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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JN 2 1392

06/02/1592

MEMORANDUM:

Subject: I.D. No. 003125-URA

New Chemical Screen: NTN 33893 Technical, and 75%,

21.4%, 2.5% and 0.62% Formulations

Myron S. Ottley, Ph. D. From:

Section IV

Tox. Chem. No. 497E HED Proj. No. 0177747 Submission No. S417300

Toxicology Branch I Health Effects Division (H7509C) Chem. I.D. No. 129099

To:

Dennis Edwards, Jr./Portia Jenkins (PM19)

Registration Division (H7505C)

Thru:

Marion P. Copley, D.V.M., D.A.B.T. Marion V. Section Head
Section IV, Toxicology Branch I 429/92 Health Effects Division (H7509C)

CONCLUSIONS

NTN 33893 Technical and Formulations pass the pre-review toxicology screen for a non-food use chemical, as evaluated by the registration Acceptance Criteria.

ACTION REQUESTED

Toxicology Branch I has been requested to review data submitted by Miles Corp. to determine whether they meet the criteria for pre-review toxicity screen for a non-food use chemical. The following data are required to be present and acceptable for review:

Table 1. Data Requirements

Guidel	ine No.	Description	Test Substance
81	1-1	Acute Oral - Rat	EP* & TGAI**
83	1-2	Acute Dermal	EP & TGAI
83	1-3	Acute Inhal Rat	EP & TGAI
8:	1-4	Prim. Eye Irrit Rat	EP & TGAI
8:	1-5	Prim. Dermal Irrit.	EP & TGAI
8:	1-6	Dermal Sensitization	EP & TGAI
82	2-1	90-Day Feeding (rodent/nonrodent)	TGAI
8:	2-2	21-Day Dermal	TGAI
8:	3-3	Developmental 1 species	TGAI
8	4-2	Gene Mutation Structural Chromosomal Abber.	TGAI
.8	4-4	Other Genotoxic Effects	TGAI

^{*} End Use Product **

RESULTS

Table 2 lists the studies included in the present submission by Miles Corporation in an effort to complete the screen on NTN 33893 Technical and Formulations. Study numbers and Guideline numbers are indicated. Studies not required, but included in this submission for support and/or comment purposes were not screened. A list of all data submitted in this action is attached.

As indicated in Table 2, some data were submitted under a separate action. The Technical Grade and Lower concentration formulations (2.5% and 0.62%) were previously evaluated. Data requirements for the 0.62% formulation were waived. The data submitted on the 2.5% formulation were used to support the waiver. After considering the previously evaluated studies, and taking into account the data screened in this submission, it appears that sufficient data have been submitted to satisfactorily meet the Acceptance Criteria for the Subdivision F pre-review screen.

^{*} Technical Grade Active Ingredient

Table 2. Studies Evaluated and Judged Adequate for Review Under Subdivision F Acceptance Criteria.

GUIDELINE NUMBER	STUDY TYPE	Technical /Formul.	STUDY NUMBER (S)
81-1	Acute Oral - Rat	Technical 21% Form. 75% Form. 2.5 Form.	T 2033060* 89-012-DV 91-012-JJ 89-012-DY*
81-2 81-2	Acute Dermal - Rat Acute Dermal - Rabbit	Technical 21% Form. 75% Form. 2.5 Form.	T 5033063* 89-025-EB 91-022-JH 89-025-DS*
81-3	Acute Inhalation - Rat	Technical 21% Form. 75% Form. 2.5 Form	T 2025951** T 3025952** T 4025953** 89-042-EG 91-042-JZ 89-042-DX**
81-4	Primary Eye Irritation Rabbit	Technical 21% Form. 75% Form. 2.5 Form.	T 8025515* 89-335-DZ 91-335-JK 89-335-DT*
81-5	Primary Dermal Irritation Rabbit	Technical 21% Form. 75% Form. 2.5 Form.	T 8025515* 89-325-DU 91-325-JG 89-325-ED*
81-6	Dermal Sensitization Guinea Pig	Technical 21% Form. 75% Form. 2.5 Form.	T 9025651* 89-324-DO 91-324-JC 89-324-DN
82-1 82-1	Subchronic Feeding - Rat Subchronic Feeding - Dog	Technical Technical	101949 100176
82-2	21-Day Dermal - Rabbit Dog	Technical	100688
83-3	Dëvelopmental Toxicity Rabbit	Technical	98572

