6-18-91

MRID No. 414764-03

JUN 1 8 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 / April 1985; 42.2% METAM-sodium; an aqueous solution.

3. **STUDY TYPE:** Avian Dietary LC_{50} Test.
Species Tested: Mallard (Anas platyrhynchos L.).

4. **CITATION:** Munk, R., 1986. Avian Dietary LC_{50} Test of METAM-SODIUM (Aqueous Solution) to the Mallard Duck. Project No. 32W232/8518. Study performed by BASF Aktiengesellschaft, Agricultural Research and Development, Limburgerhof, West Germany. No. 86/0522. Submitted by BASF Corporation, Agricultural Chemicals, Research Triangle Park, North Carolina. MRID No. 414764-03.

5. **REVIEWED BY:**

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Signature: Rosemary Graham Mora
Date: 4/24/91

6. **APPROVED BY:**

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Wildlife Toxicologist
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Signature: Michael L. Whitten
Date: 4-24-91

Henry T. Craven, M.S.
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Date: 6/11/91

7. **CONCLUSIONS:** The study appears to be scientifically sound but does not meet the requirements for an avian dietary LC_{50} study. Based on nominal concentrations, the LC_{50} was 1835.7 ppm a.i. These results indicate that METAM-sodium is slightly toxic to the mallard. The NOEC was 78.1 ppm a.i. The actual concentrations to which the birds were exposed could not be determined.

6 hrs

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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 9-day old mallard ducks (Anas platyrhynchos L.), hatched by Heinz Bohnen, Mülheium/Ruhr, Germany. The chicks were hatched "from eggs of animals indistinguishable from wild birds."

B. **Test System:** Each pen, located in building BASF - Z 454 (an air conditioned room), was constructed of iron wire (1.3 X 0.65 X 1.30 m) with wire mesh (10 X 10 mm) flooring. Birds were exposed to fluorescent lighting for 16 hours daily. The test room temperature was 22°C and relative humidity was about 50% - 80%.

C. **Dosage:** Acute dietary LC_{50} test. Nominal dietary concentrations selected for the study were 185, 556, 1667, and 5000 mg/kg diet (ppm, formulated test substance). These concentrations were not adjusted to reflect the percentage of active ingredient of the test substance used.

D. **Design:** A group of ten birds were randomly assigned to a control group and four treatment groups. All birds were fed "Ssniff" experimental diet. The contents of this diet were included in the report. Food and water were supplied ad libitum before the study and throughout the test.

The test diets were prepared separately by "preparing a premix in a mixing bowl. These premixes were then mixed with meal form basal diet..." The birds were fed ad libitum the appropriate dietary concentrations for five days, and then given untreated food for three days. The control birds received the basal diet throughout the study.

"As it was assumed that the test substance could not be sufficiently stable in the diet at higher temperature the feed was cooled down to about 4°C before the test substance was added and the final mixtures were stored at about 4°C. Each day the feed in the hoppers was completely replaced by the respective mixtures stored

int he refrigerator. The stability will be analytically verified in the course of another test with bobwhite quails using the same feed and mixing procedure ..." Samples were also taken for analyses of homogeneity and verification of treatment concentrations.

Observations for mortality, and signs of toxicity and other abnormal behavior were made daily for the duration of the study, except for Day 8 on which day (for technical reasons) no observations were made. Birds were weighed by group at test initiation and on Days 5 and 8. Daily mean food consumption per bird was determined based upon the group food consumption per day. Means were determined for Days 0-5 and Days 6-8.

Birds were weighed individually on Days 0, 5, and 8. The mean body weight was calculated for each cage.

E. **Statistics:** "The statistical evaluation of the body weight was performed by one-way analyses (ANOVA) followed by Dunnet's test..."

12. **REPORTED RESULTS:** No mortality occurred in the control, 185, 556, and 1667 ppm concentrations; no symptoms were demonstrated throughout the test period.

Sixty percent mortality was demonstrated in the 5000 ppm nominal concentration. No pronounced signs of toxicity were demonstrated by any of test birds (Table 1, attached).

During the exposure period a concentration related reduction in feed consumption was observed in the three highest test substance concentrations (Table 2, attached). During the post-exposure period feed consumption rates were similar to that of the control.

There was a substance related reduction in body weight gain in the two highest concentrations (1667 and 5000 mg/kg) at the end of the exposure period (Table 3, attached). This reduction in body weight gain persisted until Day 8.

