US EPA ARCHIVE DOCUMENT

122804
SHAUGHNESSEY NO.

2
REVIEW NO.

EEB BRANCH REVIEW

DATE: IN 8-26-83 OUT 10/14/83

FILE OR REG. NO. 618-EUP-10

PETITION OR EXP. PERMIT NO.

DATE OF SUMBMISSION 7-18-83

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RD ACTION CODE/TYPE OF REVIEW 701/EUP

TYPE PRODUCT(S): I, D, H, F, N, R, S Insecticide

DATA ACCESSION NO(S).

PRODUCT MANAGER NO. G. LaRocca (15)

PRODUCT NAME(S) Avermectin B. (MK-936)

COMPANY NAME Merck Sharp & Dohme Research Laboratories

SUBMISSION PURPOSE Submission of data (avian) to support EUP and as discussed in 4-28-83 meeting with EEB representatives

SHAUGHNESSEY NO.	CHEMICAL, & FORMULATION	% A.I.
122804	Avermectin B1	91%

Avermectin

The purpose of this submission was to provide more toxicity data.

103 Toxicological Properties

Three studies were submitted and validated.

103.2.1 Avian Acute Oral LD50

Test Species: Bobwhite Quail

Test Material: 91% pure Avermectin

LD50: >2000 mg/kg (equivalent to a 100% pure a.i.)

Category: Core

103.2.2 Avian 8-day Dietary LC50

Test Species: Bobwhite Quail

Test Material: 91% pure Avermectin

LC50: 3102 ppm (adjusted to equal a 100% a.i. test material).

Category: Core

Test Species: Mallard Duck

Test Material: 91% pure Avermectin

LC50: 383 ppm (adjusted to 100% a.i. equivalent)

Category: Core

107 Conclusions

The three studies submitted fulfilled the guideline requirements for the 3 basic avian studies.

Daniel Rieder 10/14/83
Daniel Rieder
Wildlife Biologist
Ecological Effects Branch, HED

Norman Cook 10-14-83
Norm Cook
Head, Section 2
Ecological Effects Branch, HED

Norman Cook for 10-14-83
Clayton Bushong
Branch Chief
Ecological Effects Branch, HED

DATA EVALUATION REPORT

1. CHEMICAL: Avermectin (MK-936)

2. FORMULATION: 91% a.i.

Shaughnessey Number:

3. CITATION: Beavers, Joann B. 1983. An Acute Oral Toxicity in Bobwhite Quail with MK-936. An unpublished report prepared by Wildlife International Ltd. for Merck Sharp & Dohme Research Laboratories. Acc# 250762

4. REVIEWER: Daniel Rieder
Wildlife Biologist
EEB/HED

5. REVIEW DATE: 10/6/83

6. TEST TYPE: Avian LD_{50}

   A. Species: Bobwhite Quail

   B. Material: 91% pure MK-936

7. RESULTS:

LD_{50} >2000 mg/kg. The no-effect level was less than 62.5 mg/kg. Mortalities occurred as low as 250 mg/kg.

8. REVIEWERS CONCLUSION:

This study meets guideline requirements for an avian LD_{50} and shows that MK-936 is practically non-toxic to birds.

METHODS

The test material was labeled as MK-936 technical 91% a.i.

Ten (5 male & 5 female) 12-month old bobwhite quail were tested in each of 6 treatment groups and a control. The test material was dispersed in corn oil which was intubated into the crop. The control birds received a corresponding volume of corn oil. Food was withheld for 15 hours prior to treatment. Dosages were adjusted so the reported doses are equivalent to 100% a.i.

The birds were housed indoors in cages (72 x 90 x 24 cm high). Temperature ranged from 71°F ± 4°F; Average relative humidity was 86%. The photoperiod was 17 hrs of light per day.

The birds were observed daily throughout the study and a record of mortality and toxic symptoms maintained. All birds that died during the study were subject to gross necropsy.

See attachment 1 for detailed procedures.

RESULTS

No mortality occurred in the control.

Dosage mg/kg in 100% a.i.	Mortality %
Control	0
62.5	0
125	0
250	10
500	40
1000	10
2000	40

See attachment 1 for daily mortality, results of body weight measurements and estimations of food consumption. See attachment 2 for the EEB calculations of the LC_{50}.

REVIEWERS EVALUATION

The LD_{50} is clearly greater than 2000 mg/kg. This study fulfilled guideline requirements and showed that Avermectin was practically non-toxic to Quail when administered orally. There was irregular dose mortality response but there was never greater than 50% mortality at any level.

CONCLUSION

Category: Core

Avermectin science review

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___ 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

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

X FIFRA registration data

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Attachment 2
EEB statistical analysis

AVERMECTIN MK-936 QUAIL ACUTE ORAL LD50
****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
2000	10	4	40	37.6953
1000	10	1	10	1.07422
500	10	4	40	37.6953
250	10	1	10	1.07422
125	10	0	0	.0976563
62.5	10	0	0	.0976563

THE BINOMIAL TEST SHOWS THAT 250 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 0

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	.565928	1	.187035

SLOPE = 1.22644
95 PERCENT CONFIDENCE LIMITS = .303811 AND 2.14907

LC50 = 3110.62
95 PERCENT CONFIDENCE LIMITS = 1232.32 AND 514503

LC10 = 286.635
95 PERCENT CONFIDENCE LIMITS = 17.2979 AND 620.778
****

DATA EVALUATION REPORT

1. CHEMICAL: Avermectin B1 (MK-936)

2. FORMULATION: 91% a.i.

   Shaughnessey Number:

3. CITATION: Beavers, Joann B. 1983. An Eight-Day Dietary LC_{50} in Bobwhite Quail with MK-936. A unpublished report prepared by Wildlife International Ltd. for Merck Sharp & Dohme Research Laboratories. Acc # 250763.

