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

CASWELL FILE
63 AB

SEP 26 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Avermectin (Also Called Abamectin) - 89-FL-20 - Section 18 Request by the State of Florida to Use Avermectin on Strawberries

Caswell No.: 63AB
Project No.: 9-2049A
Record No.: 250501

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William Dykstra 9/19/89

TO: Don Stubbs, PM Team 41
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THRU: Edwin Budd, Section Head
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Budd 9/25/89

Requested Action

Review section 18 request by the State of Florida to use avermectin on strawberries.

Conclusion and Recommendation

The section 18 can be toxicologically supported provided that the margin of safety (MOS) for teratogenicity based on the single-serving analysis is greater than 100 and the percent ADI utilized, based on reproductive effects, is not greater than 100 percent for the various subgroups within the U.S. population. These pivotal determinations are calculated by the TAS analyses.

The NOEL for teratogenicity to be used for single-serving analysis is 0.06 mg/kg/day, based on cleft palate in CF_1 mice. The MOS should be greater than 100.

The NOEL for the ADI calculation is 0.12 mg/kg/day, based on pup toxicity (death) in the 2-generation rat reproduction study. The uncertainty factor is 300. The percent ADI utilized for the various subgroups (especially infants and children) should not exceed 100 percent.

If RD can determine that the teratogenic MOS is not greater than 100 and/or the percent ADI utilized is greater than 100 percent, the section 18 cannot be toxicologically supported.

Review

The State of Florida requests a section 18 to use AGRI-MEK 0.15 EC (Avermectin) on strawberries to control twospotted spider-mite. The inerts in the formulation are cleared under 180.1001.

The formulation will be applied at a rate of 16 fluid ounces of product per acre. Application is to be made by ground equipment only.

Approximately 5400 acres in 1989 will be treated. This will result in a total of 405 pounds of active ingredient.

The label (attached) for the section 18 has been reviewed. The label signal word should be Warning and precautionary statements have to be changed to be correct. The new restricted use label is correct and supported by the data base.

The toxicology data base has been presented in previous memoranda (one-liners are attached). There are no data gaps.

Tolerances for avermectin and the delta-8,9-isomer have been established for citrus and cotton (contact George LaRocca, PM 15, for details).

The ADI is based on the NOEL of 0.12 mg/kg/day in the 2-generation rat reproduction study. The LEL is 0.40 mg/kg/day and the effects are increased incidence of dead pups at birth, decreased viability and lactation indices, decreased pup body weight, and increased incidence of retinal abnormalities in pups.

A 300-fold uncertainty factor (approved by both the HED and Agency RfD Committees) was utilized. This uncertainty factor provides an MOS of 100 for maternolethality in CF_1 mice

(NOEL = 0.05 mg/kg/day), an MOS of 100 for cleft palate for the delta-8,9-isomer (NOEL = 0.06 mg/kg/day), and an MOS of 300 for pup death. A 300 MOS for reproductive effects was needed because of the extreme seriousness of the reproductive effects (pup death and retinal abnormalities) at the LEL of 0.40 mg/kg/day in the rat reproduction study.

Calculation of ADI

$$ADI = \frac{NOEL}{SF}$$

$$ADI = \frac{0.12 \text{ mg/kg/day}}{300}$$

$$ADI = 0.0004 \text{ mg/kg/day}$$

The oncogenic potential of avermectin is negative in rats and mice in studies conducted at the MTD.

It should be noted that EEB has additional concerns regarding the impact of avermectin on ecological systems.

Attachments

Avermectin toxicology review

Page _____ is not included in this copy.