GUIDELINE NUMBER	STUDY TYPE	Technical /Formul.	STUDY NUMBER (8)
84-2	Gene Mutations	Technical	100668,101276 T 6030111 100661,100662 98584, 99676 102655,99262
	Structural Chromosomal Aberrations	Technical	100666,100678 99257, 100021
84-4	Bacterial DNA Repair	Technical	100665,102613 101275, 98573

Studies reviewed under previous action and found to be <u>acceptable</u> to support regulation.

Not all of the Mutagenicity studies evaluated under this screen met Acceptance Criteria. However, sufficient studies of similar design did meet the Acceptance Criteria to avoid invalidating the screen in this area. Following is a list of cytogenetics (84-2) studies, conducted on the Technical, not meeting acceptance criteria:

Report No.	MRID No.
102652	422563-47
102654	422563-48
100664	422563-66
100663	422563-68
100680	422563-69

DATA REVIEW AND ACCEPTANCE

Acceptance of the data in this submission, at this stage, does not constitute a Core Classification. This is an Acceptance Criteria Screen only. Detailed review of each study and the supporting documents is required before final conclusions can be drawn on the acceptability of the data.

Acceptance Criteria forms for each study submitted and evaluated are currently in the possession of the Reviewer. They will eventually be stored in the Caswell file as a group, or attached singly to individual DERs.

^{**} Studies reviewed under previous action and found to be <u>not acceptable</u> to support regulation.

Nittachmat VI == X

TRANSMITTAL DOCUMENT

1. Name and Address of Submitter:

MILES INC.
AGRICULTURE DIVISION
P.O. Box 4913
Kansas City, Missouri 64120

John S. Thornton, Manager Registrations Research and Development (816) 242-2255

2. Regulatory Action in Support of Which This Package is Submitted:

The studies listed in Section 4 of this document are submitted to support the registration of five <u>new</u> insecticide products containing a <u>new</u> active ingredient - NTN 33893. Specifically, the new products are NTN 33893 Technical, NTN 33893 75% Concentrate, NTN 33893 0.62% Granular, NTN 33893 2.5% Granular and NTN 33893 2. Regulatory actions on this active ingredient have been assigned to Mr. Dennis H. Edwards, Jr., Product Manager 19, Registration Division.

3. <u>Transmittal Date</u>:

March 16, 1992

4. <u>List of Submitted Studies</u>:

MRTO No.

Study No. PRODUCT CHEMISTRY

- "Product Chemistry of BAY NTN 33893 2.5% Granular," EPA Guideline Nos. 61-1 to 61-2(b), 62-1 to 62-3, 63-1 to 63-21, and 64-1, Miles Brochure No. 1767, T.D. Talbott, 38 p.
- "Product Chemistry of BAY NTN 33893 240 FS," EPA Guideline Nos. 61-1 to 61-2(b), 62-1 to 62-3, 63-1 to 63-21 and 64-1, Miles Brochure No. 1766, T.D. Talbott, 43 p.

WILDLIFE AND AQUATIC ORGANISMS BATA REQUIREMENTS

3 "Acute Toxicity of NTN 33893 to <u>Hyalella</u>
<u>azteca</u>," EPA Guideline No. 72-2, Miles Report
No. 101960, D. England and J. Bucksath, 29 p.

