.0 mg a.i./L
Percent swim-up - 1.2, 4.9, 9.8, and 19.0 mg a.i./L
Length - 2.3, 4.9, 9.8 and 19.0 mg a.i./L
Weight - 1.2, 4.9, 9.8, and 19.0 mg a.i./L

Although there is no clear dose response for the weight
data, percent swim-up or fry survival (no significant
effects occurred at 2.5 mg a.i./L), EEB aquatic biologists

concur that the significant difference from control in all three parameters cannot be disregarded as biological variability. Therefore, a NOEC was not determined for the three parameters. The study will be classified as supplemental; however, a new study does not have to be performed unless the registrant wishes to refute the presumption of chronic effects that these data suggest.

D. Adequacy of the Study:

- (1) **Classification:** Supplemental; study does not have to be repeated.
- (2) **Rationale:** A NOEC was not determined for fry survival, percent swim-up or weight.
- (3) **Repairability:** No.

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NTN FISH ELS, LENGTH DATA

File: FISHEARL Transform: NO TRANSFORM

t-test of Solvent and Blank Controls

Ho:GRP1 MEAN = GRP2 MEAN

GRP1 (SOLVENT CRTL) MEAN =	27.8344	CALCULATED t VALUE =	3.3111
GRP2 (BLANK CRTL) MEAN =	26.9339	DEGREES OF FREEDOM =	113
DIFFERENCE IN MEANS =	0.9005		
TABLE t VALUE (0.05 (2),130) =	1.978**	SIGNIFICANT DIFFERENCE at alpha=0.05	
TABLE t VALUE (0.01 (2),130) =	2.614**	SIGNIFICANT DIFFERENCE at alpha=0.01	

NTN FISH ELS, LENGTH DATA

File: FISHEARL Transform: NO TRANSFORM

SUMMARY STATISTICS ON TRANSFORMED DATA TABLE 1 of 2

GRP	IDENTIFICATION	N	MIN	MAX	MEAN
1	SOLVENT	60	23.274	32.221	27.834
2	1.3	48	17.379	30.565	27.038
3	2.5	58	19.868	30.940	26.650
4	5.0	52	23.263	29.713	26.669
5	10.0	56	23.602	36.073	26.835
6	20.0	51	19.019	28.756	25.422

NTN FISH ELS, LENGTH DATA

File: FISHEARL Transform: NO TRANSFORM

SUMMARY STATISTICS ON TRANSFORMED DATA TABLE 2 of 2

GRP	IDENTIFICATION	VARIANCE	SD	SEM
1	SOLVENT	2.533	1.592	0.205
2	1.3	6.021	2.454	0.354
3	2.5	4.613	2.148	0.282
4	5.0	2.311	1.520	0.211
5	10.0	3.741	1.934	0.258
6	20.0	3.425	1.851	0.259

NTN FISH ELS, LENGTH DATA

File: FISHEARL Transform: NO TRANSFORM

ANOVA TABLE

SOURCE	DF	SS	MS	F
				3.6

Between	5	165.652	33.130	8.880
Within (Error)	319	1190.262	3.731	
Total	324	1355.914		

Critical F value = 2.29 (0.05,5,120)
 Since $F > \text{Critical } F$ REJECT H_0 : All groups equal

NTN FISH ELS, LENGTH DATA
 File: FISHEARL Transform: NO TRANSFORM

BONFERRONI T-TEST - TABLE 1 OF 2 Ho: Control < Treatment

GROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	SOLVENT	27.834	27.834		
2	1.3	27.038	27.038	2.129	
3	2.5	26.650	26.650	3.331	*
4	5.0	26.669	26.669	3.183	*
5	10.0	26.835	26.835	2.786	*
6	20.0	25.422	25.422	6.557	*

Bonferroni T table value = 2.36 (1 Tailed Value, P=0.05, df=120,5)