Pages 4 through 10 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

TOXCHEM NO. 063AB- Avermectin B1 FILE LAST PRINTED: 06/01/89

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Teratology Species: mice Merk Sharpe & Dohme 84-722-0; 1/8/86	Avermectin B, delta 8,9-isomer; Lot# 03, 99% pure	265564	Maternal NOEL < 1.5 mg/kg (mortality). Teratogenic NOEL < 1.5 mg/kg/day (cleft palate). Doses: 1.5, 3.0, 6.25, 12.5, 25 & 50 mg/kg/day in preg. CF1 mice on GD 6-15.		Minimum 005850
Teratology Species: mice Merk Sharpe & Dohme 84-722-1; 4/29/85	Avermectin B, delta-8,9 isomer	265564	Maternal NOEL = 0.1 mg/kg/day. Maternal LEL = 0.5 mg/kg/day Teratogenic NOEL = 0.05 mg/kg/day; Teratogenic LEL = 0.1 mg/kg/day (cleft palate). A/D ratio = 0.1/0.05 = 2.0. Doses tested in CF1 strain by gavage: 0.05, 0.1, 0.5, & 1 mg/kg on GD6-15		Minimum 005850
Teratology Species: mice Merk Sharpe & Dohme 85-710-0; 6/4/85	Avermectin B, delta-8,9 isomer; Lot 03; 99% pure	265564	Maternal > 0.06 mg/kg (HDT). Teratogenic NOEL > 0.06 mg/kg (HDT). Doses: 0, 0.01, 0.03, and 0.06 mg/kg/day in CF1 mice by gavage on GD 6-15		Minmum 005850
Teratology Species: mice Merk Sharpe & Dohme 85-710-1; 9/16/85	Avermectin B, delta-8,9 isomer; lot 3; 99% pure	265564	Teratogenic LEL = 0.1 mg/kg (cleft palate). Teratogenic NOEL = 0.03 mg/kg in CF1 mice. Doses: 0, 0.03, 0.1, & 0.5 mg/kg/day in CF1 mice. Maternal NOEL = 0.1 mg/kg; Maternal LEL = 0.5 mg/kg (mortality in 1/25) A/D ratio = 0.1/0.03 = 3.33		Minimum 005850
Teratology Species: mice Merk Sharpe & Dohme 84-721-0; 3/4/85	Avermectin B1b (component of MK-0936 technical)	265572	Developmental NOEL > 0.075 mg/kg. Maternal NOEL = 0.05 mg/kg/day Maternal LEL = 0.075 mg/kg/day (mortality in 2 mice after 6 doses). Doses: 0, 0.025, 0.05, 0.075, 0.1 mg/kg/day in CF1 mice by gavage on GD 6-15.		Accepatble 005850
Reproduction-2 generation Species: rat Argus Research Labs TT82-9010; 5/10/84	MK-0936 Tech. Lot L-676	265576	Maternal NOEL = 0.12 mg/kg/day. LEL = 0.40 mg/kg/d (HDT). retinal rosette in F1b & F2b weanlings, incr. in dead pups at birth, decr. viability indices, decr. lactation indices & decr. body wt. Doses in Sprague Dawley: 0, 0.05, 0.12, 0,40 mg/kg/day.		Supplementary 005850 Minimum 006447
Teratology Species: rat Merk Sharpe & Dohme TT#82-705-1; 11/10/82	MK-0936 Tech. 94%; Lot# L-686,863-00V50	249152	Range finding: Levels tested by gavage in Sprague Dawley str: 0, 0.25, 0.5, 1.0 & 2.0 mg/kg/day [redacted] Maternal NOEL = 1.0 mg/kg Maternal LEL = 2.0 mg/kg/day		Supplementary 004114
Teratology Species: rat Merk Sharpe & Dohme TT#82-705-0; 11/20/82	MK-0936 Tech. 94%; Lot L-676,863-00V50	249152	Teratogenic NOEL > 1.6 mg/kg/day (HDT). Maternal NOEL > 1.6 mg/kg/day Fetotoxic NOEL > 1.6 mg/kg/day. Doses by gavage in Sprague Dawley str: 0, 0.4, 0.8, & 1.6 mg/kg/day.		Supplementary 004114 Minimum 004335
Teratology Species: rat Merk Sharpe & Dohme TT77-701-0	Avermectin B1a	247291	PILOT STUDY: Teratogenic NOEL = 1.6 mg/kg/day. Terata LEL = 3.2 mg/kg/d incr. in the number of visceral & skeletal malformations at 3.2 mg/kg/day Levels tested = 0.8, 1.6, 3.2 mg/kg/day by gavage in CRCD str.		Supplementary 001815