- "Growth and Survival of the Midge (Chironomus tentans)," There is no EPA Guideline No. for this study, Miles Report No. 101985, G.G. Gagliano, 43 p.
- "NTN 33893 Technical: Acute Effect on New Shell Growth of The Eastern Oyster, <u>Crassostrea virginica</u>," EPA Guideline No. 72-3, Miles Report No. 101978, J. Wheat and G. Ward, 54 p.
- "Assessment of the Potential Ecological and Biological Effects of NTN 33893 on Aquatic Ecosystems as Measured in Fiberglass Pond Systems," EPA Guideline No. 72-7, Miles Report No. 102600, J. Moring, J. Kennedy and J. Wiggins, 791 p.
- 7 "Evaluation of the Foliar Half-life and Distribution of NTN 33893 in Turf," There is no EPA Guideline No. for this study, Miles Report No. 102605, J. Lin, 164 p.
- 8 "NTN 33893: Turf Runoff Predictions and Microcosm Loading Rates." There is no EPA Guideline No. for this study, Miles Report No. 102601, J. Lin and R. Graney, 85 p.
- 9 "Freld Measurement of NTN 33893 (Imidacloprid)
 Runoff From Small Turf Plots in Miles Research
 Park, Stilwell, Kansas," There is no EPA
 Guideline No. for this study, Miles Report No.
 102606, J. Lin, 135 p.
- "Ecological Effects Summary and Risk Assessment for NTN 33893 Turf Insecticide: 240 PS Formulation," There is no EPA Guideline No. for this study, Miles Report No. 102602, R. Graney and D. Fischer, 63 p.

TOXICOLOGY DATA REQUIREMENTS

422563-11

"An Overview of the Toxicology of NTN 33893 and its Metabolite WAK 3839," There is no EPA Guideline No. for this study, Miles Report No. 102657, G.K. Sangha and L. Machemer, 134 p.

422563-12

"Acute Oral Toxicity Sudy with BAY NTN 33893 75 WP-WS in Rats," EPA Guideline No. 81-1, Miles Report No. 101283, L. Sheets and S. Phillips, 20

422563 13 13 "Acute Oral Toxicity Study with BAY NTN 33893 240 F.S. in Rats," EPA Guideline No. 81-1, Miles Report No. 100010, L. Sheets, 19 p. "Acute Dermal Toxicity Study with BAY NTN 33893 14 75 WP-WS in Rats," EPA Guideline No. 81-2, Miles Report No. 101281, L. Sheets and R. Gilmore, 19 422563-15-15 "Acute Dermal Toxicity Study with BAY NTN 33893 240 F.S. in Rabbits, " EPA Guideline No. 81-2, Miles Report No. 100002, L. Sheets, 18 p. "Acute Four-Hour Inhalation Toxicity Study with BAY NTN 33893 75% WP-WS in Rats, * EPA Guideline 422861-01 No. 81-3, Miles Report No. 101913, D. Warren, 34 422861-02 "Acute Four-Hour Inhalation Toxicity Study with 422565-17 BAY NTN 33898 240 F.S. in Rats," EPA Guideline No. 81-3, Miles Report No. 100012, D. Warren, 28 4225-63-1818 "Primary Eye Irritation Study with BAY NTN 33893 75 WP-WS in Rabbits," EPA Guideline No. 81-4, Miles Report No. 101259, L. Sheets and S. Phillips, 17 p. 422563-1919 "Primary Eye Irritation Study with BAY NTN 33893 240 F.S. in Rabbits," EPA Guideline No. 81-4, Miles Report No. 99815, L. Sheets, 17 p. 425573-530 "Primary Dermal Irritation Study with BAY NTN 33893 75 WP-WS in Rabbits," EPA Guideline No. 81-5, Miles Report No. 101278, L. Sheets and S. Phillips, 17 p. 422573-2/21 "Primary Dermal Irritation Study with BAY NTN 33893 240 F.S. in Rabbits," EPA Guideline No. 81-5, Miles Report No. 99816, L. Sheets, 16 p. 4 22563-322 "Dermal Sensitization Study with BAY NTN 33893 75 WP-WS in Guinea Pigs," EPA Guideline No. 81-6, Miles Report No. 101282, L. Sheets and S. Phillips, 23 p. 422563-23 23 "Dermal Sensitization Study with BAY NTN 33893 240 F.S. in Guinea Pigs," EPA Guideline No.

81-6, Miles Report No. 100003, L. Sheets, 21 p.

