RHÔNE-POULENC

TOXICOLOGY DEPARTMENT
P.O. BOX 12014, 2 T.W. ALEXANDER DRIVE
RESEARCH TRIANGLE PARK, NC 27709
(919) 549-2000 TELEFAX (919) 549-8525
INTERNATIONAL TELEX NUMBER 4999378–ANSWERBACK APC RTP

Contains NO CBI

October 5, 1992

A

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

8EHQ-92-12599

8892001083

INIT

Document Processing Center (TS-790)
Office of Toxic Substances
US Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID No.: 8ECAP - 0004

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN 5266, Princeton, NJ 08543-5266) and its subsidiary Rhône-Poulenc Ag Company, the attached study report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for a TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA.

The enclosed study report provides information on MC 5714. The CAS number and name for this chemical are 24814-29-7 and N-[5-(1,1-dimethyl)-1,3,4-thiadiazol-2-yl]-N'-methylurea. This chemical was synthesized for pesticide research and development approximately 15 to 20 years ago. To our knowledge, a pesticide application on this chemical has never been submitted to EPA under the Federal Insecticide, Fungicide, and Rodenticide Act.

No claims of confidentiality are made for this submission. The title of the enclosed report is "Acute Oral Toxicity Study in Rats Compound: Mobil 5714 80% Wettable Powder". The following is a summary of the adverse effects observed in this study.

This study is being submitted under Section 8(e) because of observed clinical signs. Respiratory depression, ataxia, clonic convulsions, loss of righting reflex, ptosis, piloerection, straub tail, tremors, and decreased locomotor activity were observed in animals surviving to study termination as well as those dying during the study. The oral LD50 was determined to be 2000 mg/kg.

No previous TSCA Section 8(e) notices have been submitted on this chemical. In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

RECEIVED 3/14/95

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,

Glenn S. Simon, PhD, DABT
Director of Toxicology

Cannon Laboratories, Inc.

P. O. Box 3627, Reading, Pa. 19605 (215) 375-4536

STUDY: ACUTE ORAL TOXICITY IN RATS

COMPOUND: MOBIL 5714 80% WETTABLE POWDER

SUBMITTED TO:

MOBIL CHEMICAL COMPANY
RESEARCH AND DEVELOPMENT LABORATORIES
P.O. BOX 240
EDISON, NEW JERSEY 08817

DATE: OCTOBER 18, 1974

LABORATORY NUMBER: 4E-4129

AUTHORIZED SIGNATURE G. K. Park

TITLE Dir Biological Services

Cannon Laboratories, Inc.

TABLE OF CONTENTS

	PAGE
AUTHORIZATION	1
METHOD	2
SUMMARY AND CONCLUSION	4
TABLES AND FIGURES	5

Cannon Laboratories, Inc.

This investigation was authorized in a letter from the Mobil Chemical Company, Research and Development Laboratories, P. O. Box 240, Edison, New Jersey, dated September 13, 1974.

For this testing procedure the material "Mobil 5714 80% Wettable Powder" received by this laboratory on September 16, 1974, was used.

Cannon Laboratories, Inc.

METHOD:

Fifty male Wistar derived albino rats weighing between 200 and 300 grams were obtained from a local supplier for use in this experiment. The animals were housed individually and permitted a standard laboratory diet (Purina Rat Chow) plus water ad libitum.

The test animals were fasted for a period of approximately twenty-four hours prior to testing at which time appropriate amounts of the test material was prepared to yield a final concentration of 1g/5ml H_2O and administered by gastric gavage to ten rats per group, on a gm/kg B.W. basis, to achieve the desired dose levels. Each animal received the desired dosage in a single administration. The test groups were established as follows:

NO. OF GROUP	ANIMALS PER GROUP	DOSE (gm/kg B.W.)	TEST MATERIAL
I	10	1.00	"Mobil 5714"
II	10	2.00	"Mobil 5714"
III	10	3.00	"Mobil 5714"
IV	10	4.00	"Mobil 5714"
V	10	---	Control

The animals were observed for mortality rates and signs of toxicity at one, three, six, twenty-four, forty-eight, seventy-two hours, and daily thereafter for a total of fourteen days. Body weights were taken initially and at seven and fourteen days.

