6-18-91

MRID No. 414764-02

JUN 16 1991
JUN 16 1991
JUN 18 1991

DATA EVALUATION RECORD

1. **CHEMICAL:** Sodium Methyldithiocarbamate (METAM-sodium). Shaughnessey Number: 039003.

2. **TEST MATERIAL:** METAM-sodium. Test Substance No. 85/232; Batch No. ZH 130 585; 42.2% METAM-sodium; an aqueous solution.

3. **STUDY TYPE:** Avian Single Dose Oral LD_{50} Test. Species Tested: Bobwhite quail (Colinus virginianus).

4. **CITATION:** Munk, R., 1985. Avian Single Dose Oral LD_{50}, METAM-SODIUM (Aqueous Solution) to the Bobwhite Quail. Project No. 11W0232/8559. Study performed by BASF Aktiengesellschaft, Agricultural Research and Development, Limburgerhof, West Germany. No. 86/0521. Submitted by BASF Corporation, Agricultural Chemicals, Research Triangle Park, North Carolina. MRID No. 414764-02.

5. **REVIEWED BY:**

Rosemary Graham Mora, M.S.
Associate Scientist
KBN Engineering and
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Signature: Rosemary Graham Mora
Date: 4/12/91

6. **APPROVED BY:**

Michael L. Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
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Signature: Michael L. Whitten
Date: 4-12-91

Henry T. Craven, M.S.
Supervisor, EEB/HED
USEPA

Signature: Henry T. Craven
Date: 6/11/91

7. **CONCLUSIONS:** The study appears to be scientifically sound and meets the requirements for an avian single dose oral LD_{50} study. The LD_{50} was 211 mg/kg, based on dosages adjusted for the percentage of active ingredient (42.2%). These results indicate that METAM-sodium is moderately toxic to bobwhite quail. The NOEL could not be determined.

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8. **RECOMMENDATIONS:** N/A

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were 4 to 5 month old bobwhite quail (Colinus virginianus), maintained by BASF. The birds were "visually indistinguishable from wild birds."

B. **Test System:** Each pen, located in building BASF - Z 454 (an air conditioned room), was constructed of stainless steel (0.59 X 0.45 X 0.26 m) with wire mesh flooring. Birds were exposed to fluorescent lighting for 16 hours daily. The test room temperature was 21°C and relative humidity was about 50% - 60%.

C. **Dosage:** Acute single dose oral LD_{50} test. Nominal dosages selected for the study were 125, 250, 500, 1000, and 2000 mg/kg (formulated test substance). These dosages were not adjusted to reflect the percentage of active ingredient of the test substance used.

D. **Design:** A group of ten birds each was randomly assigned to the control group and five treatment groups. Each concentration and the control consisted of two pens each containing 5 males and 5 females. All birds were fed "Ssniff" experimental diet. The composition of the diet was included in the report. Untreated food and water were supplied ad libitum before and throughout the test, except during a 24-hour period immediately prior to dosing.

The test dosages were prepared by diluting the test substance with "bidistilled" water as appropriate to obtain the desired dosage. The test dosage was administered to the birds by gavage into the crop. The volume of solution given to each bird was 10 milliliters per kilogram of body weight. The control birds were given the equivalent amount of "bidistilled" water.

Observations for mortality and toxic signs were made twice on the day of test initiation and daily thereafter. Birds were weighed individually at test

initiation and Day 14. Daily mean food consumption per bird was determined based upon the group food consumption per day. Means were determined separately for male and female birds.

E. **Statistics:** The statistical evaluation of the body weight was performed followed by a Dunnet's test.

"As the mortality values obtained in this study were not adequate for the calculation of the LD_{50}-value, the LD_{50} was estimated."

12. **REPORTED RESULTS:** No mortality occurred in the negative control group or the two lowest dosage groups. No clinical signs of toxicity were observed in the control or in the lowest dosage group (125 mg/kg).

In the 250 mg/kg dosage group, some birds demonstrated the following signs of toxicity: on Day 1, soft or fluid feces; and on Day 10 - 11, difficulties in walking and ruffled feathers (Table 2, attached). No other signs of toxicity were demonstrated at 250 mg/kg.