4225-3-24 2	"NTN 33893 Study for Acute Oral Toxicity to Mice," There is no EPA Guideline No. for this study, Miles Report No. 100039, W. Bomann, 48 p.
25	"NTN 33893 Acute Toxicity Study on Mice," There is no EPA Guideline No. for this study, Miles Report No. 100681, Y. Nakazato, 6 p.
4-22533-26 20	"NTN 33893 (c.n. Imidacloprid [proposed] Study for Acute Intraperitoneal Toxicity in Rats," There is no EPA Guideline No. for this study, Miles Report No. 100689, F. Krotlinger, 67 p.
422730-01 21	"NTN 33893 (Proposed Common Name: Imidacloprid) Subacute Inhalation Toxicity Study on the Rat According to OECD Guideline No. 412," There is no EPA Guideline No. for this study, Miles Report No. 100262, J. Pauluhn, 662 p.
422563-2728	"NTN 33893 Subchronic Toxicity Study on Wistar Rats (Administration in the Feed for 96 Days)," EPA Guideline No. 82-1, Miles Report No. 100036, R. Eiben, 489 p.
402563-28 29	on Dogs in Oral Administration (Thirteen-Week Study Feeding)," EPA Guideline No. 82-1, Miles Report No. 100176. J. Ruf. 305 p.
422563-30 31	"NTN 33893 Techn. Study for Subacute Dermal Toxicity in the Rabbit," EPA Guideline No. 82-2, Miles Report No. 100688, W. Flucke, 140 p.
422573 -31 31	"28-Day Oral Range-Finding Toxicity (Feeding) Study with NTN 33893 Techn. in the Dog," There is no EPA Guideline No. for this study, Miles Report No. 99656, I. Bloch, 172 p.
422563-3136 (3Vol.)	"NTN 33893 (Proposed Common Name: Imidacloprid) Chronic Toxicity and Cancerogenicity Studies on Wistar Rats (Administration in Food Over 24 Months)," EPA Guideline No. 83-1, Miles Report No. 100652, R. Eiben and G. Kaliner, 1323 p.
402562-35 ³⁵	"NTN 33893 (Proposed Common Name: Imidacloprid) Chronic Toxicity and Carcinogenicity Studies on Wistar Rats (Administration in Food Over 24 Months) Supplementary MTD Study for Two-Year Study T 1025699," EPA Guideline No. 83-1, Miles Report No. 101931, R. Eiben, 971 p.

422563-33	34	"Expert Opinion on the Occurrence of Mineralized Particles in the Colloid of the Thyroid Glands in Aging Rats," There is no EPA Guideline No. for this study, Miles Report No. 102658, G. Kaliner, 7 p.
422562-34	35	"NTN 33893 Pilot Range-Finding Study for a Chronic Toxicity Study on Wistar Rats (Ninety-Eight Day Feeding Study)," There is no EPA Guideline No. for this study, Miles Report No. 99672, R. Eiben, 147 p.
422.730-2	36	"52-Week Oral Toxicity (Feeding) Study with NTN 33893 Technical in the Dog," EPA Guideline No. 83-1, Miles Report No. 100015, T. Allen, Th. Frei, H. Luetkemeier, O. Voegel, K. Biedermann and J. Wilson, 454 p.
402573-35	37	"NTN 33893 (proposed common name Imidacloprid) Carcinogenicity Study on B6C3F1 Mice (Administration in the Food for 24 Months), EPA Guideline No. 83-1, Miles Report No. 100693, B. Watta-Gebert, 1318 p.
422563-36	38	"NTN 33893 (Proposed Common Name: Imidacloprid) Carcinogenicity Study in B6C3F1 Mice (Supplementary MTD Testing for Study T 5025710 With Administration in Diet Over a 24-Month Period), "EPA Guideline No. 83-1, Miles Report No. 101929, B. Watta-Gebert, 732 p.
422563-37	39	"NTN 33893 Pilot Range-Finding Study for a Cancerogenesis Study on B6C3F1 Mice (One Hundred Seven Day Feeding Study)," There is no EPA Guideline No. for this study, Miles Report No. 99808, R. Eiben, 119 p.
422563-38	40	"Embryotoxicity Study (Including Teratogenicity) With NTN 33893 Technical in the Rat," EPA Guideline No. 83-3, Miles Report No. 98571, H. Becker, W. Vogel and Ch. Terrier, 288 p.
422563-411	41	"Embryotoxicity Study (Including Teratogenicity) With NTN 33893 Technical in the Rabbit," EPA Guideline No. 83-3, Miles Report No. 98572, H. Becker and K. Biedermann, 237 p.
422563-40	42	"NTN 33893 Technical (Proposed C.N. Imidacloprid) Multiple Generation Reproduction Study in Rats," EPA Guideline No. 83-4, Miles Report No. 100647, P. Suter, K. Biedermann, H. Luetkemeier, J. Wilson and Ch. Terrier, 1729 p.