Mortality data are given in Table I. Signs of toxicity and other changes in physical appearance and behavior are presented for each rat in Table II. Initial, seven day and fourteen day body weights are presented in Table III.

The twenty-four hour and fourteen day LD50 determinations (see Figure I) were calculated in accordance with the method of Miller and Tainter (Experimental Biology and Medicine, 57, pp 261-264, 1944).

Cannon Laboratories, Inc.

SUMMARY

Male rats administered oral dose levels of 1,00 to 4.00 gms/kg B.W. of Mobil Company sample "Mobil 5714 80% Wettable Powder" exhibited respiratory depression, ataxia, clonic convulsions, loss of righting reflex, ptosis, piloerection, straub tail, tremors, decreased locomoter activity, and dose-related mortality.

The acute oral LD50 for fifty male rats at 24 hours was 2.45 $\pm$ 0.31 g/kg B.W. and at 14 days, was 2.00 $\pm$ 0.32 g/kg B.W..

York Terrell
Technician in Charge

Geoffrey Parke
Director of Biological Services

TABLE I

MORTALITY FOR THE ACUTE ORAL TOXICITY

STUDY OF MOBIL 5714 80% WETTABLE POWDER IN RATS

DOSE (gm/kg B.W.)	NO. PER GROUP	HOUR						DAY											TOTAL
		1	3	6	24	48	72	4	5	6	7	8	9	10	11	12	13	14	
1.00	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2.00	10	0	0	1	2	1	1	0	0	0	0	0	0	0	0	0	0	0	5
3.00	10	0	4	1	2	1	0	0	0	0	0	0	0	0	0	0	0	0	8
4.00	10	0	3	5	2	-	-	-	-	-	-	-	-	-	-	-	-	-	10
Control	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

TABLE 2

CLINICAL OBSERVATIONS FOR THE ACUTE ORAL TOXICITY STUDY OF MOBIL 5714 80% WETTABLE POWDER

DOSE (gm/kg B.W.)	ANIMAL NUMBER	HOUR 1	3	6	24	48	72	DAY 4	5	6	7	8	9	10	11	12	13	14
1.0	1	D	D-Pt-P	D-P-St	D-Pt A	D	N	N	N	N	N	N	N	N	N	N	N	N
	2	D-Pt	R-Rr	Rr-R	D-St	N	N	N	N	N	N	N	N	N	N	N	N	N
	3	D-P	D-P-Pt	Pt-D A	D-St	D	D	N	N	N	N	N	N	N	N	N	N	N
	4	D	D-P	R-P-Pt	D-A	D	N	N	N	N	N	N	N	N	N	N	N	N
	5	D	D	D-A-Pt	D	N	N	N	N	N	N	N	N	N	N	N	N	N
	6	D-Pt	D-P-Pt	D-Pt-P	D-P	D	D	N	N	N	N	N	N	N	N	N	N	N
	7	D-Pt	D-P-Pt	D-P	D	N	N	N	N	N	N	N	N	N	N	N	N	N
	8	D-Rr	D-Pt-Rr	Pt-R-Rr	D-Pt-St	D	N	N	N	N	N	N	N	N	N	N	N	N
	9	D	D-Rr	D-Rr-Pt	D-Pt	N	N	N	N	N	N	N	N	N	N	N	N	N
	10	D	D-P-Pt	D-P-Pt	D-P	D	N	N	N	N	N	N	N	N	N	N	N	N