NTN FISH ELS, LENGTH DATA
 File: FISHEARL Transform: NO TRANSFORM

BONFERRONI T-TEST - TABLE 2 OF 2 Ho: Control < Treatment

GROUP	IDENTIFICATION	NUM OF REPS	Minimum Sig Diff (IN ORIG. UNITS)	% of CONTROL	DIFFERENCE FROM CONTROL
1	SOLVENT	60			
2	1.3	48	0.882	3.2	0.796
3	2.5	58	0.839	3.0	1.185
4	5.0	52	0.863	3.1	1.165
5	10.0	56	0.846	3.0	1.000
6	20.0	51	0.867	3.1	2.412

NTN FISH ELS, LENGTH DATA
 File: FISHEARL Transform: NO TRANSFORM

ANOVA TABLE

SOURCE	DF	SS	MS	F
Between	5	165.652	33.130	8.880
Within (Error)	319	1190.262	3.731	

Handwritten mark: a checkmark and the number 7.

 Total 324 1355.914

Critical F value = 2.29 (0.05,5,120)
 Since F > Critical F REJECT Ho:All groups equal

NTN FISH ELS, LENGTH DATA
 File: FISHEARL Transform: NO TRANSFORM

TUKEY method of multiple comparisons

GROUP	IDENTIFICATION	TRANSFORMED MEAN	ORIGINAL MEAN	GROUP					
				0	0	0	0	0	0
				6	3	4	5	2	1
6	20.0	25.422	25.422	\					
3	2.5	26.650	26.650	*	\				
4	5.0	26.669	26.669	*	.	\			
5	10.0	26.835	26.835	*	.	.	\		
2	1.3	27.038	27.038	*	.	.	.	\	
1	SOLVENT	27.834	27.834	*	*	*	.	.	\

* = significant difference (p=0.05)
 Tukey value (6,319) = 4.10

. = no significant difference
 s = 3.731

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NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

t-test of Solvent and Blank Controls

Ho:GRP1 MEAN = GRP2 MEAN

 GRP1 (SOLVENT CRTL) MEAN = 0.9166 CALCULATED t VALUE = 3.2630
 GRP2 (BLANK CRTL) MEAN = 0.8007 DEGREES OF FREEDOM = 111
 DIFFERENCE IN MEANS = 0.1159

 TABLE t VALUE (0.05 (2),130) = 1.978** SIGNIFICANT DIFFERENCE at alpha=0.05
 TABLE t VALUE (0.01 (2),130) = 2.614** SIGNIFICANT DIFFERENCE at alpha=0.01

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

SUMMARY STATISTICS ON TRANSFORMED DATA TABLE 1 of 2

GRP	IDENTIFICATION	N	MIN	MAX	MEAN
1	SOLVENT	59	0.521	1.371	0.917
2	1.5	45	0.206	1.479	0.794
3	2.0	55	0.299	1.270	0.821
4	5.0	51	0.193	1.389	0.801
5	10.0	56	0.249	1.405	0.782
6	20.0	49	0.109	1.045	0.628

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

SUMMARY STATISTICS ON TRANSFORMED DATA TABLE 2 of 2

GRP	IDENTIFICATION	VARIANCE	SD	SEM
1	SOLVENT	0.045	0.211	0.028
2	1.5	0.053	0.229	0.034
3	2.0	0.043	0.208	0.028
4	5.0	0.058	0.240	0.034
5	10.0	0.052	0.228	0.030
6	20.0	0.035	0.188	0.027

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

ANOVA TABLE

SOURCE	DF	SS	MS
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Between	5	2.290	0.458	9.542
Within (Error)	309	14.684	0.048	
Total	314	16.974		

Critical F value = 2.29 (0.05,5,120)
 Since F > Critical F REJECT Ho:All groups equal