422563-41

"NTN 33893 Reverse Mutation Assay (Salmonella typhimurium and Escherichia coli)," EPA Guideline No. 84-2, Miles Report No. 101276, M. Watanabe, 28 p.

422563-12 44

"NTN 33893 Mutagenicity Study for the Detection of Induced Forward Mutations in the CHO-HGPRT Assay in Vitro," EPA Guideline No. 84-2, Miles Report No. 98584, H. Lehn, 33 p.

4 22513-4345

"NTN 33893 Salmonella/Microsome Test to Evaluate for Point Mutagenic Effects," EPA Guideline No. 84-2, Miles Report No. 98570, B. Herbold, 45 p.

422573-44 46

"NTN 33893 In Vivo Cytogenetic Study of the Bone Marrow In Chinese Hamster to Evalute for Induced Clastogenic Effects," EPA Guideline No. 84-2, Miles Report No. 100021, B. Herbold, 36 p.

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"NTN 33893 In Vitro Cytogenetic Study with Human Lymphocytes for the Detection of Induced Clastogenic Effects," EPA Guideline No. 84-2, Miles Report No. 99262, B. Herbold, 36 p.

422563 -46 48

"NTN 33893 Sister Chromatid Exchange in Bone Marrow of Chinese Hamsters In Vivo," EPA Guideline No. 84-2, Miles Report No. 99257, B. Herbold, 36 p.

422565-47 49

"NTN 33893 Micronucleus Test on the Mouse to Evaluate for Clastogenic Effects," EPA Guideline No. 84-2, Miles Report No. 102652, B. Herbold, 31 p.

422563-4850

"Mouse Germ-Cell Cytogenetic Assay with NTN 33893," EPA Guideline No. 84-2, Miles Report No. 102654, W. Volkner, 27 p.

422563-4951

"Clastogenic Evaluation of NTN 33893 in an In Vitro Cytogenetic Assay Measuring Sister Chromatid Exchange in Chinese Hamster Ovary (CHO) Cells," EPA Guideline No. 84-2, Miles Report No. 102655, R. Taalman, 24 p.

422563-50 52	"Sister Chromatid Exchange Assay in Chinese Hamster Ovary Cells," EPA Guideline Nos. 84-3 and 84-4, Miles Report No. 99676, D. Putman, M. Morris, 26 p.
422553-57 53	"NTN 33893 Rec-assay with Spores in the Bacterial System," EPA Guideline No. 84-4, Miles Report No. 101275, M. Watanabe, 25 p.
4225 63 753 54	"Mutagenicity Test on NTN 33893 In the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay," EPA Guideline No. 84-4, Miles Report No. 98573, M. Cifone, 29 p.
422562-53 55	"NTN 33893 Test on S. Cerevisiae D7 to Evaluate for Induction of Mitotic Recombination," EPA Guideline No. 84-4, Miles Report No. 102653, B. Herbold, 28 p.
4225 63 54 56	"Methylene-[14C] Imidacloprid: Metabolism Part of the General Metabolism Study in the Rat," EPA Guideline No. 85-1, Miles Report No. 101999, O. Klein and W. Karl, 101 p. plus page 78A and 78B for a total of 103 p.
42 2563 -53 -57	"[14C]-NTN 33893: Investigations on the Distribution of the Total Radioactivity in the Rat by Whole-Body Autoradiography," There is no EPA Guideline No. for this study, Miles Report No. 87264, O. Klein, 28 p.
4225 33 - 57	"[14C]-NTN 33893: Biokinetic Part of the General Metabolism Study in the Rat," EPA Guideline No. 85-1, Miles Report No. 87265, O. Klein, 97 p.
4 22563-57 59	"[Imidazolidine-4,5-14C] Imidacloprid: Investigation of the Biokinetic Behaviour and Metabolism in the Rat," EPA Guideline No. 85-1, Miles Report No. 102617, O. Klein and A. Brauner, 86 p.
422563-5360	"A Liquid Chromatographic Method for the Determination of NTN 33893 in Inhalation Chamber Atmospheres," There is no EPA Guideline No. for this study, Miles Report No. 99874, K. Moore, 14 D.