D= Decreased locomotor activity

St= Straub tail

A= Ataxia

N= Normal

R= Respiratory depression

P= Piloerection

Pt= Ptosis

Rr= Loss of righting reflex

TABLE 2

CLINICAL OBSERVATIONS FOR THE ACUTE ORAL TOXICITY STUDY OF MOBIL 5714 80% WETTABLE POWDER

DOSE (gm/kg B.W)	ANIMAL NUMBER	HOUR 1	3	6	24	48	72	DAY 4	5	6	7	8	9	10	11	12	13	14
2.0	1	D-Pt	D-Pt-P	D-Pt-P	D-P A	D-P-Pt	DEATH											
	2	D	Pt-D	D-P-Pt	D-P A	D-P-Pt-St	D-P	N	N	N	N	N	N	N	N	N	N	N
	3	Rr-R	Rr-R	R-Pt Rr	DEATH													
	4	P-Pt	D-P-Pt	D-P-Pt	D-P-Pt	D-P-Pt	D	N	N	N	N	N	N	N	N	N	N	N
	5	D-Pt	D-P-Pt	D-P-Pt	P-D-Pt	DEATH												
	6	D	D-P	D-P	D-P	D-P	D	N	N	N	N	N	N	N	N	N	N	N
	7	P-Pt	D-P-Pt	P-Pt	D-P	D	N	N	N	N	N	N	N	N	N	N	N	N
	8	R-Rr	R-Rr-Pt	R-Rr-Pt	DEATH													
	9	R	R-P-Pt	DEATH														
	10	R-Pt	P-Pt	P-Pt	P-Pt-A		D-P	N	N	N	N	N	N	N	N	N	N	N

A= Ataxia

R= Respiratory depression

D= Decreased locomotor activity

Rr= Loss of righting reflex

DEATH= Death

St= Straub tail

N= Normal

P= Piloerection

Pt= Ptosis

TABLE 2

CLINICAL OBSERVATIONS FOR THE ACUTE ORAL TOXICITY STUDY OF MOBIL 5714 80% WETTABLE POWDER

DOSE (gm/kgB.W.)	ANIMAL NUMBER	HOUR 1	3	6	24	48	72	DAY 4	5	6	7	8	9	10	11	12	13	14
3.0	1	R-Pt-P	DEATH															
	2	R-Cc	DEATH															
	3	R-T	Pt-R-Rr	Pt-R Rr	DEATH													
	4	D-A	Pt-R-Rr	R-Pt Rr	DEATH													
	5	R-Rr	R-Rr	DEATH														
	6	R-Rr	DEATH															
	7	R-Cc	DEATH															
	8	R-T	R-T	R-Rr	Pt-R-Rr		DEATH											
	9	D-T	R-T	R-A	D-P	P	D	N	N	N	N	N	N	N	N	N	N	N
	10	Pt-R-T	R-Pt-A	P-Pt-D	D-P	D	N	N	N	N	N	N	N	N	N	N	N	N

A= Ataxia

Cc= Clonic convulsions

D= Decreased locomoter activity

DEATH= Death

N= Normal

R= Respiratory depression

Rr= Loss of righting reflex

P= Piloerection

Pt= Ptosis

T= Tremors

TABLE 2

CLINICAL OBSERVATIONS FOR THE ACUTE ORAL TOXICITY STUDY OF MOBIL 5714 80% WETTABLE POWDER

DOSE (gm/kg B.W.)	ANIMAL NUMBER	HOUR 1	3	6	24	48	72	DAY 4	5	6	7	8	9	10	11	12	13	14
4.0	1	R-Rr	DEATH															
	2	R-Pt-P	R-Pt-Rr		DEATH													
	3	R-Rr	R-Rr	R-Rr	DEATH													
	4	R-Rr	DEATH															
	5	R-Rr	DEATH															
	6	R-T	R-Cc	DEATH														
	7	R-Rr	R-Cc	DEATH														
	8	R-Rr	R-Rr	R-Rr	DEATH													
	9	R-T	R-T	DEATH														
	10	R-P-Pt	R-Cc	DEATH														

Cc= Clonic convulsions

DEATH= Death

R= Respiratory depression

Rr= Loss of righting reflex

P= Piloerection

Pt= Ptosis

T= Tremors

TABLE 3

INDIVIDUAL BODY WEIGHTS (GRAMS)

