6-14-91

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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

Subject: Review of Avian Single Dose Oral LD50 for S-Fenvalerate

From: James W. Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C) 6/14/91

To: Lois Rossi, PM 74
Reregistration Branch
Special Review and Reregistration Division (H7508C)

The Ecological Effects Branch (EEB) has completed its review of the avian single dose oral LD50 study submitted by E.I. du Pont de Nemours & Company, Haskell Laboratory for Toxicology & Industrial Medicine. The following is a brief summary of the data reviewed:

1. CITATION: Campbell, Susan , Gregory J. Smith, and K.A. Hoxter. 1991. Technical Asana: An acute oral toxicity study with the Northern Bobwhite Wildlife international Ltd. Project No.: 112-231A. Study performed by Wildlife International Ltd., Easton, Maryland. Submitted by E.I. du Pont de Nemours & Company, Haskell Laboratory for Toxicology & Industrial Medicine, Newark, Delaware. MRID No. 416984-01.

   CONCLUSIONS: This study appears to be scientifically sound. The no effect level is less than 125 mg/kg. The calculated LD50 is 381 mg/kg with 95% confidence intervals of 125 mg/kg to positive infinity.

   Should you have any questions in regards to these comments, please contact Renee Lamb at 557-0294.

(1)

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DATA EVALUATION RECORD

1. **CHEMICAL:** S-Fenvalerate Shaughnessey Number: 109303

2. **TEST MATERIAL:** S-Fenvalerate--Benzeneacetic acid, 4-chloro-alpha-(1-methylethyl)-, cyano(3-phenoxyphenyl)-methyl ester, [S-R*,R*]-,; purity 98.6% by analysis; a brown viscous liquid.

3. **STUDY TYPE:** An acute oral toxicity study with the Northern Bobwhite quail Colinus virginianus.

4. **CITATION:** Campbell, Susan, K.A. Hoxter, and G. Smith. 1991. Technical Asana: An acute oral toxicity study with the Northern Bobwhite Wildlife International Ltd. Project No.: 112-231A. Study performed by Wildlife International Ltd., Easton, Maryland. Submitted by E.I. du Pont de Nemours & Company, Haskell Laboratory for Toxicology & Industrial Medicine, Newark, Delaware. MRID No. 416984-01.

5. **REVIEWED BY:**

Renee Lamb
Biologist
Ecological Effects Branch (H7507C)
Environmental Fate & Effects Division

Signature: Renee Lamb
Date: 6/7/91

6. **APPROVED BY:**

Ann Stavola
Head, Section 5
Ecological Effects Branch (H7507C)
Environmental Fate & Effects Division

Signature: Ann Stavola
Date: 6/12/91

7. **CONCLUSIONS:** This study appears to be scientifically sound and in accordance with EPA guideline requirements. The calculated LD_{50} value is 381 mg/kg with a 95% confidence interval of 125 mg/kg to positive infinity. The NOEL is less than 125 mg/kg.

8. **RECOMMENDATIONS:** N/A

9. **BACKGROUND:** N/A

10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A

11. **MATERIALS AND METHODS:**

A. **TEST ANIMALS:** The birds, Bobwhite quail Colinus virginianus, were 23 weeks old and appeared to be in good health at test initiation. They were purchased from Fritt's Quail Farm in Phillipsburg, New Jersey 08865. The birds were from the same hatch, pen-reared, healthy and phenotypically indistinguishable from wild birds. All birds were acclimated to the facilities for 3 weeks prior to test initiation.

B. **TEST SYSTEM:** Test birds were housed indoors in pens manufactured by Georgia Quail Farm Manufacturing Co. (Model #0010) measuring approximately 78 x 51 cm. with ceiling heights ranging from 20-25 cm. due to the slope of the floors. Each dosage group was assigned two pens; each containing either five females or five males.

The temperature was maintained at an average of 24°C ± 1°C with an average relative humidity of 60% ± 10%. The photoperiod was 8 hours of light per day during acclimation and maintained throughout the study. The birds were exposed to approximately 130 lux (12.03 foot candles) of illumination throughout the test, provided by fluorescent lighting.

C. **DOSAGE:** Treatment levels were based upon known toxicity data. Groups of ten quail were assigned to five different treatment and one control group. Nominal dosages used were 125, 250, 500, 1000, and 2000 milligrams of Technical Asana per kilogram of body weight. All birds received a constant dosage volume of 4 milliliters per kilogram of body weight. The control group was dosed with diluent only.

The test substance was dispersed in corn oil. The dosages and LD_{50} were not adjusted for purity of the test substance.

D. **DESIGN:** After the 3 week acclimation period, the birds were fasted for at least 15 hours prior to dosing. At test initiation, a single dose of the test substance was orally intubated directly into the crop or proventriculus of the birds using a stainless steel cannula.