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

BONFERRONI T-TEST - TABLE 1 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	SOLVENT	0.917	0.917		
2	1.5	0.794	0.794	2.821	*
3	2.0	0.821	0.821	2.340	
4	5.0	0.801	0.801	2.749	*
5	10.0	0.782	0.782	3.293	*
6	20.0	0.628	0.628	6.820	*

Bonferroni T table value = 2.36 (1 Tailed Value, P=0.05, df=120,5)

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

BONFERRONI T-TEST - TABLE 2 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	NUM OF REPS	Minimum Sig Diff (IN ORIG. UNITS)	% of CONTROL	DIFFERENCE FROM CONTROL
1	SOLVENT	59			
2	1.5	45	0.102	11.2	0.122
3	2.0	55	0.097	10.6	0.096
4	5.0	51	0.099	10.8	0.115
5	10.0	56	0.096	10.5	0.135
6	20.0	49	0.100	10.9	0.289

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

ANOVA TABLE

SOURCE	DF	SS	MS	F
Between	5	2.290	0.458	9.542
Within (Error)	309	14.684	0.048	

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 Total 314 16.974

Critical F value = 2.29 (0.05,5,120)
 Since F > Critical F REJECT Ho:All groups equal

NTN 33893 WEIGHT DATA FISH ELS
 File: WEIGHTFEL Transform: NO TRANSFORM

TUKEY method of multiple comparisons

GROUP	IDENTIFICATION	TRANSFORMED MEAN	ORIGINAL MEAN	GROUP					
				0	0	0	0	0	0
				6	5	2	4	3	1
6	20.0	0.628	0.628	\					
5	10.0	0.782	0.782	*	\				
2	1.5	0.794	0.794	*	.	\			
4	5.0	0.801	0.801	*	.	.	\		
3	2.0	0.821	0.821	*	.	.	.	\	
1	SOLVENT	0.917	0.917	*	*	.	.	.	\

