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

AUG 12 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: Review of studies submitted by Du Pont for Asana technical (Esfenvalerate)

To: George LaRocca PM 15
Registration Division, H7508C

From: Doug Urban, *Joe H.T. Caven 8/9/91* Acting Branch Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C)

The Ecological Effects Branch (EEB) has completed its review of the studies submitted by Du Pont for Asana technical. The following is a brief summary of the data reviewed. If you have any questions, please contact Renee Lamb at 557-0294.

1. CITATION: Driscoll, Cindy, K. Hoxter, and G. Smith. 1990. Asana Technical: A dietary LC₅₀ study with the mallard Wildlife International Ltd. Project No.: 112-230 FIFRA guideline 71-2. Study performed by Wildlife International Ltd., Easton, Maryland. Submitted by E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, Delaware 19711. MRID No. 416378-02.

CONCLUSIONS: This study appears to be scientifically sound and meets the guideline requirements for an avian acute oral dietary study. The LC₅₀ was determined to be 4894 ppm with a 95% confidence interval of 1780 ppm and + infinity. The NOEL is 562 ppm.

2. CITATION: Driscoll, Cindy, K. Hoxter, G. Smith, and M. Jaber. 1990. Asana Technical: A dietary LC₅₀ study with the Northern Bobwhite Wildlife International Ltd. Project No.: 112-229 FIFRA Guideline 71-2. Study performed by Wildlife International Ltd., Easton, Maryland. Submitted by E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, Delaware 19711. MRID No. 416378-03.

CONCLUSIONS: This study appears to be scientifically sound and meets the guideline requirements for an avian acute oral dietary study. The LC₅₀ was determined to be greater than 5620 ppm, the NOEL is 1000 ppm.

DATA EVALUATION RECORD

1. **CHEMICAL:** Asana Technical
Shaughnessey Number 109303
2. **TEST MATERIAL:** Asana Technical, Esfenvalerate
(Benzeneacetic acid, 4-chloro-alpha-(1-methylethyl)-,
cyano(3-phenoxyphenyl)- methyl ester, [S-(R*,R*)]-, 98.6%
purity, a brown viscous fluid.
3. **STUDY TYPE:** Dietary LC₅₀ study with the Northern Bobwhite.
4. **CITATION:** Driscoll, Cindy, K. Hoxter, G. Smith, and M.
Jaber. 1990. Asana Technical: A dietary LC₅₀ study with
the Northern Bobwhite Wildlife International Ltd. Project
No.: 112-229 FIFRA Guideline 71-2. Study performed by
Wildlife International Ltd., Easton, Maryland. Submitted by
E.I. du Pont de Nemours and Company, Haskell Laboratory for
Toxicology and Industrial Medicine, Newark, Delaware 19711.
MRID No. 416378-03.

5. **REVIEWED BY:**

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

Signature: *Renee Lamb*
Date: 7/24/91

6. **APPROVED BY:**

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

Signature: *Ann Stavola*
Date: 8/9/91

7. **CONCLUSIONS:** This study appears to be scientifically sound
and meets the guideline requirements for an avian acute oral
dietary study.

The LC₅₀ was determined to be greater than 5620 ppm, the
NOEL is 1000 ppm.

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 10 days of age and in good health upon test initiation. They were all from the same hatch, pen-reared and phenotypically indistinguishable from wild birds. The birds were hatched at Wildlife International on February 5, 1990.
- B. TEST SYSTEM: All birds were housed indoors in brooding pens manufactured by Beacon Steel Products, Co (model no. B735Q). The pens measured approximately 72 X 90 cm. with ceiling heights of approximately 23 cm.
- C. DOSAGE: Treatment levels were based upon known toxicity data. Each of 6 groups were fed diets containing either 0, 562, 1000, 1780, 3160, or 5620 ppm of the test substance. The control birds received carrier only, equivalent to the greatest amount used in the treated diets.
- D. DESIGN: Each test group, and the control, were assigned a pen containing 10 birds. The chicks were immature and were not differentiated by sex. They were acclimated for 10 days prior to test initiation.

The birds were fed a game ration ad libitum throughout the test. The temperature averaged $38^{\circ}\text{C} \pm 2^{\circ}\text{C}$ in the brooding compartment of the pens. Average ambient room temperature was $23^{\circ}\text{C} \pm 6^{\circ}\text{C}$ with an average relative humidity of $31\% \pm 15\%$. The photoperiod was maintained at 16 hours of light per day during acclimation and throughout the test. The birds were exposed to approximately 130 lux (12.03 foot candles) of illumination.

Birds were observed daily for signs of toxicity and abnormal behaviors. Body weights by group were measured upon test initiation and on day 5, and at termination on day 8. Average estimated feed consumption was determined for each group for the exposure period, days 0-5, and for the post-exposure period days 6-8.

The test diets were prepared by mixing the test substance into the diet with corn oil (2% concentration). An amount of diet sufficient to last the five day exposure period was presented to the birds

upon initiation of the test. The dietary concentrations were not adjusted for purity of the test substance.