INERT INGREDIENT INFORMATION IS NOT INCLUDED

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Teratology Species: rabbit Merk Sharpe & Dohme TT# 82-706-1	MK-0936 Tech. 94% pure Lot L-767863-00V50	249152	RANGE FINDING: Maternal NOEL = 2.0 mg/kg/day. Mat LEL = 3.0 mg/kg/day		Supplementary 004114
Teratology Species: rabbit Merk Sharpe & Dohme TT #82-706-01	MK-0936 Tech 84% pure; Lot L-767863-00V50	249152	Teratogenic NOEL = 1.0 mg/kg/day. Terata LEL = 2.0 mg/kg/day (cleft palate and clubbed foot). Developmental NOEL = 1.0 mg/kg/day. Developmental LEL = 2.0 mg/kg/day (delayed ossification of sternebrae, metacarpals and phalanges). Maternal NOEL = 1.0 mg/kg/day. Maternal LEL = 2.0 mg/kg/day (decr. body weight. food consumption & water consumption).		Supplementary 004114 Minimum 004335 007227
Teratology Species: rabbit Merk Sharpe & Dohme TT76-24-A;77-702-0	Avermectin B1a	247291	PILOT STUDY: Teratogenic NOEL = 0.5 mg/kg/day. T Teratogenic LEL = 1.0 mg/kg/day (incr. in number of visceral malformation & skeletal variations). Doses (gavage) 0.25, 0.5, 1, 2, 4 mg/kg.		Supplementary 001815
Teratology Species: mice Merk Sharpe & Dohme TT# 77-705-0	C-076 (Avermectin B1a) Lot P 20	246894	Teratogenic NOEL = 0.2 mg/kg/day. Teratogenic LEL = 0.4 mg/kg/day (cleft palate). Maternal NOEL < 0.1 mg/kg/day (mortality). Doses by gavage in CF1 str - 0, 0.1, 0.2, 0.4 & 0.8 mg/kg/day.		Supplementary 001535 Minimum 005850
Teratology Species: mice Merk Sharpe & Dohme TT# 76-723-0	C-076 (Avermectin B1a)	246894	Teratogenic NOEL < 0.4 mg/kg/day (cleft palate) Note - fetuses at 0.1 and 0.2 mg/kg were not examined. Maternal NOEL < 0.1 mg/kg (mortality) Levels tested by gavage: 0.1, 0.2, 0.4 & 0.8 mg/kg/day.		Supplementary 001535
Teratology Species: mice Merk Sharpe & Dohme TT# 76-723-3	C-076 (Avermectin)	246894	Teratogenic NOEL < 0.2 mg/kg/day (cleft palate) NOte - fetuses at 0.1 mg/kg were not examined. Maternal NOEL < 0.1 mg/kg/day (LDT) (mortality). Doses (gavage): 0, 0.1, 0.2, 0.4, & 0.8 mg/kg/day.		Supplementary 001535
Reproduction-1 generation Species: rat Merk Sharpe & Dohme TT# 77-706-0	C-076 (Avermectin)		NOEL < 0.5 mg/kg/day (LDT). (decr. pup survival & growth rate between 1 to 21 days; delay in opening of eyes). Levels tested by gavage in Charles River CD str. 0, 0.5, 1.0 & 3.0 mg/kg/day (only females).		Supplementary 001535
Reproduction-1 generation Species: rat Merk Sharpe & Dohme TT# 77-712-0	C-076 (Avermectin)	246894	NOEL = 0.1 mg/kg/day. LEL = 0.2 mg/kg/day (one pup had spastic movements, decr. pup wts; delayed incisor eruption). Levels tested by gavage: 0, 0.1, 0.2, & 0.4 mg/kg/day. This study is considered a teratology study with only postnatal evaluation & not a true reproduction study since males were not tested.		Supplementary 001535