A post-mortem macroscopic examination of all surviving birds was conducted and "no substance related effects" could be observed. Examination of those birds which had died in the highest concentration revealed general hyperemia and discoloration of the liver (gray-brown).

Results of analyses of test substance homogeneity and concentration were presented (Tables 4 and 5, respectively,

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attached). Deviations in homogeneity and concentration of the test substance diets may have been the result of "the chemical structure of the test compound in the diet." The diet was analyzed "about a half year after the test had been run. Although the substance-diet mixtures had been stored at about -20°C this long storage of the samples in the deep freezer might have influenced the analytical results."

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute LC_{50} based on nominal concentrations of METAM-sodium in the test diets was about 5000 ppm. Based on the analysis of actual test concentrations, the LC_{50} was about 4000 ppm. The NOEC based on the nominal concentration was 185 ppm.

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 made. 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, ASTM, and SEP guidelines except for the following deviations:

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

No observations were made on Day 8 of the test period.

B. **Statistical Analysis:** The reviewer used EPA's Toxanal computer program (attached, printout) to calculate the LC_{50} value. The LC_{50} was 1835.7 ppm (adjusted to a.i. concentration), using the binomial test method. These values are different from the author's values which were estimated and which did not reflect the percent active ingredient.

C. **Discussion/Results:** The LC_{50} value (5000 ppm) presented by the author did not reflect the percentage of active ingredient of the test substance. The test concentrations based on percentage active ingredient were 78.1, 234.6, 703.5, and 2110 ppm a.i.

Nominal test concentrations were presented as "mg/kg diet." The reviewer assumed that this was milligrams of test substance to kilograms of feed (or parts per million).

Chemical analysis of the test diets was performed on samples which had been stored at -20°C for a period of one-half year. This delay may have been responsible for the wide range of values for homogeneity and concentration. Furthermore, since the author stated that the test chemical is not stable at room temperature, the actual concentration to which the birds were exposed can not be determined.

If observations of behavior had been made on day 8 it is probable that the findings would not change the status of the test substance.

A range finding test prior to performance of this test would have better defined the toxic range of this test substance to the mallard.

Only four test substance concentrations were used for this study. Five or six concentrations are recommended.

Based on nominal concentrations the test substance is slightly toxic to the mallard. The study appears to be scientifically sound but does not meet the requirements for an avian dietary LC_{50} study.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

(2) **Rationale:** The actual concentrations to which the birds were exposed cannot be determined.

(3) **Repairability:** No.

15. **COMPLETION OF ONE-LINER:** Yes; April 24, 1991.

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4. RESULTS

4.1. Mortality

Mortality occurred only in the highest dose group (5000 mg/kg).

TABLE 1

Group No.	Concentration (mg/kg diet)	Time of death (cumulative mortality)								
		Substance feeding period						Post-exposure period		
		Day						Day		
		0	1	2	3	4	5	6	7	8
0	0 (untreated control)	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10
1	185	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10
2	556	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10
3	1667	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10
4	5000	0/10	1/10	1/10	2/10	3/10	6/10	6/10	6/10	6/10

4.2. LC_{50}

The LC_{50} related to nominal concentrations is about 5000 mg/kg diet.

The LC_{50} related to analytically detected concentrations is determined to be about 4000 mg/kg diet.

Highest concentration tested causing no mortality: 1667 mg/kg diet

Minimum concentration causing 100% mortality: greater than 5000 mg/kg diet

4.3. Clinical signs

No pronounced toxic signs were observed; partly weak and underdeveloped chicks were seen in all groups including the control. In deviation from the protocol it was not looked for clinical signs on the last day of the post-exposure period for technical reasons.

4.4. Feed consumption

Group mean feed consumption (g/bird/day)

TABLE 2

Day	Group No. (concentration mg/kg)				
	0 (untreated control)	1 (185)	2 (556)	3 (1667)	4 (5000)
1	28.4	33.4	22.2	12.2	4.7
2	43.8	50.4	37.0	26.1	8.4
3	47.6	55.5	37.6	27.5	6.8
4	52.7	66.3	47.3	33.4	9.1
5	87.1	92.2	62.8	38.1	10.2
mean (days 1 - 5; exposure period)	51.9	59.6	41.4	27.5	7.8
6	66.3	70.7	69.0	56.8	60.4
7	86.9	81.8	64.6	68.2	96.5
8	97.9	102.5	73.3	77.9	74.5
mean (days 6 - 8; post-exposure period)	83.7	85.0	69.0	67.6	77.1

4.7. NOEC

The "No Observed Effect Concentration" (= NOEC) was determined to be 185 mg/kg diet.