DOSE gm/kg B.W.	ANIMAL NO.	TEST DAY 0	7	14
1.0	1	200	220	298
	2	203	230	290
	3	201	227	301
	4	200	232	301
	5	210	235	302
	6	210	230	295
	7	200	227	250
	8	211	220	278
	9	207	236	296
	10	220	250	299

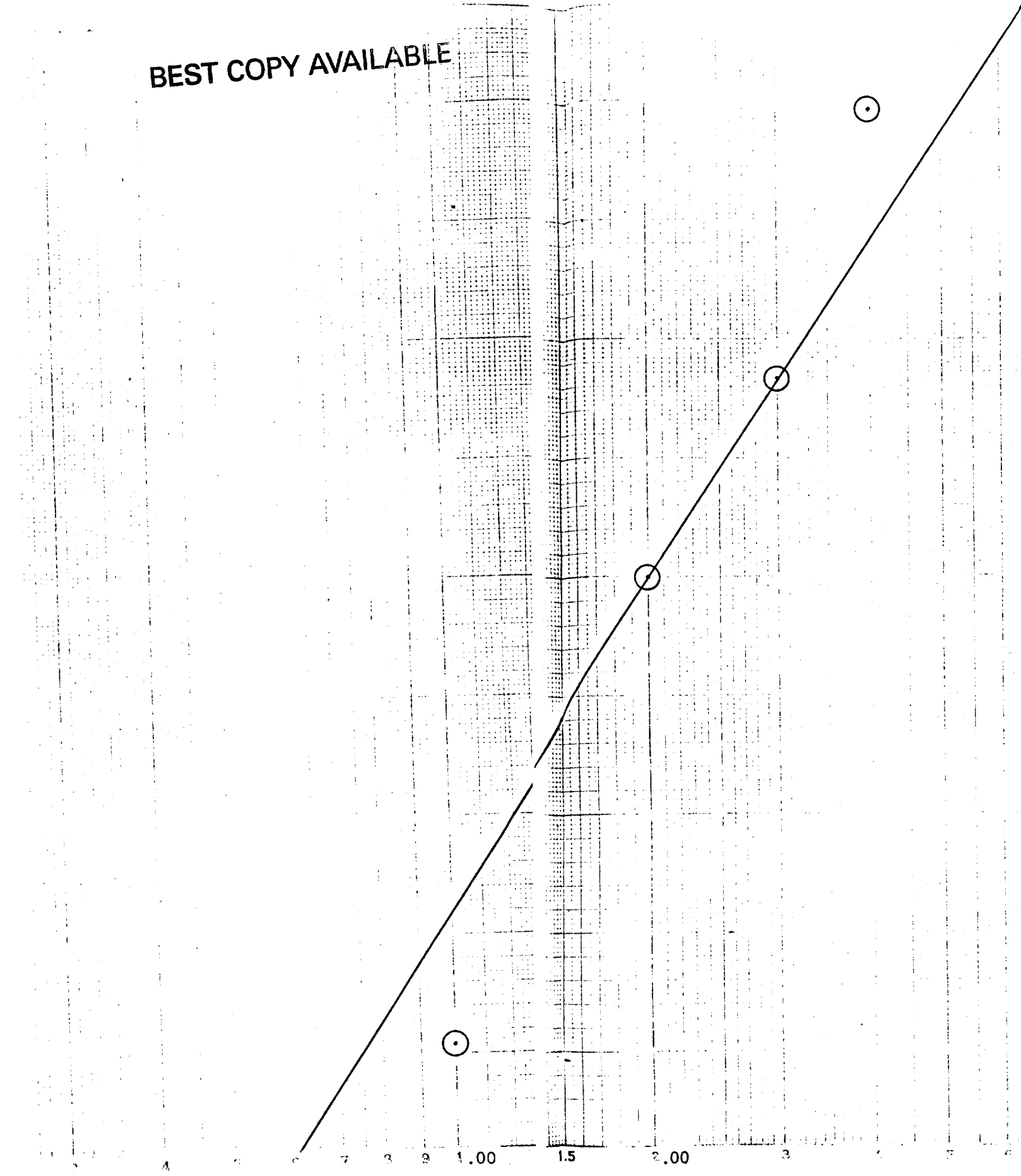
DOSE gm/kg B.W.	ANIMAL NO.	TEST DAY 0	7	14
2.0	1	210	-	-
	2	201	230	290
	3	210	-	-
	4	213	215	287
	5	215	-	-
	6	210	236	307
	7	201	250	301
	8	200	-	-
	9	200	-	-
	10	210	240	300

