6-18-91

MRID No. 411062-02

DATA EVALUATION RECORD

1. **CHEMICAL:** Sodium Methyldithiocarbamate.
Shaughnessey No. 039003.

2. **TEST MATERIAL:** Metam-Sodium; Batch No. ZH 130 585; 42.2% active ingredient.

3. **STUDY TYPE:** Freshwater Fish Static Acute Toxicity Test.
Species Tested: Rainbow Trout (Salmo gairdneri).

4. **CITATION:** Gelbke, H.P. and R. Munk. 1986. Report on the Study of Acute Toxicity of METAM-Sodium in Rainbow Trout (Salmo gairdneri Rich.). Registration Document No. 86/0511. Prepared by BASF Aktiengesellschaft, Department of Toxicology, Ludwigshafen, West Germany. Submitted by BASF Corporation Chemicals Division, Parsippany, NJ. EPA MRID No. 411062-02.

5. **REVIEWED BY:**

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6. **APPROVED BY:**

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7. **CONCLUSIONS:** This study is not scientifically sound. Numerous unexplained deviations from the guidelines collectively cast doubt on the usefulness of the results for risk assessment purposes. Under the conditions of the test, the 96-hour LC_{50} of Metam-Sodium for rainbow trout was 34.1 mg a.i./L (based on measured concentrations). Therefore, Metam-Sodium is classified as slightly toxic to rainbow trout. The NOEC, based on the absence of behavioral effects, was 2.15 mg/L (nominal).

8. **RECOMMENDATIONS:** N/A

6 hrs

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9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Rainbow trout (Salmo gairdneri) were obtained from a commercial supplier in West Germany and held in flowing dechlorinated tap water for 7-12 weeks. During holding, the temperature was 11°-20°C, the pH was approximately 7.5, the dissolved oxygen (D.O) was greater than 60% of saturation, the hardness was 2.5 mmol/L (1 mmol $CaCO_3$/L = 100 mg $CaCO_3$/L), and the alkalinity was 5.5 mmol/L. The fish were fed a commercially available fish food ad libitum. Records of disease treatments were kept.

The fish were acclimated to test conditions for 3-7 days. Weight and length of the fish were 6.6 (2.1-17.4) g and 8.3 (6.0-11.3) cm.

B. **Test System:** Vessels used in the test were glass aquaria with stainless steel frames (80 x 35 x 46 cm) containing 100 L of reconstituted water (control) or test solution. The reconstituted water was prepared to yield a total hardness of 2.5 mmol/L and an alkalinity of 0.8 mmol/L. The test temperature was 12°±2°C. A 16-hour light/8-hour dark photoperiod was used.

The test concentrations were prepared by adding appropriate amounts of a 10 g/L aqueous stock solution or test material directly to the test chambers.

C. **Dosage:** Ninety-six-hour static test. Based on preliminary tests, nine nominal concentrations (0.215, 0.464, 1.000, 2.150, 4.640. 10.000, 21.500, 46.400 and 100.000 mg/L) and dilution water controls were used. Testing took place on three separate dates, but it is unclear which concentrations were tested during each test.

D. **Design:** Ten fish were distributed to each test chamber. Biomass loading rate in the aquaria was 0.3-1.1 g/L. All chambers were observed at 1, 4, 24, 48, 72, and 96 hours for mortality and sublethal effects.

The D.O., pH, and temperature were monitored every 24 hours in the test aquaria containing live fish.

The concentrations of Metam-Sodium were measured in all test solutions at test initiation and in several concentrations at termination using HPLC.

E. **Statistics:** The 96-hour median lethal concentration (LC_{50}) was calculated using probit analysis.

12. **REPORTED RESULTS:** Measured concentrations are given in Table 1 (attached). At test initiation and termination, measured concentrations were 81.0 to 96.7% and 37.2 to 93.5% of nominal, respectively.

The mortality and behavioral responses of the rainbow trout are given in Table 2 (attached). The 96-hour LC_{50}, based on measured concentrations, was given as approximately 35.18 mg a.i./L. The no-observed-effect concentration (NOEC) was given as 0.464 mg/L (nominal) which was equivalent to 0.40 mg a.i./L (measured at 1 hour).

The D.O. of the test solutions ranged from 6.5 to 11.6 or 60 to 107.4% of saturation. The pH values ranged from 7.5 to 8.4. The temperature was 11°-14°C throughout the test.

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

The authors presented no conclusions.

A Quality Assurance Statement was included in the report. Another statement was included which stated that the study did not have to meet the Good Laboratory Practice requirements of 40 CFR 160.