4.8. Chemical analysis

4.8.1. Stability

c.f. item 3.3.5.2.

4.8.2. Homogeneity

TABLE 4

Nominal concentration (mg/kg diet)	Analytically detected concentration (mg/kg diet)	% of nominal concentration
185	152	82
	186	101
	203	110
	204	110
	145	78
	162	88
5000	3619	72
	3911	78
	4144	83
	3326	67
	4623	93
	3956	79

4.8.3. Concentration control

TABLE 5

Nominal concentration (mg/kg diet)	Analytically detected concentration (mg/kg diet)	% of nominal concentration
185	175	95
556	480	86
1667	1152	69
5000	3930	79

The chemical determinations were performed by Dr.rer.nat. W. Dreher, APE/RU; method: GC

The deviations of the analytically detected concentrations (homogeneity and concentration control) may be due to the chemical structure and the predictable instability of the test compound in the diet; for technical reasons it was not possible to perform the analyses for about half a year after the study had been run. Although the substance-diet mixtures had been stored at about -20°C this long storage of the samples in the deep freezer might have influenced the analytical results.

4.8.4. Residues in the diet

The feed is assayed periodically for contaminants. In view of the aim and duration of the study the contaminants contained in commercial feed should have no influence on the results.

4.8.5. Analyses of drinking water

The drinking water is regularly assayed for contaminants by the municipal authorities of Frankenthal and the Technical Services of BASF Aktiengesellschaft. In view of the aim and duration of the study there are no special requirements exceeding the specifications of the drinking water.

(9)

TABLE 3
~~TABLE 2~~

BASF TOXICOLOGY
PROJECT NUMBER 32W232/8518

LC50 - MALLARD DUCK (CHICKS)

GROUP MEANS

BODYWEIGHT

PRINT DATE 1-OCT-85

		day 0 BODYWT G	day 5 BODYWT G	day 8 BODYWT G	
GROUP 0					
0 MG/KG	M	78.2	178.3	269.4	244.5%
	SD	20.8	48.2	71.7	
	N	10	10	10	
GROUP 1			* 124.0 %	51%	
185 MG/KG	M	80.5	177.7	258.1	220.6%.
	SD	21.9	46.0	56.6	
	N	10	10	10	
GROUP 2			120.8%	45%	
556 MG/KG	M	80.6	146.9	213.4	~~82.5%~~
	SD	21.6	47.2	64.2	164.8%
	N	10	10	10	
GROUP 3			92.3 %	45%	
1667 MG/KG	M	79.6	104.3**	189.2*	137.8%
	SD	24.0	37.4	67.5	
	N	10	10	10	
GROUP 4			31%	81.4%	
5000 MG/KG	M	73.5	71.1**	140.6**	91.3%.
	SD	23.1	13.0	31.9	
	N	10	4 -3.8%	4 97.7	

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

86/0522 0032

PRINTOUT

ROSEMARY GRAHAM MORA METAM-SODIUM ANAS PLATYRHYNCHOS ,04-08-91

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
2110	10	6	60.00001	37.69531
703.5	10	0	0	9.765625E-02
234.6	10	0	0	9.765625E-02
78.1	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 0 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 1835.669

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.

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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}

_____ LD_{50} = _____ mg/kg (95% C.L. _____) Control Mortality (%) = _____

Species

Slope = _____ # Animals/Level = _____ Age (Days) = _____

Lab

Sex = _____

_____ _____

14-Day Dose Level mg/kg/(% Mortality)

MRID # ( ), ( ), ( ), ( ), ( )

Comments:

8-Day Dietary LC_{50}

42.2% LC_{50} = 1835.7 ppm (95% C.L. 0, ∞) Control Mortality (%) = 0%

Species

Anas platyrhynchos Slope = — # Animals/Level = 10 Age (Days) = 9

Lab

BASF Sex = ND

RWM 4/8/91 Supplemental

8-Day Dose Level ppm /(% Mortality)

MRID # 78.1 (0%), 234 (0%), 703.5 (0%), 2110 (60%), ( )

414764-03

Comments: Only four test substance concentrations were employed. Based on nominal conc. of active ingredient.

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