Weights of each bird was recorded at initiation and at test termination.

The birds were fed a game bird ration throughout acclimation and testing. Food and water were provided ad libitum throughout the study.

E. **STATISTICS:** The mortality data were analyzed using a computer program by C.E. Stephan (3). The binomial probability method was used to determine the LD_{50} and the 95% confidence interval.

12. **REPORTED RESULTS:**

Control group birds were normal in appearance and behavior throughout the test with no mortalities occurring.

At the 125 mg/kg dosage, there were no mortalities, but there was one bird exhibiting slight lower limb weakness approximately five hours after dosing. This was the only sign of toxicity in this group, all other birds appeared normal.

There was 20% mortality (2 of 10) in the 250 mg/kg dosage group. Hyperexcitability, a ruffled appearance, and lower limb weakness were first noted approximately 3.5 hours after dosing at this level. other signs including muscular fasciculations and head twitching were noted as time progressed. By the end of Day 0, all birds were showing signs of toxicity. On Day 1, two birds were found dead, and three birds exhibited some signs of toxicosis. After Day 6, all birds were noted as normal in appearance and behavior and remained so until termination.

At the 500 mg/kg dosage level, there was 70% mortality (7 out of 10). Birds began experiencing similar signs of toxicosis as the 250 mg/kg group approximately 3.5 hours following dosing. Mortalities began (6) on the morning of Day 1. By the afternoon of Day 1, the last mortality occurred and the others showed some improvement. All survivors were noted as remaining the same through the morning of Day 8, after which they appeared normal until termination.

Mortality in the 1000 mg/kg dosage group was 100 % (10 of 10). All birds began to show signs of toxicosis approximately 3.25 hours after dosing, and progressively worsened throughout Day 0 and were found dead on the morning of Day 1.

In the 2000 mg/kg dosage group, the first mortality was found only 3.10 hours after dosing. This was the first of 8 mortalities (80%) in this group. Signs of toxicosis included hyperexcitability, lower limb weakness, ruffled appearance, loss of coordination nd righting reflex, depression and reduced reaction to external stimuli (sound and movement). Early on Day 1, three other mortalities occurred and three birds were nearly comatose. By the afternoon of Day 1, three more

birds were dead and another was nearly comatose. The last mortality was noted on the morning of Day 2. The two remaining birds began to improve gradually, with all signs of toxicosis disappearing by Day 8.

There was a reduction in food consumption for all birds at 500, 1000, and 2000 mg/kg from Day 0 through 3. Also there was a dose responsive loss in body weight in all groups from Day 0 through 3.

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

The author concluded that the acute oral LD_{50} for the northern bobwhite exposed to technical asana as a single oral dosage was 381 mg/kg with a 95% confidence interval of 125 mg/kg to infinity. An accurate slope of the dose response curve was not calculated. The no mortality level was 125 mg/kg. The NOEL was less than 125 mg/kg.

"This study was conducted to conform with Good Laboratory Practices as published by the US EPA, OPP in 40 CFR Part 160 with the following exception: samples of the dosing solutions were not taken for confirmation of the test concentrations, stability or homogeneity." This statement was signed by representatives of Wildlife International, the sponsor and the submitting company.

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

A. **TEST PROCEDURE:** This test is in accordance with EPA's SEP protocol with the following exception:

Photoperiod was maintained at 8 hours of light per day. SEP recommends 10 hour light/ 14 hour dark lighting regime.

B. **STATISTICAL ANALYSIS:** Using the EPA statistic program "Toxanal", the LD_{50} value of 381 mg/kg was confirmed by the reviewer. (See attached)

C. **DISCUSSION/RESULTS:** This study appears to be scientifically sound with a calculated LD_{50} value of 381 mg/kg with a 95% confidence interval of 125 mg/kg and positive infinity. The NOEL is less than 125 mg/kg.

D. **ADEQUACY OF STUDY:**

(1) **CLASSIFICATION:** Core

(2) **RATIONALE:** N/A

(3) **REPAIRABILITY:** N/A

15. **COMPLETION OF ONE-LINER:** Yes, June 7, 1991.

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
2000	10	8	80	5.46875
1000	10	10	100	9.765625E-02
500	10	7	70	17.1875
250	10	2	20	5.46875
125	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 125 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 381.1084

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
4	.214883	382.1076	214.1772	588.3987

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	1.802006	3.278149	2.002722E-02

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 2.644511
95 PERCENT CONFIDENCE LIMITS =-.9054494 AND 6.194471

LC50 = 452.8638
95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 = 149.8744
95 PERCENT CONFIDENCE LIMITS = 0 AND 446.7376

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