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

A. **Test Procedure:** The test procedures were generally in accordance with protocols recommended by the guidelines, but deviated as follows:

The results for a number of test concentrations were obtained using separate tests, two and five weeks after the definitive test. All test levels should be initiated on the same day.

The presentation of the analytical results was very confusing. All test solutions were measured on day 0, but only seven out of twelve were measured at the completion of the tests. No explanations were given.

The test material is 57.8% inert or carrier ingredients. A concurrent control containing the concentration of inert or carrier ingredients equal to that found in the highest test concentration should have been part of the test design.

The hardness of the dilution water, 2.5 mmol/L (250 mg/L), was higher than recommended (no greater than 200 mg/L).

Each nominal concentration was approximately 46% of the next highest concentration. The guidelines recommend that each concentration be at least 60% of the next highest concentration.

The period of time between test solution preparation and test initiation was not given in the report. Fish should be placed into the test solutions within 30 minutes of solution preparation.

The report does not state if the fish were fed during the test.

The system used to control temperature was not described in the report.

Temperature must be monitored continuously or at least every 6 hours (if the test vessels are located in a water bath). Temperature in this study was probably monitored every 24 hours.

The acclimation period of the rainbow trout to the dilution water and temperature was 3-7 days. The SEP recommends that the acclimation period to the test conditions be at least two weeks.

Fish weight ranged from 2.1 to 17.4 g which was larger than recommended (0.1-5 g).

The recommended test temperature for rainbow trout is 12°C. The temperature during the test was as high as 14°C.

A 30-minute dawn/dusk simulation is recommended in the SEP. No transition period between light and dark was used in the study.

The biological loading (0.3-1.1 g/L) in the test was higher than recommended (0.8 g/L).

Rainbow trout mortality during the "period of adaptation" was 5.6%. If this period is the same as an acclimation period, then these fish should not have been used in the test. A group of fish are acceptable if 3% mortality or less occurred during acclimation.

The D.O. during the test was as high as 11.6 mg/L (107.4% of saturation). Dissolved oxygen concentrations should remain at or below 100% of saturation.

B. **Statistical Analysis:** The reviewer used EPA's Toxanal program and the results given in Table 3 (attached) to calculate the 96-hour LC_{50} value as 34.1 mg a.i./L with 95% confidence interval of 20.1-87.8 mg a.i./L (see attached printout).

C. **Discussion/Results:** Numerous deviations from the guidelines weaken this study. In addition, the test design (i.e. including in the definitive test results test levels performed at a later date) and analytical measurements (i.e. only a few of the concentrations were measured at test termination with no explanation) cast doubt on the validity and usefulness of the results. The presentation of the study results was somewhat confusing. The reviewer was unable to determine which test levels were tested on each test day. Perhaps the results could be more useful if the results of each test were separated into individual tests. It is unacceptable to combine results from 2 or 3 tests to determine the LC_{50} value.

Under the conditions of the test, the 96-hour LC_{50} of 34.1 mg a.i./L (based on the results in Table 3) classifies Metam-Sodium as slightly toxic to rainbow trout. The NOEC given by the authors was 0.464 mg/L, but, based on the results in Table 2, the NOEC appears to be 2.15 mg/L (nominal concentration).

D. **Adequacy of the Study:**

(1) **Classification:** Invalid.

(2) **Rationale:** Numerous deviations from the guidelines collectively cast doubt on the usefulness of the data for risk assessment purposes.

(3) **Repairability:** No.

15. **COMPLETION OF ONE-LINER FOR STUDY:** Yes, 03-21-91.

TABLE 1

85/232
RAINBOW TROUT
(SALMO GAIRDNERI RICH.)

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY

RESULTS :

NOMINAL CONC. (MG/L)	ANALYTICALLY DETECTED CONCENTRATIONS (MG/L)					
	1 H	4 H	24 H	48 H	72 H	96 H
0.215	0.18					0.08 -
0.464	0.40					
1.000	0.90					
2.150	1.90					
4.640	3.90					
1.000	0.81					3.80 -
2.150	2.01					0.62 -
4.640	4.46					
10.000	9.07					3.74 -
21.500	20.8					
46.400	44.2					20.1 -
100.000	85.9					39.9 -
						87.8 -
0.000						
0.000						
0.000						

TABLE 2

85/232
RAINBOW TROUT
(SALMO GAIRDNERI RICH.)