TABLE 3

INDIVIDUAL BODY WEIGHTS (GRAMS)

DOSE gm/kg B.W.	ANIMAL NO.	TEST DAY 0	7	14	DOSE gm/kg B.W.	ANIMAL NO.	TEST DAY 0	7	14
3.0	1	200	-	-	4.0	1	210	-	-
	2	210	-	-		2	215	-	-
	3	207	-	-		3	216	-	-
	4	211	-	-		4	207	-	-
	5	201	-	-		5	201	-	-
	6	200	-	-		6	200	-	-
	7	200	-	-		7	200	-	-
	8	207	-	-		8	210	-	-
	9	210	237	288		9	222	-	-
	10	215	249	296		10	200	-	-

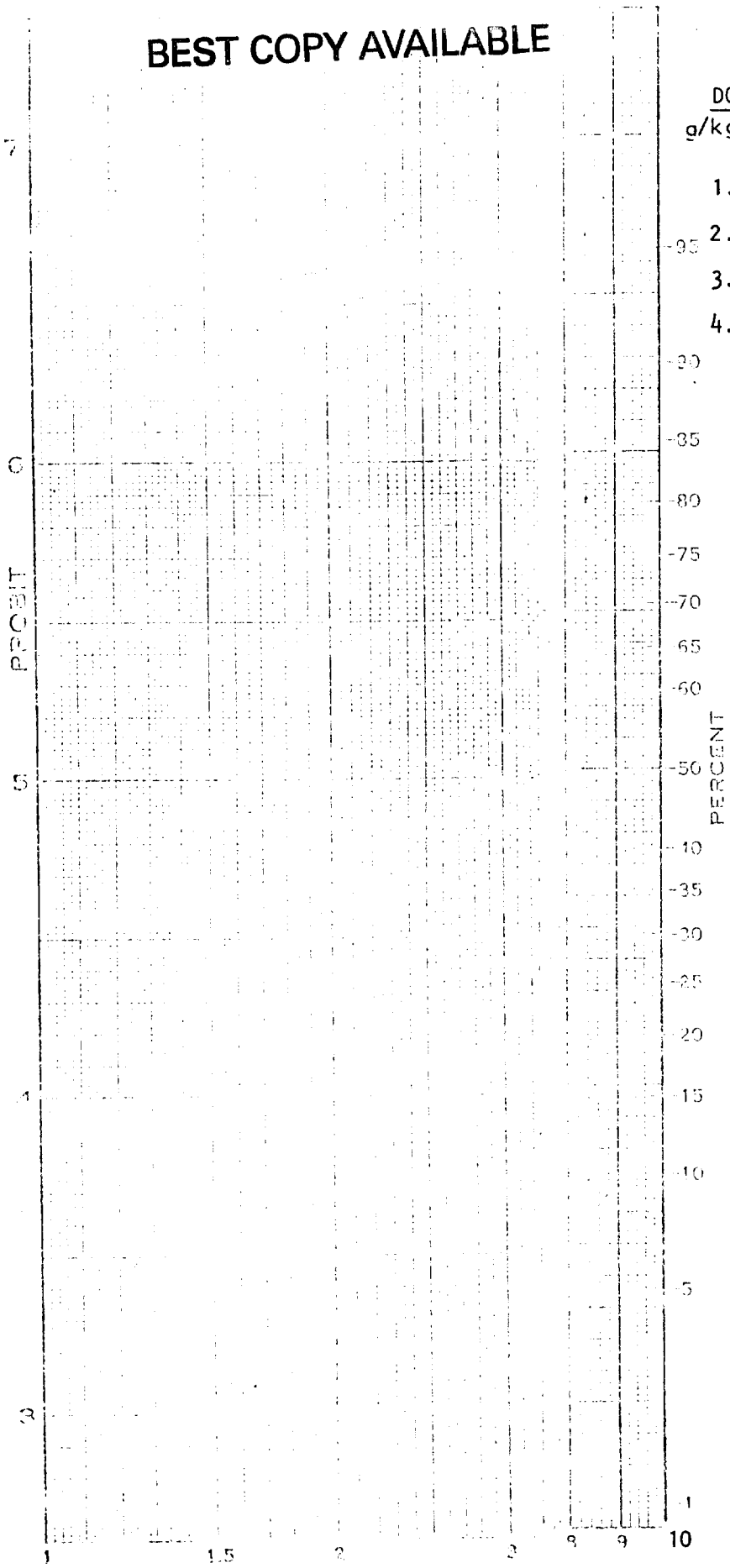