* = significant difference (p=0.05)
 Tukey value (6,309) = 4.10

. = no significant difference
 s = 0.048

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DATA EVALUATION RECORD

1. **CHEMICAL:** NTN 33893.
Shaughnessey No. 129059 (129099).
2. **TEST MATERIAL:** NTN 33893 240FS (active ingredient Imidacloprid).
3. **STUDY TYPE:** Supplemental to Guidelines 141-1 and 141-2. Integrated Pest and Pollinators Investigation. Species Tested: Worker Honey Bee (Apis mellifera), Alfalfa Leafcutting Bee (Megachile rotundata) and Alkali Bees (Nomia melanderi).
4. **CITATION:** Mayer, D.F., J.D. Lunden and M.R. Husfloen. 1991. Integrated Pest and Pollinator Investigations 1991 (Including Honey Bee Toxicity to NTN 33893). Report No. 103815. Conducted by Department of Entomology, Irrigated Agriculture Research and Extension Center, Washington State University, Rt. 2, Box 2953-A, Prosser, WA 99350-9687. Submitted by Miles Inc., Kansas City, MO. EPA MRID No. 424805-03.
5. **REVIEWED BY:**
Dana Lateulere, Biologist
Ecological Effects Branch
Environmental Fate and
Effects Division
Signature: *Dana Lateulere*
Date: *11/18/92*
6. **APPROVED BY:**
Ann Stavola, Section Head #5
Ecological Effects Branch
Environmental Fate and
Effects Division
Signature: *Ann Stavola*
Date: *12/9/92*
7. **CONCLUSIONS:** This study does not fulfill the requirements for a Foliar Residue Honey Bee Toxicity test; the data was submitted as supplemental information for the study forthcoming. Bees exposed to 0.025 lb a.i./A, ~~two~~ to eight hour old residues had 12 to 13% mortality; bees exposed to 0.05 lb a.i./A, two to eight hour old residues showed mortality ranging from 14 to 20% and bees exposed to 0.1 lb a.i./A, ~~two~~ to eight hour old residues ranged from 14 to 19% mortality. A topical toxicity test was performed; the LD50 was determined to be 0.0439 ug/bee (this value is lower than the LD50 of 0.078 ug/bee determined in an earlier submission, MRID No. 422730-03). The Foliar Residue study is still required, Guidline #141-2.
8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:** Based on LD50 values that determined NTN 33893 to be very highly toxic to bees (LD50 = .078, MRID No. 422730-03), Residual Foliar Testing was required.
10. **DISCUSSION OF INDIVIDUAL TESTS:** Three tests were performed: Residual Bee Poisoning Bioassay, LD50 Topical Drop Insecticide Tests on Bees, LC50 Microsprayer Insecticide Tests on Adult Bees. Results and conclusions were reported for the Residual testing only; results were reported in tabular form for the Topical Drop test.
11. **MATERIALS AND METHODS:**
- A. **Test Animals:** - Worker Honey bees (HB) were obtained from the top frames of colonies and anesthetized with CO₂ to facilitate handling. Alfalfa leafcutting bees (LC) were emerged in an incubation chamber at 85°F., allowed to fly in the lab, and collected off the windows. Alkali bees (AB) were collected from nesting sites and chilled at 35°F. to facilitate handling.
- B. **Test System:** - Tests were conducted with insecticides applied with a R&D CO₂ pressurized sprayer at a rate of 26 gallons per acre using a hand-held boom with 4 nozzles applied to 0.01 acre plots of first or second growth alfalfa. Field-weathered residual test exposures were replicated 4 times with 4 foliage samples per treatment and time interval. Samples consisting of about 500 cm of foliage taken from the upper 15 cm portions of plants and clipped to 1-inch lengths, were placed in plastic petri dishes (15 cm diameter) whose tops and bottoms were separated by a wire screen (6.7 meshes/cm) insert (45 cm long and 5 cm wide).
- C. **Dosage:** Test levels were 0.025, 0.05 and 0.01 lb a.i./A of NTN 3383 240FS.
- D. **Design:** Residual test exposures were replicated 4 times by caging 30 to 40 worker HB, 20 to 25 LB or 20 to 25 AB with each of four foliage samples per treatment and time intervals. Bees in cages were fed syrup (1:1 ratio) in a wad of cotton (5 x 5 cm), and the bees held at 75 degrees F. for 24 hour mortality counts.
- E. **Statistics:** n/a.
12. **REPORTED RESULTS:** NTN 33893 240FS at 0.025, 0.05 and 0.1 lb a.i./A was non-hazardous to alkali, alfalfa leafcutting and honey bees if applied in late evening. A topical toxicity test was also performed, the LD50 was reported as 0.0439 ug/bee for NTN 33893 240FS.

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13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:

Quality Assurance and Good Laboratory Practice statements were included in the report indicating that the study did not apply to the requirements of 40 CFR Part 160.

Conclusions were only given for the Residual Bee Poisoning Bioassay - "When 8 hour residues cause less than 25% mortality, the material is probably safe to use around bees if applied in late evening after bees have quit foraging for the day. NTN as tested would qualify as non-hazardous to these three pollinating bees if applied in late evening".

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:

A. Test Procedure: The test procedures do not follow the protocols recommended by EPA, as this study was not submitted to satisfy the guideline requirement, only to supplement other data.

B. Statistical Analysis: No analysis was performed.

C. Discussion/Results: This study does not fulfill the guideline requirements for Foliar Residue Honey bee testing. This data will be used to supplemental the toxicity database of NTN 33893. Guideline #141-2 is still required.

There was mortality at all levels tested in the residue study; however, no clear dose response was apparent. The topical LD50 of 0.0439 ug/bee is lower than the original LD50 of 0.078 ug/bee determined in MRID No. 422730-03. (No reasoning was given for this difference.)

D. Adequacy of the Study:

(1) Classification: Supplemental.

(2) Rationale: Data submitted to supplement, not to fulfill requirements.

(3) Repairability: n/a.