- E. **STATISTICS:** Data was analyzed using the computer program of C.E. Stephan. This program uses the probit method to calculate the LC_{50} value and the 95% confidence interval. The pattern of mortality made it necessary to estimate the LC_{50} value by a visual inspection of the mortality data.

12. REPORTED RESULTS:

There were 0 mortalities in the control, and all birds seemed normal in appearance and behavior throughout the test.

There were 0 mortalities at the 562 and 1000 ppm concentrations. All birds were normal in appearance and behavior.

One mortality at the 1780 ppm concentration was not considered treatment related. No signs of toxicity were noted, and upon necropsy of the bird, it was found to have severe lesions of toe picking.

Signs of toxicity (lethargy) were noted in three birds in the 3160 ppm concentration treatment group. One bird was found dead on day 4, and one bird was noted with lethargy and a ruffled appearance. From the morning of day 5 until termination, all birds were normal in behavior and appearance.

In the 5620 ppm concentration, signs of toxicity were also noted, one bird was found dead on the morning of day 1 and two birds were found dead on the morning of day 3. All remaining birds were noted as normal in behavior and appearance from day 3 until termination.

There was a dose responsive reduction in body weight gain at the 1780, 3160 and 5620 ppm concentrations during the exposure period when compared to the control. There was no apparent effect on feed consumption at any test levels.

Gross necropsies were performed on two birds. One bird, dead at 5620 ppm, was noted to have a slight contusion on the foot and an erythematous beak. No other lesions were observed. The other bird, dead at 1780 ppm, showed evidence of toe picking, dehydration, and autolysis was also noted throughout the abdominal cavity.

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

The reported LC₅₀ based on visual inspection of the data was determined to be greater than 5620 ppm, the highest concentration tested. The NOEL was 1000 ppm, based on the reduction of body weight gain at the 1780 ppm concentration.

The report stated that the study was conducted under good laboratory practice standards and is signed by a quality assurance officer.

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:

o Group body weights were measured at test initiation and termination, SEP recommends individual body weights at these times.

- B. STATISTICAL ANALYSIS: The results were such that no statistics could be used to analyze the data.

- C. DISCUSSION/RESULTS: This study appears to be scientifically sound and meets the guideline requirements for an avian acute oral dietary study.

The LC₅₀ was determined to be greater than 5620 ppm, the NOEL is 1000 ppm.

- D. ADEQUACY OF STUDY:

(1) CLASSIFICATION: Core

(2) RATIONALE: N/A

(3) REPAIRABILITY: N/A

15. COMPLETION OF ONE-LINER: Yes, July 23, 1991.

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
5620	10	3	30	17.1875
3160	10	1	10	1.074219
1780	10	1	10	1.074219
1000	10	0	0	9.765625E-02
562	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 3160 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 .8897672 1
 .8469496

SLOPE = 2.211904
 95 PERCENT CONFIDENCE LIMITS = .1254709 AND 4.298337

LC50 = 9834.42
 95 PERCENT CONFIDENCE LIMITS = 4961.255 AND 1.012735E+12

LC10 = 2621.697
 95 PERCENT CONFIDENCE LIMITS = 34.6325 AND 5549.631

DATA EVALUATION RECORD

1. **CHEMICAL:** Asana Technical
Shaughnessey Number 109303
2. **TEST MATERIAL:** Asana Technical, Esfenvalerate
(Benzeneacetic acid, 4-chloro-alpha-(1-methylethyl)-,
cyano(3-phenoxyphenyl)- methyl ester, [S-(R*,R*)]-, 98.6%
purity, a brown viscous fluid.
3. **STUDY TYPE:** Dietary LC₅₀ study with the mallard
4. **CITATION:** Driscoll, Cindy, K. Hoxter, and G. Smith. 1990.
Asana Technical: A dietary LC₅₀ study with the mallard
Wildlife International Ltd. Project No.: 112-230 FIFRA
guideline 71-2. Study performed by Wildlife International
Ltd., Easton, Maryland. Submitted by E.I. du Pont de
Nemours and Company, Haskell Laboratory for Toxicology and
Industrial Medicine, Newark, Delaware 19711. MRID No.
416378-02.
5. **REVIEWED BY:**

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

Signature: *Renee Lamb*
Date: 7/24/91
6. **APPROVED BY:**

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

Signature: *Ann Stavola*
Date: 8/9/91
7. **CONCLUSIONS:** This study appears to be scientifically sound
and meets the guideline requirements for an avian acute oral
dietary study.