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CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Teratology-10 day oral Species: mice pregnant Merk Sharpe & Dohme TT# 77-717-1	C-076 (Avermectin) Lot P 34	246894	Maternal NOEL = 0.05 mg/kg/day. Maternal LEL = 0.075 mg/kg/day (mortality Levels tested by gavage in CF str: 0.025, 0.050, 0.075 & 0.1 mg/kg/day.		Minimum 001535
Terat-10 day Mat feeding tox. Species: mice Merk Sharpe & Dohme TT 83-705-1; 4/11/84	MK-0936 Tech.	073759 073761	NOEL = 0.1 mg/kg/day. LEL = 0.30 mg/kg/day (death, tremors). Levels tested: 0, 0.1, 0.3, 0.6 mg/kg/day in pregnant CF1 strain.		Supplementary 004751 Minimum 005850
Teratology Species: mouse Merk Sharpe & Dohme TT88-713-0; 11/1/88	Citrus derived polar degr adates of abamectin (L-93 0,463)	409127-01	Maternal NOEL > 1.0 mg/kg/day (HDT); Developmental NOEL > 1.0 mg/kg/ day (HDT). Doses = 0 (vehicle control), 100 mg/kg/day (carrier con- tol), and 0.25, 0.50, and 1.0 mg/kg/day (citrus-derived polar degra- dates) in CF1 mice. See review for details.		Minimum 007081
Teratology Species: rat Merk Sharpe & Dohme TT87-715-0; 6/7/88	Delta-8,9-isomer of abame ctin L-652,280-000N005 (91.6% pure)	407134-03	Negative for developmental effects up to 1.0 mg/kg/day (HDT). NOEL for maternal toxicity is 1.0 mg/kg/day (HDT). Doses = 0, 0.25, 0.50, and 1.0 mg/kg/day. Sprague-Dawley rats by gavage during days 6 to 17 of gestation.		Minimum 007080
Reproduction-1 generation Species: rat Merk Sharpe & Dohme TT87-716-0; 6/7/88	Delta-8,9-isomer of abame ctin L-652,280-000N005 (91.6% pure)	407134-04	The NOEL for reproductive effects (parental females and pups only) is 0.40 mg/kg/day (HDT). Males were not tested. Doses = 0, 0.06, 0.12, 0.40 mg/kg/day to Sprague-Dawley rats by daily oral gavage.		Supplementary 007080
Teratology Species: mouse Merk Sharpe & Dohme TT87-717-0; 6/7/88	Polar degradates of abame ctin L-930,406-000N001 (polar degradates from th in film dish photolysis)	407134-06	Negative for developmental effects up to 1.0 mg/kg/day (HDT). NOEL for maternal toxicity is 1.0 mg/kg/day (HDT). Doses = 0, 0.25, 0.50, and 1.0 mg/kg/day. CF1 mice by gavage during days 6 to 15 of gestation.		Minimum 007080
Teratology Species: mice Merk Sharpe & Dohme TT-77-706-0	Avermectin B1a (component of MK-0936 Tech.)	265572	Levels tested: 0, 0.025, 0.05, 0.075 and 0.1 mg/kg/day in CF1 strain by gavage on gestation days 6-15. Developmental NOEL > 0.075 mg/kg/day. Maternal NOEL = 0.05 mg/kg/day. Maternal LEL = 0.075 mg/kg/day (mortality in 2 mice after 6 doses).		Acceptable 005850
Feeding-1 year Species: dog Merk Sharpe & Dohme TT#82-104-0; 9/15/87	MK-0936 Tech.	265574 403755-10	NOEL = 0.25 mg/kg/day. LEL = 0.50 mg/kg/day (high incidence of mydriasis in males & females. Mortalities at 1.0 mg/kg/day. Doses (in diet) of beagles = 0.25, 0.50 and 1.0 mg/kg/day.		Supplementary 005850 Guideline 007093
Feeding/oncogenic-2 year Species: rat Merk Sharpe & Dohme TT#82-099-0; 8/27/85	MK-0936 Tech	265575 400696-01 405178-01	Oncogenic potential: negative up to 2.0 mg/kg/day (HDT). NOEL = 1.5 mg/kg/day. LEL = 2.0 mg/kg/day (MTD). Effects at LEL were treatment-induced tumors in both sexes. Body wt. increases in males & females at all doses. Doses: 0, 0.75, 1.5 & 2.0 mg/kg/day in Sprague Dawley rats (levels of test material in diets adjusted biweekly).		Supplementary 005850 Minimum 007093