Fifty, one-hundred, and one-hundred percent mortality was demonstrated in the 500, 1000, and 2000, mg/kg nominal dosages, respectively (Table 1, attached). Signs of toxicity demonstrated by birds in these dosage groups included apathy, prone position, soft or fluid feces, and ruffled feathers. In addition, one bird each in the 500 and 1000 mg/kg dosage groups demonstrated side position and hanging wing, respectively (Table 2, attached).

A dose related reduction in feed consumption and body weight gain was apparent in the 250, 500, and 1000 mg/kg dosages (Tables 3, 6 and 7, attached). In the 2000 mg/kg no uptake of feed could be measured.

A post-mortem macroscopic examination of all birds was revealed crop wall thickening and skin fusion in the 125, 250, and 500 mg/kg dosage groups. Signs of general congestive hyperemia were observed in those birds which had died during the test period.

Results of analysis of the lowest test substance concentration was presented (Table 4, attached).

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute LD_{50} is estimated to be 500 mg/kg (formulated substance). The no mortality level is 250 mg/kg.

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Due to the substance related findings in all dosage groups during the post mortem examinations the NOEL "should be lower than 125 mg/kg body weight."

The report included the following Good Laboratory Practices statement: "This study was conducted prior to the effective date of 40 CFR part 160 for studies of this nature. Therefore there is no Sponsor of Study Director of record for signature of this compliance statement." The statement was signed by a BASF representative. A Quality Assurance Statement was included. The report was also signed by the study Director and other representatives of the BASF toxicology department.

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

A. Test Procedure: The test procedures were in accordance with Subdivision E, and SEP guidelines except for the following deviations:

Food consumption for each group was not monitored for the period of pretreatment.

The amount of test material and/or diluent dosed per bird was not reported.

B. Statistical Analysis: The reviewer used EPA's Toxanal computer program (attached, printouts) to calculate the LD_{50} value. Since there was only one dosage at which the mortality was between 0 and 100%, neither the probit method nor the moving average method could be used. Results of the binomial test show that the LD_{50} to be 500 mg/kg (95% confidence limits: 250-1000 mg/kg. Based on nominal dosages adjusted for the percent active ingredient (42.2%) the LD_{50} is 211 mg/kg (95% confidence limits: 105.5-422 mg/kg).

C. Discussion/Results: Due to substance related findings in all dosage groups, the NOEL could not be determined.

Results of the study indicate that the test substance is moderately toxic to bobwhite quail. The study appears to be scientifically sound and meets the requirements for an avian single dose oral LD_{50} study.

D. Adequacy of the Study:

(1) Classification: Core.

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

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

15. **COMPLETION OF ONE-LINER:** Yes; April 12, 1991.

Cumulative mortality

Table 1

5 male (= m) and 5 female (= f) birds/test group

Test group	Dose level mg/kg	Day of the study															
		0*		0**		1		2		3		4		5		6	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f
0	0 (carrier control)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	125	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	250	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	500	0	0	0	0	0	1	0	2	0	2	0	2	0	2	0	2
4	1000	0	0	0	0	4	4	4	4	4	4	4	4	4	4	4	4
5	2000	0	0	0	0	5	5	5	5	5	5	5	5	5	5	5	5

Test group	Dose level mg/kg	Day of the study															
		7		8		9		10		11		12		13		14	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f
0	0 (carrier control)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	125	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	250	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	500	0	2	1	2	2	3	2	3	2	3	2	3	2	3	2	3
4	1000	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
5	2000	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

* = shortly after administration
** = about 3 to 5 hours after administration

Symptoms (clinical signs)

Table 2

5 male (= m) and 5 female (= f) birds/test group

Test group	Dose level mg/kg	Day of the study																	
		0*		0**		1		2		3		4		5		6		7	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f
0	0 (carrier control)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1	125	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
2	250	n.d.	n.d.	n.d.	n.d.	D	(D)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
3	500	n.d.	n.d.	n.d.	(A1)	A5, D, G5	A2, B2, D, G2, L5	A1, D, G3	n.d.	A3, G3	n.d.	A4, G4	n.d.	n.d.	n.d.	n.d.	n.d.	A1, S1	n.d.
4	1000	n.d.	n.d.	(A2)	(A3)	A1, D, G1	A2, B2, D, G2	A1 D, G1	A1 D, G1	A1	A1, G1	A1	A1, G1	n.d.	n.d.	n.d.	n.d.	A1, W1	-
5	2000	A5	A5	A4 B2 G4	A4 B1 G3	D	A1 D G1	-	-	-	-	-	-	-	-	-	-	-	-