BEST COPY AVAILABLE



CALCULATION FOR S. E.

24 Hours

FIGURE I



DOSE g/kg B.W.	MORTALITY %	PROBIT
1.00	0	3.04
2.00	30	4.48
3.00	70	5.52
4.00	100	6.96

Probit 6 (84%) = 3.60

Probit 4 (16%) = 1.66

2S = 1.94

2N = 40

$$S.E. = \frac{2S}{\sqrt{2N}} = \frac{1.94}{\sqrt{40}} = \frac{1.94}{6.32} = .31$$

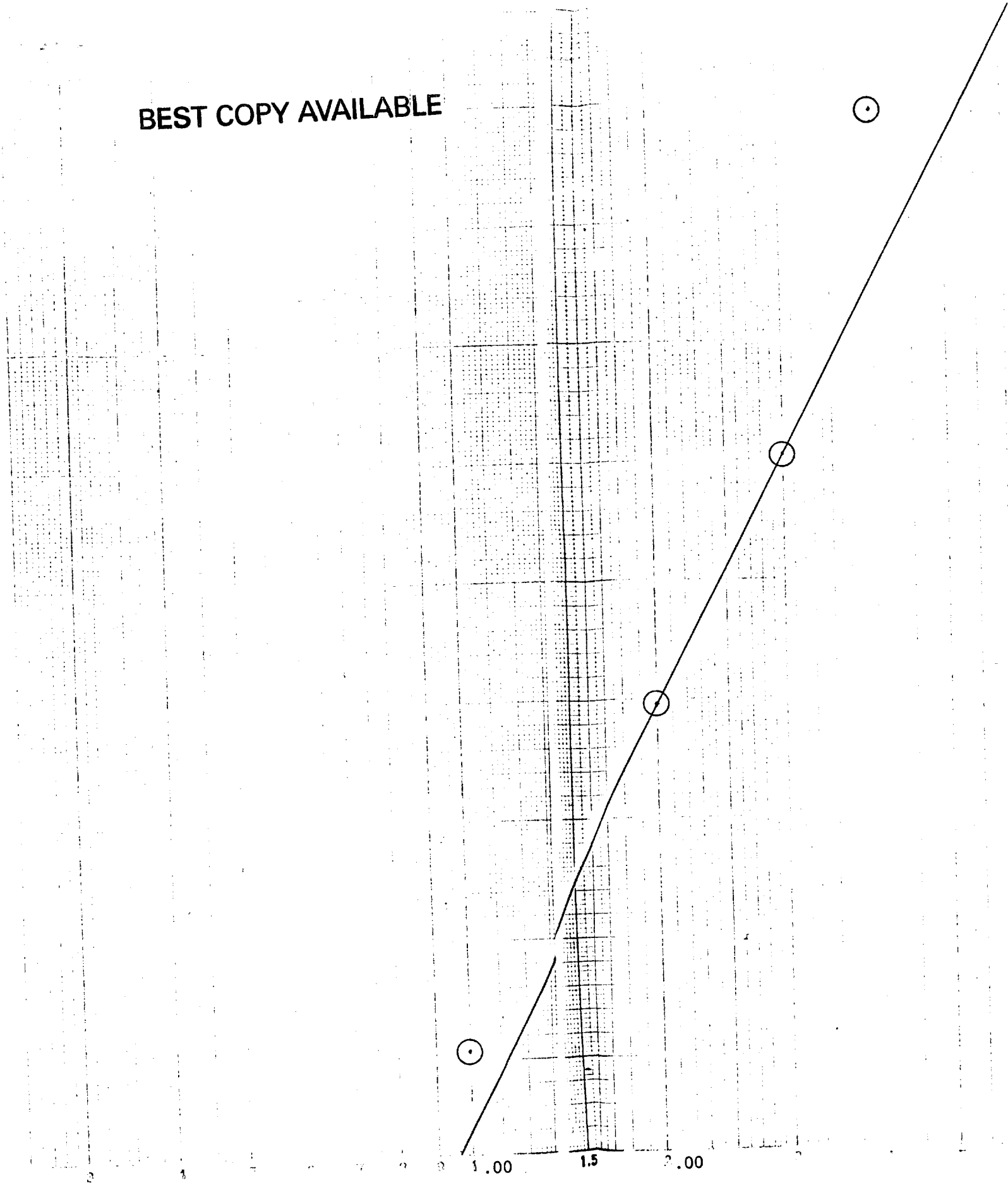
LD50 = 2.45 $\pm$ .31 g/kg B.W.