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CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Feeding/Oncogenic 21 months Species: mice Merk Sharpe & Dohme TT/83-002-0-1,2,3; 8/27/85	MK-0936 Tech (Avermectin B1)	400696-02 403755-12	Oncogenic potential: negative up to 8 mg/kg/day (HDT). NOEL = 4 mg/kg/day LEL = 8.0 mg/kg/day (MTD). Effects at LEL were increased mortality in males, tremors and body weight loss in females, dermatitis in males and extramedullary hematopoiesis in spleen of males. Doses: 0, 2.0, 4.0, and 8.0 mg/kg/day in CD-1 mice (levels of test material in diets adjusted biweekly).		Minimum 007093
Dermal- 9 days Species: rabbit Merk Sharpe & Dohme TT# 83-2967	MK-0936 EC formulation Avid		Toxicity greater in rabbits unoccluded at 1000 mg/kg than in rabbits occluded at 1000 mg/kg.		Supplementary 003967
Dermal- 23 days Species: rabbit Merk Sharpe & Dohme TT# 83-066-0; 5/4/84	MK-0936 EC formulation Avid		NOEL < 250 mg/kg (LDT) (testicular degeneration). Doses: 0, 250, 500 & 1000 mg/kg.		Minimum 003967
Dermal- 24 days Species: rabbit Merk Sharpe & Dohme TT 83=2947	MK-0936 EC formulation Avid		NOEL < 125 mg/kg (LDT) (testicular degeneration). Levels tested: 0, 125, 250, 500 & 1000 mg/kg.		Minimum 003967
Feeding-18 week Species: dog Merk Sharpe & Dohme TT 76-073-0	C-076 (Avermectin)	246895	NOEL = 0.25 mg/kg/day. LEL = 0.5 mg/kg/day (body tremors, one death, pathology of liver, decreased body weight). Levels tested by gavage in beagles: 0, -.24, 0.5, 2.0 & 8.0 mg/kg/day.		Supplementary 001535 Minimum 004114
Feeding-98 day Species: rat Merk Sharpe & Dohme TT 77-043-0	C-076 (Avermectin) Lot P 22	246895	NOEL > 0.4 mg/kg/day (HDT) Levels tested by gavage = 0, 0.1, 0.2, 0.4 mg/kg/day. Rats used in this study had previously been exposed in utero to the test material at the respective concentrations: 0, 0.01, 0.2 & 0.4 mg/kg/day.		Supplementary 001535 Minimum 004114
Dermal-3 week Species: rabbit	Avermectin Tech		Requirement is waived.		003252
Dermal-3 week Species: rabbit Merk Sharpe & Dohme TT-84-045-0; 8/28/84	MK-0936 EC based formulation	254601	NOEL for testicular effects = 125 mg/kg/day. LEL = 250 mg/kg/day (decr. testicular wt. & histological seminiferous tubule degeneration.) Levels tested: 0, 31, 62.5, 125, 250, 1000 mg/kg in N. Z. White strain.		Minimum 004331