Key to symptoms: A = apathy, B = prone position, D = soft or fluid feces, G = ruffled feathers, H = injuries from fighting (head), K = convulsions, L = difficulties in walking (ataxia), S = side position, W = hanging wings, Z = trembling

Figure behind key to symptom = number of birds affected (e.g. A_2 = 2 birds affected)
n.d. = no symptoms detectable
( ) = partly or slight
- = no animals alive

* = shortly after administration
** = about 3 to 5 hours after administration

5 male (= m) and 5 female (= f) birds/test group

Test group	Dose level mg/kg	Day of the study													
		8		9		10		11		12		13		14	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f
0	0 (carrier control)	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1	125	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
2	250	n.d.	n.d.	n.d.	n.d.	L_5	G_1	G_3, L_3	G_1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
3	500	A_2, G_2	A_1, L_1	A_3, G_3	G_1	G_1, L_3	n.d.	G_1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	?
4	1000	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5	2000	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Key to symptoms: A = apathy, B = prone position, D = soft or fluid feces, G = ruffled feathers, H = injuries from fighting (head), K = convulsions, L = difficulties in walking (ataxia), S = side position, W = hanging wings, Z = trembling

Figure behind key to symptom = number of birds affected (e.g. A_2 = 2 birds affected)
n.d. = no symptoms detectable
? = unclear raw data
- = no animals alive

Table 3

Mean feed consumption (g/bird/day)*, calculated from the feed consumption/cage/day

- male birds -

Day	Test group					
	0 (0 mg/kg)	1 (125 mg/kg)	2 (250 mg/kg)	3 (500 mg/kg)	4 (1000 mg/kg)	5 (2000 mg/
0	-	-	-	-	-	-
1	18.8	15.5	5.7	1.6	7.4	-
2	15.6	14.8	7.4	0.1	0.0	-
3	18.2	17.9	6.9	1.8	0.4	-
4	16.3	16.2	5.4	2.8	1.3	-
5	13.6	14.3	5.5	4.1	1.2	-
6	17.0	17.2	8.8	5.6	2.0	-
7	18.2	25.0	16.4	7.6	1.7	-
8	9.2	18.7	15.5	5.3	-	-
9	23.2	14.7	11.0	15.0	-	-
10	16.9	16.3	14.0	14.9	-	-
11	17.6	17.8	14.9	17.7	-	-
12	14.0	18.3	15.0	22.3	-	-
13	11.1	12.0	7.4	9.3	-	-
14	16.5	19.8	22.0	26.0	-	-
Mean	16.2	17.0	11.1	9.6	2.0	-

* The birds that were found dead in their cages on the respective day of the determination of the feed consumption are not included in the calculations and thus in the feed consumption figures.

Table 3
(contin

Mean feed consumption (g/bird/day)*, calculated from the feed consumption/cage/day

- female birds -

Day	Test group					
	0 (0 mg/kg)	1 (125 mg/kg)	2 (250 mg/kg)	3 (500 mg/kg)	4 (1000 mg/kg)	5 (2000 mg/
0	-	-	-	-	-	-
1	17.7	15.4	6.9	3.1	2.7	-
2	14.7	13.1	9.3	1.3	0.0	-
3	16.1	14.9	11.6	4.0	0.7	-
4	14.6	14.4	9.2	4.6	0.4	-
5	13.3	13.7	8.6	5.0	3.2	-
6	14.1	15.5	9.0	7.0	1.9	-
7	16.6	21.2	18.1	13.5	-	-
8	6.9	11.0	15.7	9.6	-	-
9	14.6	18.5	14.5	19.0	-	-
10	14.4	14.4	13.9	15.5	-	-
11	18.5	20.0	18.4	16.8	-	-
12	18.6	18.3	17.0	18.3	-	-
13	11.2	11.6	10.7	10.4	-	-
14	20.4	20.9	20.6	20.4	-	-
Mean	15.1	15.9	13.1	10.6	1.5	-

* The birds that were found dead in their cages on the respective day of the determination of the feed consumption are not included in the calculations and thus in the feed consumption figures.

TABLE 4.