N= # of Animals between Probit 3.5 & 6.5

BEST COPY AVAILABLE

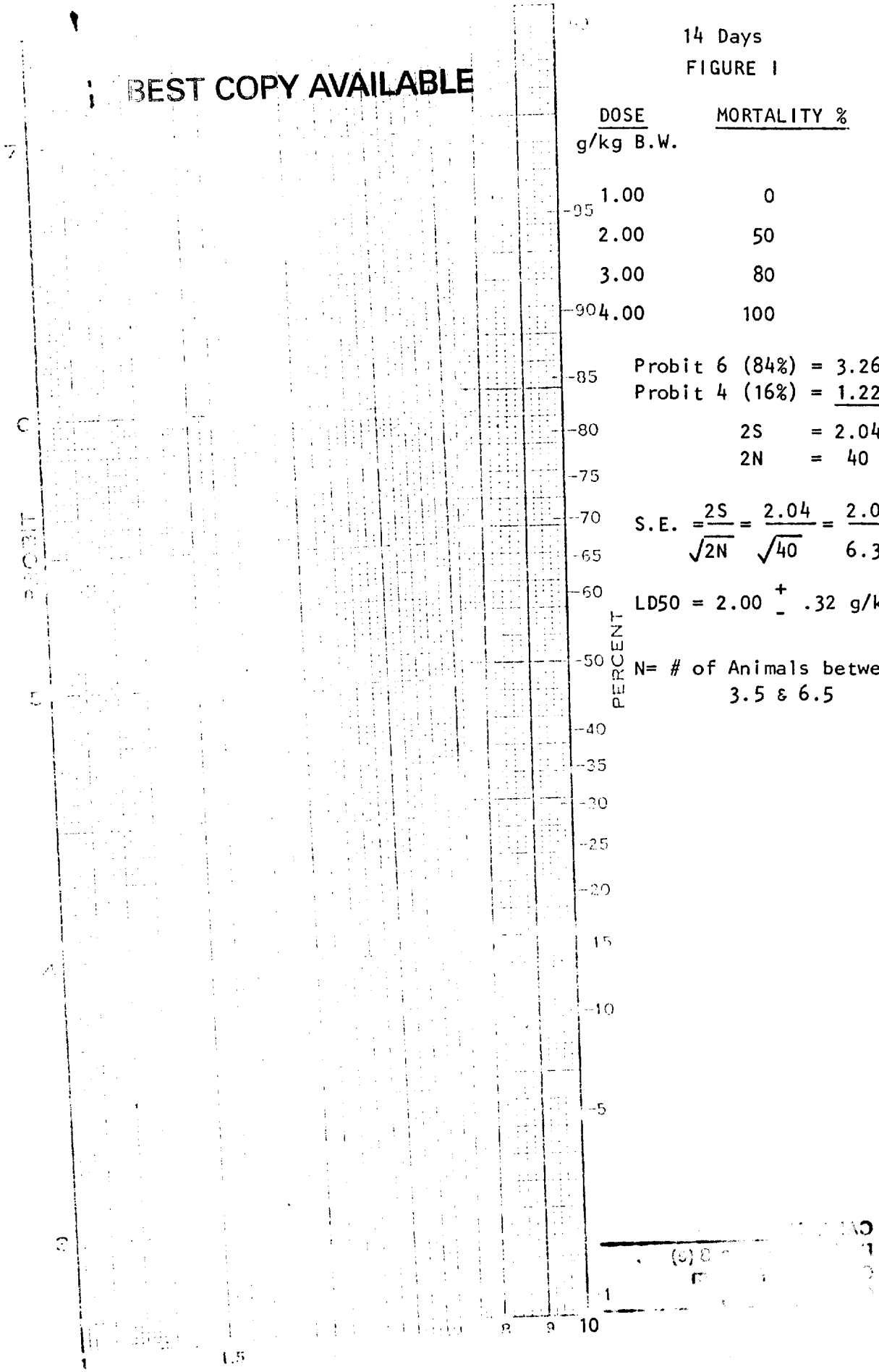
WINTHROP LOGARITHMIC - PROBIT

BEST COPY AVAILABLE



CALCULATION FOR S.E.

BEST COPY AVAILABLE



14 Days

FIGURE I

DOSE g/kg B.W.	MORTALITY %	PROBIT
1.00	0	3.04
2.00	50	5.00
3.00	80	5.84
4.00	100	6.96

Probit 6 (84%) = 3.26
Probit 4 (16%) = 1.22

2S = 2.04
2N = 40

$$S.E. = \frac{2S}{\sqrt{2N}} = \frac{2.04}{\sqrt{40}} = \frac{2.04}{6.32} = .32$$

LD50 = 2.00 $\pm$ .32 g/kg B.W.

N= # of Animals between Probit 3.5 & 6.5

CAP ID No. A-AG-MAM-0771
Reviewed for Sec. 8 (e)
Compliance Program
On 6/23/92 By MAM

Triage of 8(e) Submissions

Date sent to triage: MAY 0 9

NON-CAP CAP

Submission number: 12599A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.):

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1,2 **pages** 1,2, DATA

Notes:

Contractor reviewer : PM **Date:** 4/26/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092-12599 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/05/92 OTS DATE: 10/13/92 CSRAD DATE: 03/14/95

CHEMICAL NAME:
Urea, N-[5-(1,1-dimethyl)-1,3,4-thiadiazol-2-yl]-N'-methyl-
MC 5714

CAS#
24814-29-7
"

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	RAT	LOW	R&D	
CAS SR	NO	NO (CONTINUE)		MED	Pesticide	
	DETERMINE	REFER		HIGH		

COMMENTS

-CPSS- 0927952113

0 0 0 0 0 0 0 0 0 0 0
> <ID NUMBER>
8(E)-12599A

> <TOX CONCERN>
L

> <COMMENT>
ACUTE ORAL TOXICITY IN MALE RATS IS LOW CONCERN BASED ON AN LD50 OF 2.45 G/KG. DOSE (G/MG) AND MORTALITY: 1.0 (0/10), 2.0 (5/10), 3.0 (8/10), AND 4. 0 (10/10). CLINICAL SIGNS INCLUDED DEPRESSED RESPIRATION, ATAXIA, CLONIC CONVULSIONS, LOSS OF RIGHTING REFLEX, PTOSIS, PILOERECTION, STRAUB TAIL, TREMORS, AND DECREASED LOCOMOTOR ACTIVITY.

$$$$