"A Liquid Chromatographic Method for the 400563 -59 Determination of NTN 33893 in Aqueous Dose Mixtures," There is no EPA Guideline No. for this study, Miles Report No. 99875, K. Moore, 14 422563-60 62 "NTN 37571 Oral Acute Toxicity Study on Rats," EPA Guideline No. 81-1, Miles Report No. 100683, Y. Nakazato, 6 p. 422563-61 "WAK 3839 Acute Oral Toxicity Study in Rats (Preliminary Study), " EPA Guideline No. 81-1, Miles Report No. 100682, Y. Nakazato, 6 p. 422563-62 64 "WAK 3839 Subchronic Toxicological Study on Rats (Twelve-Week Administration in Drinking Water)," EPA Guideline No. 82-1, Miles Report No. 101949, F. Krotlinger, 359 p. 422563-6365 "WAK 3839 Reverse Mutation Assay (Salmonella typhimurium and Escherichia coli), " EPA Guideline No. 84-2, Miles Report No. 100668, M. Watanabe, 26 p. 425563-60,66 "WAK 3839 Mutagenicity Study for the Detection of Induced Forward Mutations in the V79-HGPRT Assay In Vitro, " EPA Guideline No. 84-2, Miles Report No. 100662, H. Lehn, 32 p. 4225 3 2 -65 -67 "WAK 3839 Mutagenicity Study for the Detection of Induced Forward Mutations in the CHO-HGPRT Assay In Vitro, " EPA Guideline No. 84-2, Miles Report No. 100661, H. Lehn, 32 p. 422563-16 "WAK 3839 or NTN 37571 Micronucleus Test on the Mouse After Intraperitoneal Injection," EPA Guideline No. 84-2, Miles Report No. 100664, B. Herbold, 38 p. 422553-6769

422563-1810 "WAK 3839 Micronucleus Test on the Mouse After Oral Application," EPA Guideline No. 84-2, Miles Report No. 100663, B. Herbold, 39 p.

Report No. 100679, M. Usami, 10 p.

"NTN 37571 Micronucleus Test on the Mice after I.P. Treatment, EPA Guideline No. 84-2, Miles 422563-69 71

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"NTN 37571 Micronucleus Test on the Mice After Oral Treatment Pilot Study, " EPA Guideline No. 84-2, Miles Report No. 100680, M. Usami, 10 p.

"Chromosome Aberration Assay in Chinese Hamster V79 Cells In Vitro with WAK 3839," EPA Guideline No. 84-2, Miles Report No. 100666, A. Heidemann,

73

"NTN 37571 In Vitro Cytogenetic Assay Measuring Chromosome Aberrations in CHO-K1 Cells," EPA Guideline No. 84-2, Miles Report No. 100678, M. Usami, 13 p.

422563-72

"Unscheduled DNA Synthesis in Primary Hepatocytes of Male Rats In Vitro with WAK 3839, " EPA Guideline No. 84-4, Miles Report No. 100665, R. Fautz, 31 p.

"Imidacloprid - WAK 3839: Comparison of Biokinetic Behaviour and Metabolism in the Rat Following-Single Oral Dosage and Investigation of the Metabolism After Chronic Feeding of Imidacloprid to Rats and Mice, " EPA Guideline No. 85-1, Miles Report No. 100645, O. Klein, 85

PLANT PROTECTION DATA REQUIREMENTS

76 "Growth Inhibition of Green Algae (Scenedesmus subspicatus) Cauged by NTN 33893 (Technical)," EPA Guideline No. 122-2, Miles Report No. 100098, F. Heimbach, 17 p.

"Acute Toxicity of NTN 33893 Technical to the 77 Green Algx (Selenastrum capricornutum), " EPA Guideling No. 123-2, Miles Report No. 101986, 30

NONTARGET INSECT DATA REQUIREMENTS

78 "The Acute Oral and Contact Toxicity to Honey Bees of Compound NTN 33893 Technical, " EPA guideline No. 141-1, Miles Report No. 101321, J. Cole, 13 p.