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Metabolism Species: rat Merk Sharpe & Dohme ARM-1; 9/83	Avermectin B1, tritium & C14 labelled.		68.7%-81.6% of label is excreted in the feces by day 7. T1/2 is 1.2 days.		Supplementary 003967
Dissimilation chemicals			517T (L-652, 871-00N01 polar metabolite). 517U (L-652-280-00N02 non-polar metabolite).		
Dermal absorption Species: monkey Merk Sharpe & Dohme PS#1; 6/2/86	Avermectin B1a-tritium labelled.	265590	The maximum dermal absorption of Avermectin B1a is 1% of appl. dose.		Supplementary 005850
Eff. of restraint testes morph Species: rabbit Merk Sharpe & Dohme TT# 84-088-0	None	073759	Restraint of rabbits produced testicular degeneration.		Acceptable 004395
Acute oral neurotoxicity Species:	Avermectin tech		Data requirement waived (EPA Guideline 81-7).		005648
Metabolism Species: rat Merk Sharpe & Dohme 7/22/85	MK-936 H3-Tech.; MK-936-C14 tech.	073768	No bioaccumulation; two metabolites found, 2,4-OH-ME-B1a and 3		Minimum 004751
Antidote Species: dog MSD, TT$84-085-0 12/10/84	MK-0936 Tech.	255978	Ipecac given at 15 min. after dose of MK-0936 induces vomiting and results in no comas or death in 21 dogs.		Acceptable 004395
Antidote Species:	Avermectin tech		Data requirement is waived for determining a specific antidote.		
Mutagenic-Ames Species: microbes Merk Sharpe & Dohme TT#85-8051; 3/11/86	MK-0936 Tech.	265568	Not mutagenic in Ames assay. Doses: 0, 3, 10, 30, 100 & 1000 ug/plate with & without S-9.		Acceptable 005850

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CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Mutagenic-Ames Species: microbes Merk Sharpe & Dohme TT#85-8005; 5/1/86	MK-0936 Tech.	265569	MK-0936 is not mutagenic in Ames assay without metab. activ.; the system was not tested with metab. activ. Doses: 0, 100, 300, 1000, 3000 & 10,000 ug/plate.		Accep (w TT85-8051 005850
Mutagenic-chromosome aberr. Species: CHO cells Merk Sharpe & Dohme TT#85-8631; 3/11/86	MK-0936 Tech.	265570	Avermectin was not mutagenic in vitro in CHO cells both with & without metab. activ.		Acceptable 005850
Mutagenic-Ames Species: Merk Sharpe & Dohme TT 82-8013; 8/30/83	Avermectin B1 Tech.		Not mutagenic in presence of S-9 activation. Mutagenicity without S-9 activation could not be evaluated due to absence of positive control.		Acceptable (S-9) 003967 Unacc (no S-9) 003967
Mutagenic-bone marrow cells Species: mice Merk Sharpe & Dohme TT# 83-900-6; 6/83	Avermectin Tech.		No chromosome aberrations in male mice at doses of 1.2 & 12.0 mg/kg. Female mice not tested.		Acceptable (males) 003967
Mutagenic Species: rat hepatocytes Merk Sharpe & Dohme TT828520;23;25; 4/12/83	Avermectin Tech.		*Under conditions of the study Avermectin (0.3 & 0.6mM) caused an induction of single strand DNA breaks in rat hepatocytes in vitro; there was no effect at lower doses. No effect was observed when the assay was carried out on hepatocytes from rats dosed in vivo at the LD50 dose level (10.6 mg/kg).		Acceptable 003967
Mutagenic Species: mammalian cells Merk Sharpe & Dohme TT82-8506,10,19; 3/8/83	Avermectin Tech.		MK-0936, Avermectin, was not mutagenic for V-79 cells under the condition of the assay, but in the presence of S-9 appeared to have a mutagenic potential, provided the test cells had an approp. level of sensitivity.		Acceptable 003967
Mutagenic-Ames Species: Merk Sharpe & Dohme TT76-8052	C-076 (B1a)	246894	Negative for mutagenicity.		Acceptable 001535
Mutagenic-Ames Species: bacteria Merk Sharpe & Dohme TT87-8046; 6/7/88	Delta-8,9-isomer of abamectin L-652,280-000N005 (91.6% pure)	407134-02	Negative for mutagenicity up to 3000 ug/plate in S. typhimurium TA97a, TA98, TA100, TA1535 and in E. coli WP 2 uvrA and WP 2 uvrA pKM101 (both with and wiyhout metabolic activation).		Acceptable 007080
Mutagenic-Ames Species: bacteria Merk Sharpe & Dohme TT87-8047 and; 6/7/88	Polar degradates of abamectin L-930,406-000N001 (polar degradates from th in film dish photolysis)	407134-05	Negative for mutagenicity up to 10,000 ug/plate in S. typhimurium TA97a, TA98, TA100, TA1535 and E. coli WP2, WP2uvrA, and WP2uvrA pKM 101 (both with and without metabolic activation).		Acceptable 007080