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY

RESULTS :

NOMINAL CONC. (MG/L)	NUMBER OF FISH	DEAD FISH AFTER 1 H	4 H	24 H	48 H	72 H	96 H
0.215	10	0	0	0	0	0	0
0.464	10	0	0	0	0	0	0
1.000	10	0	0	0	0	0	0
2.150	10	0	0	0	0	0	0
4.640	10	0	0	0	0	0	0
1.000	10	0	0	0	0	0	0
2.150	10	0	0	0	0	0	0
4.640	10	0	0	0	0	0	0
10.000	10	0	0	0	0	0	0
21.500	10	0	0	0	0	0	0
46.400	10	0	0	0	0	0	0
100.000	10	0	0	0	0	5	7
					10	10	10
0.000	10	0	0	0	0	0	0
0.000	10	0	0	0	0	0	0
0.000	10	0	0	0	0	0	0

NOMINAL CONC. (MG/L)	SYMPTOMS 1 H	4 H	24 H	48 H	72 H	96 H
0.215						
0.464						
1.000						
2.150						
4.640						
1.000						Y
2.150					Y	Y
4.640					Y	Y
10.000				V	Y	Y
21.500				V	Y	Y
46.400				V	Y	Y
100.000				Y	LN	L
			T			
0.000						
0.000						
0.000						

EXPLANATION OF SYMPTOMS:

A=APATHY
B=ABDOMINAL DISTENSION
E=EXOPHTHALMOS
F=ESCAPE REFLEX
H=HYPERREFLEXIA
K=CONVULSIONS
L=GASPING
N=NARCOTIC-LIKE STATE
T=TUMBLING
U=RESTLESSNESS
V=DISCOLORATION
W=HEADSTAND
X=ACCELERATED RESPIRATION
Y=LYING ON THE BOTTOM

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TABLE 3

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RAINBOW TROUT
(SALMO GAIRDNERI RICH.)

BASF AKTIENGESELLSCHAFT
DEPARTMENT OF TOXICOLOGY

ANALYTICALLY DETECTED CONCENTRATIONS

FISH TOXICITY : AFTER 96H

CONCEN-TRATION (MG/L)	NUMBER OF FISH START	AFTER	DEAD FISH 96H	MOR-TALITY (%)	CONCEN-TRATION USED
0.080	10		0	0.0	
0.620	10		0	0.0	
3.740	10		0	0.0	
3.800	10		0	0.0	
20.100	10		0	0.0	*
39.900	10		7	70.0	*
87.800	10		10	100.0	

LC50 ABOUT 35.18 (VALUE OF INTERPOLATION)

LOUIS M. RIFICI METAM-SODIUM SALMO GAIRDNERI 3-20-91

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
87.8	10	10	100	9.765625E-02
39.9	10	7	70	17.1875
20.1	10	0	0	9.765625E-02
3.8	10	0	0	9.765625E-02
3.74	10	0	0	9.765625E-02
.62	10	0	0	9.765625E-02
.08	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 20.1 AND 87.8 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 34.1191

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 No. 039003 Chemical Name Sodium Methyldithiocarbamate Chemical Class ____ Page 1 of 1

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Validatic Status
14-Day Single Dose Oral LD_{50}		LD50 = mg/kg (95% C.L.) Contr. Mort.(%)=		
Species ____		Slope= # Animals/Level= Age(Days)= Sex =		
Lab		14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
14-Day Single Dose Oral LD_{50}		LD50 = mg/kg. (95% C.L) Contr. Mort.(%)=		
Species ____		Slope= # Animals/Level= Age(Days)= Sex =		
Lab		14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Age(Days)= Sex =		
Lab ____		8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L) Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Age(Days)= Sex =		
Lab ____		8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
48-Hour LC_{50}		LC50 = pp__ (95% C.L.) Contr. Mort.(%)= Sol. Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Temperature =		
Lab ____		48-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
96-Hour LC_{50}		LC50 = 34.1 *ppm (95% C.L. binomial test 20.1 - 87.8) Con. Mor(%)= 0 Sol. Con. Mor.(%)= NA	LR 3/21/91	INVALID
Species Salmo gairdneri		Slope= NA , # Animals/Level= 10 Temp.= 12°C		
Lab BASF Aktiengesellschaft West Germany 42.2%		96-Hour Dose Level *ppm/(%Mortality) 0.08 (0), 0.62 (0), 3.74 (0), 3.8 (0), 20.1 (0), 39.9(70), 87.8(100)		
Acc. MRID 411062-02		Comments: *measured concentrations (TABLE 3)		
96-Hour LC_{50}		LC50 = pp__ (95% C.L) Con. Mort.(%)= Sol. Con. Mort.(%)=		
Species		Slope= # Animals/Level= Temp.=		
Lab ____		96-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		