4. REVIEWER: Daniel Rieder
   Wildlife Biologist
   EEB/HED

5. REVIEW DATE: 10/6/83

6. TEST TYPE: Avian dietary LC_{50}

   A. Species: Bobwhite Quail

   B. Material: MK-936 is 91% a.i.

7. RESULTS: The reported LC_{50} = 3102 ppm (95% C.L. = 2338 to 4393 ppm)

8. REVIEWERS CONCLUSION:

   This study meets guideline requirements for an avian LC_{50} and shows that Avermectin is slightly toxic to some upland game birds.

METHODS

The test material was MK-936 technical, 91% a.i. The test animals were 14-day old bobwhite quail. Ten birds were tested per level at 6 concentrations. Fifty birds were tested in an untreated control. Cages were 72 x 90 x 23 cm high; Appropriate diet and water were provided ad libitum; Photoperiod was 14 hours of light per day. Acetone was used as a solvent. The reported concentrations were adjusted to be equivalent to a 100% a.i. test material. The birds were fed the treated feed for 5 days then maintained on a basal (toxicant free) diet for 3 days.

Body weights and food consumption were recorded. See attachment 1 for detailed description of procedures.

RESULTS

No mortality occured in the control test group.

Concentration (ppm)	Mortality/Tested
288	0/10
511	0/10
910	0/10
1620	1/10
2876	5/10
5114	8/10

See attachment 1 for the reported results.

See attachment 2 for the statistical analysis performed "in house" using the "TOXANAL" LC_{50} generating program on the Lexitron.

REVIEWERS EVALUATION

The statistical analysis show that the LC_{50} for this group is approximately 3102 ppm with 95% C.L. of 2344 to 4415 ppm.

The study was done using acceptable protocol.

CONCLUSION

Category: Core

Avermectin science review

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Attachment 2
EEB statistics

AVERMECTIN MK-936 QUAIL 8-DAY DIETARY LC50
****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
5114	10	8	80	5.46875
2876	10	5	50	62.3047
1620	10	1	10	1.07422
910	10	0	0	.0976563
511	10	0	0	.0976563
288	10	0	0	.0976563

THE BINOMIAL TEST SHOWS THAT 1620 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 2876

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
2	.370772	3023.92	2118.57	4576.76

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
7	.28439	1	.989139

SLOPE = 4.45345
95 PERCENT CONFIDENCE LIMITS = 2.0785 AND 6.82839

LC50 = 3102.43
95 PERCENT CONFIDENCE LIMITS = 2344.15 AND 4415.94

LC10 = 1608.9
95 PERCENT CONFIDENCE LIMITS = 762.272 AND 2167.17
****

DATA EVALUATION REPORT

1. CHEMICAL: Avermectin MK-936

2. FORMULATION: 91% a.i.

   Shaughnessey Number:

3. CITATION: Beavers, Joann B. 1983. An Eight-Day Dietary LC_{50} in Mallard Duck with MK-936. An unpublished report prepared by Wildlife International Ltd. for Merck, Sharp & Dohme Research Laboratories. Acc # 250761

4. REVIEWER: Daniel Rieder
   Wildlife Biologist
   EEB/HED

5. REVIEW DATE: 10/11/83

6. TEST TYPE: Avian 8-day Dietary LC_{50}

   A. Species: Mallard Duck

   B. Material: 91% a.i. Avermectin

7. RESULTS:

   LC_{50} = 383.6 ppm 95% C.L. = 302 to 486

8. REVIEWERS CONCLUSION:

   The study meets guideline requirements for an avian LC_{50} and shows that Avermectin is nightly toxic to some waterfowl.

METHODS

See attachment 1 "Materials and Methods" for a detailed description of procedure provided by the registrant.

RESULTS

See attachment 1 "Results" for the reasearchers account of the test results to include mortality data, food consumption and weight changes. The reported LC_{50} was 385 ppm (95% C.L. = 302 to 487 ppm)

REVIEWERS EVALUATION

See attachment 2 for the statistical calculations. These agree with the reported statistics. The no-effect level is 162 ppm. This is based on food consumption, weight gain and toxic symptoms exhibited by the test birds.

The study followed acceptable protocol. Note that reported concentrations are 100% a.i. equivalent.

CONCLUSION

Category: Core

Avermectin science review

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Attachment
EEB statistical analysis

AVERMECTIN MK-936 MALLARD 8-DAY DIETARY LC50
****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
1620	10	10	100	.0976563
910	10	10	100	.0976563
511	10	8	80	5.46875
288	10	2	20	5.46875
162	10	0	0	.0976563

THE BINOMIAL TEST SHOWS THAT 162 AND 910 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 383.625

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
4	.113806	384.121	275.982	496.831

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
8	.316771	1	.991468

SLOPE = 7.2564
95 PERCENT CONFIDENCE LIMITS = 3.17232 AND 11.3405

LC50 = 383.641
95 PERCENT CONFIDENCE LIMITS = 302.456 AND 486.705

LC10 = 256.393
95 PERCENT CONFIDENCE LIMITS = 141.415 AND 319.968
****