Nominal concentration (g/l)	Analytically detected concentration (g/l)	% of nominal Concentration
12.5	12.9; 13.5 mean 13.2	105.6

TABLE 6

BASF TOXICOLOGY
PROJECT NUMBER 11W0232/8559 LD 50 METAM-NA

GROUP MEANS BODYWEIGHT PRINT DATE 17-FEB-88

M A L E S		day 0 BODYWT G	day 14 BODYWT G	
GROUP 0				
0 MG/KG	M	171.1	190.1	11.1%
	SD	11.6	12.2	
	N	5	5	
GROUP 1				
125 MG/KG	M	167.9	186.7	11.2%
	SD	9.6	8.0	
	N	5	5	
GROUP 2				
250 MG/KG	M	169.4	164.7	-2.8%
	SD	9.1	24.1	
	N	5	5	
GROUP 3				
500 MG/KG	M	165.6	156.5*	-5.5%
	SD	8.3	13.5	
	N	5	3	
GROUP 4				
1000 MG/KG	M	165.4	0.0	
	SD	7.5	0.0	
	N	5	0	
GROUP 5				
2000 MG/KG	M	172.1	0.0	
	SD	19.3	0.0	
	N	5	0	

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

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TABLE 7

BASF TOXICOLOGY
PROJECT NUMBER 11W0232/8559 LD 50 METAM-NA

GROUP MEANS BODYWEIGHT PRINT DATE 17-FEB-86

F E M A L E S		day 0 BODYWT G	day 14 BODYWT G	
GROUP 0				
0 MG/KG	M	166.2	193.1	14.8%
	SD	10.7	10.8	
	N	5	5	
GROUP 1				
125 MG/KG	M	166.8	187.4	12.4%
	SD	9.3	10.1	
	N	5	5	
GROUP 2				
250 MG/KG	M	169.4	183.2	8.2%
	SD	8.3	9.0	
	N	5	5	
GROUP 3				
500 MG/KG	M	167.6	158.3**	-5.6%
	SD	10.3	1.0	
	N	5	2	
GROUP 4				
1000 MG/KG	M	164.7	0.0	
	SD	6.9	0.0	
	N	5	0	
GROUP 5				
2000 MG/KG	M	167.8	0.0	
	SD	12.2	0.0	
	N	5	0	

Statistics: Anova + Dunnetts tests * P<0.05 ** P<0.01 two sided (Statistical unit = animal)

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ROSEMARY MORA METAM-SODIUM COLINUS VIRGINIANUS 4-5-91

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
844	10	10	100	9.765625E-02
422	10	10	100	9.765625E-02
211	10	5	50	62.30469
105.5	10	0	0	9.765625E-02
52.75	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 105.5 AND 422 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 211

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE
PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE
NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

****

Based on dosages corrected for 42.2% active ingredient.

ROSEMARY MORA METAM-SODIUM COLINUS VIRGINIANUS 4-5-91

****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
2000	10	10	100	9.765625E-02
1000	10	10	100	9.765625E-02
500	10	5	50	62.30469
250	10	0	0	9.765625E-02
125	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 250 AND 1000 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 500

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE
PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE
NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

****

Based on nominal dosages, not corrected for 42.2% active ingredient.

Shaughnessey # 039003 Chemical Name METAM-sodium Chemical Class _____ Page 1 of 1

Study/Species/Lab/ MRID #	Chemical % a.i.	Results	Reviewer/ Date	Validation Status
14-Day Single Oral LD_{50}	42.2%	LD_{50} = 211 mg/kg (95% C.L. 105.5 - 422) Control Mortality (%) = 0		
Species: Colinus virginianus		Slope = — # Animals/Level = 10 Age (Days) = 120-150 Sex = 5♂/5♀	RVM 4/12/91	Core
Lab: BASF				
MRID #: 414764-02		14-Day Dose Level mg/kg/(% Mortality): 125 (0), 250 (0), 500 (50), 1000 (100), 2000 (100)		
		Comments: LD_{50} above based on active ingredient of nominal concentration.		
8-Day Dietary LC_{50}	_____	LC_{50} = pp (95% C.L.) Control Mortality (%) =		
Species		Slope = # Animals/Level = Age (Days) =		
Lab		Sex =	_____	_____
MRID #		8-Day Dose Level pp /(% Mortality): ( ), ( ), ( ), ( ), ( )		
		Comments:		

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