3-27-92

MRID No. 420553-08.

DATA EVALUATION RECORD

1. **CHEMICAL:** NTN 33893
   Shaughnessy No. ~~129059~~ 129099

2. **TEST MATERIAL:** Technical NTN 33893, 97.4%

3. **STUDY TYPE:** Avian Acute LD50 Test, Bobwhite Quail (Colinus virginianus).

4. **CITATION:** Toll, P.A. 1990. "Technical NTN 33893: An Acute Oral LD50 With Bobwhite Quail" Mobay Corporation, Agricultural Chemicals Division Research and Development Department, Biochemistry/Ecological Effects, 17745 South Metcalf, Stilwell, Kansas 66085-9104. Report Number 100059. Submitted by Mobay Corporation, P.O. Box 4913, Kansas City, Missouri 64120-0013. USEPA MRID No. 420553-08.

5. **REVIEWED BY:**

   Dana Lateulere, Biologist
   Ecological Effects Branch
   Environmental Fate and
   Effects Division

   Signature: Dana Lateulere
   Date: 3/27/92

6. **APPROVED BY:**

   Ann Stavola, Section Head, 5
   Ecological Effects Branch
   Environmental Fate and
   Effects Division

   Signature: Ann Stavola
   Date: 3/27/92

7. **CONCLUSIONS:** This study is scientifically sound and fulfills guideline requirements. The acute oral LD50 for NTN 33893 to bobwhite quail was determined to be 152.3 mg/kg with a confidence interval of 102.7 - 227.0 mg/kg, based on the Probit method. The NOEC is 25 mg/kg, the LOEC is 50 mg/kg - based on feed consumption and body weight. Based on the LD50, NTN 33893 is classified as moderately toxic to bobwhite quail.

8. **RECOMMENDATIONS:**

9. **BACKGROUND:** This study is submitted as part of a data package for an EUP and for registration requirements.

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Adult (17 week-old) bobwhite quail were obtained from Barrett's Quail Farm, Houston, Texas. All quail were from the same hatch and appeared phenotypically similar to birds from wild populations. The birds were examined upon receipt and daily thereafter throughout the 21-day acclimation period. There was no mortality during the acclimation period.

B. **Test System:** Birds were maintained at a temperature of 68+/-4°C and a relative humidity of 45-70%. Room lighting was maintained under a 8/16 hour light/dark cycle. Brooder bedding was changed at least weekly. Food and water were available ad libitum prior to and during the study with the exception of approximately 17-19 hours immediately prior to dosing, during which the birds were fasted.

At twenty weeks of age ten quail (5 male, 5 female) were allocated randomly to each of six treatment and two control groups. Treatment and control groups were gang housed, five per sex per level in separate brooders throughout the study.

Twenty four hours prior to dosing, birds were weighed to determine dose amount. Proper amounts of technical grade NTN 33893 were weighted into individual gelatin capsules based on the treatment level and the weight of the bird. Dosages were adjusted for percent active ingredient. Body weights were recorded at test initiation, day 7, and termination. Feed consumption for each group of five birds was recorded daily.

C. **Dosage:** Dosage concentrations were 25, 50, 100, 200, 400 and 800 mg technical NTN 33893/kg body weight.

D. **Design:** The birds received a single oral dose via the use of the gelatin capsules, then were observed for mortality and symptoms of intoxication for 14 days. Observations for mortality and clinical signs of intoxication were recorded 0.5, 1, 2 and 4 hours post-dosing, then twice daily throughout the remainder of the study (except on weekends when only one observation per day was made). At the end of the study all surviving birds were sacrificed by CO_2 asphyxiation. Necropsy examinations were conducted on all surviving birds as well as any birds that died during the course of the study.

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E. **Statistics**: The acute oral LD50 was calculated using a computer program which estimated the LD50 using one of three statistical techniques: moving average, binomial probability, or probit. The appropriate method was determined on the basis of data characteristics. For parametric procedures, body weight and feed consumption days for all treatment levels were subject to a standard one-way analysis of variance.

12. **REPORTED RESULTS**: Mortalities occurred in all exposure groups > 50 mg/kg. Mortalities were noted within 24 hours of dosing and continued through day 7. Clinical signs of toxicity were noted in all groups in which mortality occurred and consisted primarily of fluffed feather coat, hyperactivity, ataxia, immobility, and wing drop. (See Table 1).

A summary of the postmortem examination of those birds found dead during the study or sacrificed at study termination are presented in Table 3. In summary, primary observations included wastage of body musculature (emaciation), fluid filled crop, fluid and gas filled intestines and enlarged or distended and fluid filled colon.

Control groups were combined for statistical analyses in terms of body weight and feed consumption based on no significant differences between the two groups.

All exposure groups had a significant decrease in body weight on day 7; at termination all groups except the 400 mg/kg group had returned to control level body weights. All exposure groups showed decreased feed consumption during the first 24 hours after dosing. However, at termination of the study the only group which had a statistically significant decrease in feed consumed was 800 mg/kg group.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES**: Exposure levels of greater than or equal to 50 mg/kg technical NTN 33893 had a toxic effect on 20-week old bobwhite quail. The acute oral LD50 was determined to be 152 mg/kg (103-227 mg/kg 95% C.I.). Based on mortality the highest no-observed-effect-concentration (NOEC) was 25 mg/kg. The lowest observed effect concentration (LOEC) was 50 mg/kg.

Quality Assurance Inspection was conducted for compliance verification by the Quality Assurance Unit. It was also stated that this study was conducted in compliance with the Good Laboratory Practice Standards.

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

A. Test Procedure: The test procedures were in accordance with Subdivision E, and SEP guidelines.

B. Statistical Analysis: The reviewer used Toxanol to determine the LD50 and the corresponding 95% confidence interval. See attached.

C. Discussion/Results: The acute oral LD50 for NTN 33893 to bobwhite quails was determined to be 152.3 mg/kg with a 95% confidence interval of 102.7 - 227.0 mg/kg, based on the Probit method. The NOEC is 25 mg/kg, the LOEC is 50 mg/kg - based on feed consumption and body weight. Based on the LD50, NTN 33893 is classified as moderately toxic to bobwhite quail.

D. Adequacy of the Study:

(1) Classification: Core.

(2) Rationale:

(3) Repairability:

Image Reviewed

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LATEULERE NTN 33893 ACUTE ORAL LD50 BWQ

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
800	10	10	100	9.765625E-02
400	10	8	80	5.46875
200	10	6	60.00001	37.69531
100	10	4	40	37.69531
50	10	1	10	1.074219
25	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 50 AND 800 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 141.4214

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
5	.1144044	151.1685	104.8408	221.7543

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.166824	1	.8716789

SLOPE = 2.656458
95 PERCENT CONFIDENCE LIMITS = 1.571452 AND 3.741465

LC50 = 152.3366
95 PERCENT CONFIDENCE LIMITS = 102.7133 AND 227.0183

LC10 = 50.6669
95 PERCENT CONFIDENCE LIMITS = 20.95373 AND 79.21688

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