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CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Acute Dermal LD50 Species: rabbit Merk Sharpe & Dohme TT81-3021; 3/16/83	Avermectin (Technical)		LD50 = > 1600 mg/kg. Levels tested : 100, 200, 400, 800,and 1600mg/kg		Supplementary 003967
Dermal sensitization Species: guinea pig Merk Sharpe & Dohme TT83-2506; 4/15/83	Avermectin (Technical)		Negative for skin sensitization.		Minimum 003967
Acute Dermal LD50 Species: rabbit Merk Sharpe & Dohme TT83-031-0	Avermectin (MK-0936) 2.2%		One death . LD50 > 2000 mg/kg (only level tested).	3	Minimum 003967
Acute oral LD50 Species: rat Merk Sharpe & Dohme TT82-097-0	Avermectin (MK-0936) 2.2%		LD50 = 0.7222 ml/kg. Levels tested : 0, 25, 0.40, 0.64, 1.02, and 1.63 ml/kg.	3	Minimum 003967 005288
Primary dermal irritation Species: rabbit Merk Sharpe & Dohme TT-82-3036; 12/2/82	Avermectin (MK-0936)2.2%		Slight 1.63 ml/kg.	3	Minimum 003967
Primary eye irritation Species: rabbit Merk Sharpe & Dohme TT82-3035; 12/6/82	Avermectin(MK-0936) 2.2%)		Conjunctivitis and iritis which cleared after 8 days.	3	Minimum 003967
Acute inhalation LC50 Species: rat Hazleton 284-126; 5/22/79	Avermectin MK-0936) 2.2%		No deaths . LC50 > 5.73 ml/kg (nominal concentration only).	4	Supplementary 003967
Acute oral LD50 Species: rat Merk Sharpe & Dohme TT81-2879; 8/7/81	Avermectin B1 (0.022%)		No deaths. LD50 > 5.0 gm/kg. [redacted]	3	Minimum 003984
Acute Dermal LD50 Species: rabbit Merk Sharpe & Dohme TT81-2877; 8/31/81	Avermectin B1 (0.022%)		No deaths . LD50 > 2.0 gm/kg . [redacted]	3	Minimum 003984