The LC₅₀ was determined to be 4894 ppm with a 95% confidence
interval of 1780 ppm and + infinity. The NOEL is 562 ppm.
8. **RECOMMENDATIONS:** N/A

9. BACKGROUND: N/A

10. DISCUSSION OF INDIVIDUAL TESTS: N/A

11. MATERIALS AND METHODS:

- A. TEST ANIMALS: The birds, Mallard duck Anas platyrhynchos were 10 days of age and in good health upon test initiation. They were all from the same hatch, pen-reared and phenotypically indistinguishable from wild birds. The birds were obtained from Whistling Wings, Hanover, Illinois. They were hatched on February 5, 1990.
- B. TEST SYSTEM: All birds were housed indoors in brooding pens manufactured by Safeguards Products, Inc. The pens measured approximately 72 X 90 cm. with ceiling heights of approximately 25.5 cm.
- C. DOSAGE: Treatment levels were based upon known toxicity data. Each of 6 groups were fed diets containing either 0, 562, 1000, 1780, 3160, or 5620 ppm of the test substance. The control birds received carrier only, equivalent to the greatest amount used in the treated diets.
- D. DESIGN: Each test group, and the control, were assigned a pen containing 10 ducklings. The ducklings were immature and were not differentiated by sex. They were acclimated for 9 days prior to test initiation.

The birds were fed a game ration ad libitum throughout the test. The temperature averaged $32^{\circ}\text{C} \pm 2^{\circ}\text{C}$ in the brooding compartment of the pens. Average ambient room temperature was $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$ with an average relative humidity of $39\% \pm 15\%$. The photoperiod was maintained at 16 hours of light per day during acclimation and throughout the test. The birds were exposed to approximately 130 lux (12.03 foot candles) of illumination.

Birds were observed daily for signs of toxicity and abnormal behaviors. Body weights by group were measured upon test initiation and on day 5, and at termination on day 8. Average estimated feed consumption was determined for each group for the exposure period, days 0-5, and for the post-exposure period days 6-8.

The test diets were prepared by mixing the test substance into the diet with corn oil (2% concentration). The dietary concentrations were not adjusted for purity of the test substance.

- E. STATISTICS: Data was analyzed using the computer program of C.E. Stephan. This program uses the probit method to calculate the LC_{50} value and the 95% confidence interval.

12. REPORTED RESULTS:

There were 0 mortalities in the control, and all birds seemed normal in appearance and behavior throughout the test.

There were 0 mortalities at the 562 ppm concentration. Signs of toxicity were noted on the morning of day 3 through the morning of day 4. All birds appeared normal in appearance and behavior from the afternoon of day 4 until study termination.

One mortality at the 1000 ppm concentration was noted on day 5 of the test. Signs of toxicity were noted on day 3 through the morning of day 5.

Signs of toxicity were noted in the 1780 ppm concentration treatment group from day 3 through the afternoon of day 5. One bird was found dead on day 3. From the morning of day 6 until termination, all birds were normal in behavior and appearance.

In the 3160 ppm concentration, signs of toxicity were observed beginning on the morning of day 3 throughout the afternoon of day 5. Two birds were found dead, one on day 1, the other on day 5. All remaining birds were noted as normal in behavior and appearance from day 6 until termination.

At the 5620 ppm concentration, six mortalities occurred. Four birds were found dead on day 1, one on day 2, and one on day 5. Signs of toxicity were noted from day 1 through day 5. All remaining birds were noted as normal in behavior and appearance from day 6 until termination.

There was a dose responsive reduction in body weight gain at the 562, 1000, and 1780 ppm concentrations during the exposure period when compared to the control and loss of body weight at the 3160 and 5620 ppm concentrations. There was no apparent effect on feed consumption at the 1000 through 5620 ppm concentrations for this same period.

Gross necropsies were performed on five birds. Findings were considered inconclusive.

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

The reported LC₅₀ was determined to be 5274 ppm, with a 95% confidence interval of 3356 ppm to 22,965 ppm. The NOEL was less than 562 ppm, based on the effect on body weights at all test concentrations. The no mortality level was 562 ppm.

The report stated that the study was conducted under good laboratory practice standards and is signed by a quality assurance officer.

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 exceptions:

o Group body weights were measured at test initiation and termination, SEP recommends individual body weights at these times.

o Temperatures in both the brooding chambers and outside the chambers were not in accordance with SEP guidelines.

- B. STATISTICAL ANALYSIS: The data was analyzed using EEB's "Toxanal" program. See attached.

- C. DISCUSSION/RESULTS: This study appears to be scientifically sound and meets the guideline requirements for an avian acute oral dietary study.

The LC₅₀ was determined to be 4894 ppm with a 95% confidence interval of 1780 ppm and + infinity. The NOEL is 562 ppm.

- D. ADEQUACY OF STUDY:

(1) CLASSIFICATION: Core

(2) RATIONALE: N/A

(3) REPAIRABILITY: N/A

15. COMPLETION OF ONE-LINER: Yes, July 24, 1991.

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
5620	10	6	60.00001	37.69531
3160	10	2	20	5.46875
1780	10	1	10	1.074219
1000	10	1	10	1.074219
562	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 1780 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 4894.082 .

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	1.25215	4894.082	2761.389	+INFINITY

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H
3	.4479198	1

GOODNESS OF FIT PROBABILITY
.6427201

SLOPE = 2.386053
95 PERCENT CONFIDENCE LIMITS = .789144 AND 3.982963

LC50 = 5273.907
95 PERCENT CONFIDENCE LIMITS = 3356.238 AND 22969.88

LC10 = 1548.363
95 PERCENT CONFIDENCE LIMITS = 375.4393 AND 2422.563