INFORMATION WHICH MAY REVEAL THE IDENTITY OF AN INERT INGREDIENT IS NOT INCLUDED

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CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Primary dermal irritation Species: rabbit Merk Sharpe & Dohme TT83-2864; 2/1/84	Avermectin B1 (0.022%)		Slight conjunctivitis in both washed and unwashed eyes which were normal at 24 hr.[redacted]	3	Minimum 003984
Primary dermal irritation Species: rabbit Merk Sharpe & Dohme TT83-2864; 2/1/84	Avermectin B1 (0.022%)		No irritation.[redacted]	4	Minimum 003984
Acute oral LD50 Species: mice Merk Sharpe & Dohme	Avermectin C-076 (B1A)	246894	LD50 = 13.6-23.8 mg/kg.	1	Supplementary 001535
Acute oral LD50 Species: rat Merk Sharpe & Dohme	Avermectin C-076 (B1A)	246894	LD50 = 10.6 (7.7 - 14.5) mg/kg (male). LD50 = 11.3 (7.5 - 17.1) mg/kg (female) LD50 = 1.5 (1.1 - 2.2) mg/kg (weanling)	1	Supplementary 001535
Acute oral LD50 Species: mice Merk Sharpe & Dohme TT767231,TT767231	Avermectin C-076 (B1A) Avermectin C-076 (B2)	246894	Range finding . Death in mice given 0.1 , 0.25 , 1.0 , and 8.0 mg/kg/day of 0.76 (B1A) . No body weight decrease at 0.1 , 0.25 , 0.5 mg/kg/day .		Supplementary 001535
Acute inhalation LC50 Species: rat Bio/dynamics Inc. TT83-7651; 2/24/84	Avermectin MK-0936 (2.2%)	252914	LC50 = 1.033 (0.634 - 1.683) mg/L (M) LC50 = 1.141 (0.594 - 2.193) mg/L (F) LC50 = 1.062 (0.742 - 1.521) mg/L (M&F) Gravimetric: Levels tested: 0.033 - 6.5 mg/L	3	Minimum 005288
Acute Dermal LD50 Species: rabbit Merk Sharpe & Dohme TT83-064-0; 2/8/84	Avermectin (MK-0936) Technical	255978	LD50 = > 2000 mg/kg . No deaths .	3	Minimum 004394
Acute oral LD50 Species: mice Merk Sharpe & Dohme TT84-112-0; 4/9/86	Delta-8,9-isomer of Abamectin (99% pure)	265564	LD50 = >80 mg/kg (both sexes). (3/10 and 1/10 deaths in male and female, respectively at 80 mg/kg) .	2	guideline 005850
Acute oral LD50 Species: mice Merk Sharpe & Dohme TT84-2842; 6/23/86	Abamectin (MK-0936 Technical) 94% pure	265567	Pregnant CF1 mice : LD50 = 19.0 (14.0 - 25.7) mg/kg . Nonpregnant CF1 mice : LD50 = 41.3 mg/kg . Doses = 0 , 5 , 20 , 40 , and 80 mg/kg .	1	Minimum 005850

INFORMATION WHICH MAY REVEAL THE IDENTITY OF AN INERT INGREDIENT IS NOT INCLUDED

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Acute oral LD50 Species: mice Merk Sharpe & Dohme TT85-2593; 6/23/86	Abamectin MK-0936 (Tech.94.0%)	265567	Pregnant CF1 mice : LD50 = 11.8 (8.3 - 15.8) mg/kg . Nonpregnant CF1 mice : LD50 = 15.0 (10.2 - 21.1) mg/kg . Doses = 0 , 5 , 10 , 20 , 40 , and 80 mg/kg .	1	Minimum 005850
Acute oral LD50 Species: mice Merk Sharpe & Dohme TT84-107-0; 6/9/85	Avermectin B1B (MK-0936 Tech.)	265572	LD50 = 11.4 (7.6 - 16.1) mg/kg (M) LD50 = 19.8 (12.8 - 31.0) mg/kg (F) Doses = 0 ,5 , 20 , 40 , and 80 mg/kg (CF1 mice)	1	Minimum 005580
[redacted]					
Primary eye irritation Species: rabbit Merk Sharpe & Dohme TT88-085-0; 11/15/88	Avid 0.15EC	409125-01	Moderately irritating (19-43/110) in unwashed eyes and same (17-41/110) in washed eyes; corneal opacity, iritis and conjunctivitis, cleared in 9/10 eyes by day 14. One rabbit's washed eye did not clear by day 14.	2	Minimum 007082

INFORMATION REFERENCING AN UNREGISTERED PRODUCT IS NOT INCLUDED

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