

8ENQ-0296-13588



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ORIGINAL

February 15, 1996

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Office of Pollution Prevention and Toxics  
U. S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460  
ATTN: 8(e) Coordinator



88960000068

CONFIDENTIAL

Dear Sir or Madam:

**Subject:** Report submitted in accordance with the U. S. Environmental Protection Agency Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk-Section 8(e) TSCA.

The following information is submitted in accordance with the above statement. The submission pertains to 4-chlorobenzenesulphonamide (CAS# 98-64-6) and is being submitted because of adverse effects observed in an acute oral toxicity study conducted with rats.

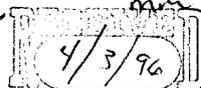
We do not believe the information in this report reasonably supports the conclusion that the substance presents a substantial risk. It is, however, being submitted to enable the Agency to draw its own conclusions.

Groups of five male rats and five female rats were administered a single dose of the test compound by gavage at dose levels of 250, 500, 1000, or 2000 mg/kg body weight. All animals at the 1000 and 2000 mg/kg dose levels and a single male and all females at the 500 mg/kg dose level died prior to study termination. The acute oral LD<sub>50</sub> for this material was calculated to be 574 mg/kg for male rats and 354 mg/kg for female rats.

Abnormal clinical signs evident during the 14-day observation period included slight to severe weakness, prostration, hypothermia, blood in the urine, a reduced amount or lack of feces, dehydration, and porphyrin nasal and/or ocular discharges. Prostration was observed only in animals which died after exposure to the test material and severe weakness was either transient or seen only in moribund animals. Although the cause of death for animals which died after exposure to the test material was not determined, the test material appeared to be a gastric irritant which caused leakage of the gastric contents into the abdominal cavity. The major treatment-related changes noted at necropsy included hemorrhage and necrosis in the glandular gastric mucosa and hyperkeratosis and acanthosis in the non-glandular gastric mucosa. In addition, leakage of the test material or gastric juices through the stomach wall resulted in necrosis and hemorrhage in the liver adjacent to the stomach. All other effects appear to represent secondary changes.

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R. Hays Bell, Ph.D., Vice-President and Director, Health, Safety, and Environment  
Eastman Kodak Company, Rochester, NY 14652-6256



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In addition to the acute oral toxicity study, we have enclosed a copy of an acute dermal irritation study in rabbits. No dermal irritation was evident when a single topical dose of 0.5 grams was left in contact with the skin under an occlusive wrap for four hours.

The test material is a site-limited intermediate used in the synthesis of another chemical. Unreacted test material is not expected to be present in the final chemical. This material is currently purchased from an outside vendor. A copy of this submission letter will be forwarded to the vendor. We are not aware of any adverse health problems associated with the use of the test material. The original health hazard evaluation of this intermediate resulted in a "Health Hazards Unknown" rating. This rating is accompanied by a statement to employees to "Avoid all contact". We will continue to handle the material in the same manner based on the new toxicology data.

Please contact me if additional information is required.

Sincerely,

A handwritten signature in cursive script that reads "R. Hays Bell".

R. Hays Bell  
(716) 722-5036

RHB:JAF

Enc.

STUDY TITLE

**4-CHLOROBENZENESULPHONAMIDE  
ACUTE ORAL TOXICITY STUDY IN THE RAT**

**HAEL NUMBER: 94-0046 KAN: 002243  
CAS REGISTRY NUMBER: 98-64-6**

**FINAL REPORT**

AUTHOR

Kenneth P. Shepard, B.S.

PERFORMING LABORATORY

Toxicological Sciences Laboratory  
Health and Environment Laboratories  
Eastman Kodak Company  
1100 Ridgeway Avenue  
B-320 Kodak Park  
Rochester, New York 14652-6272  
USA

LABORATORY PROJECT ID

HAEL Number: 94-0046

STUDY SPONSOR

Eastman Kodak Company

STUDY COMPLETION DATE

January 30, 1996

QUALITY ASSURANCE INSPECTION STATEMENT

[21 CFR 58.35(B)(7), 40 CFR 792.35(B)(7), and 40 CFR 160.35(B)(7)]

STUDY: 94-0046-1 STUDY DIRECTOR: SHEPARD, K.P.  
ACCESSION NUMBER: 002243

PAGE 1  
01/22/96

STUDY TYPE: ACUTE ORAL TOXICITY

M. James  
(AUDITOR, QUALITY ASSURANCE UNIT)

1/22/96  
DATE

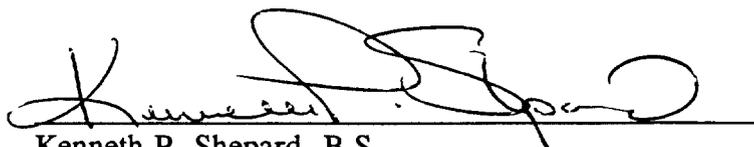
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THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY  
ASSURANCE UNIT OF HAEL, EASTMAN KODAK COMPANY ROCHESTER, N.Y.  
AND WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES:  
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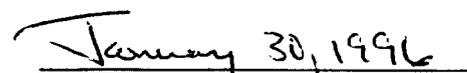
INSPECTION DATES	PHASE(S) INSPECTED	STATUS REPORT DATES
06/15/94	PROTOCOL APPENDIX/AMENDMENT SUBMISSION TEST SUBSTANCE WEIGH AND MIX WITH CARRIER TEST SYSTEM RANDOMIZATION TEST SYSTEMS WEIGHTS DOSE CALCULATIONS TEST SUBSTANCE CARRIER MIXTURE DOSING OF TEST SYSTEMS CLINICAL SIGNS-IMMEDIATE RESPONSE	
06/27/94	PROTOCOL APPENDIX/AMENDMENT SUBMISSION REPEAT - LOWER DOSES	
06/30/94	CLINICAL SIGNS AT 72 HRS.	
07/11/94	PROTOCOL APPENDIX/AMENDMENT SUBMISSION REPEAT - LOWER DOSE	
07/14/94	CLINICAL SIGNS AT 72 HRS.	
11/01/94	GROSS PATHOLOGY HISTOPATHOLOGY PATHOLOGY REPORT	11/01/94
01/22/96	FINAL REPORT REVIEW	01/22/96

**COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS**

The study described by this report was conducted in compliance with the following Good Laboratory Practice Standards:

Annex 2 of the Organization for Economic Cooperation and Development  
Guidelines for Testing of Chemicals C(81)30 (Final).

  
Kenneth P. Shepard, B.S.  
Study Director

  
Month/Day/Year

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**ABSTRACT**

**4-CHLOROBENZENESULPHONAMIDE**

**ACUTE ORAL TOXICITY STUDY IN THE RAT**

**HAEL NUMBER: 94-0046 KAN: 002243  
CAS REGISTRY NUMBER: 98-64-6**

An acute oral toxicity study was conducted with groups of five male and five female rats administered single doses of either 250, 500, 1000, or 2000 mg/kg of the test material by gavage. All animals at the 1000 and 2000 mg/kg dose level died after exposure to the test material. Additional deaths included a single male and all females at the 500 mg/kg dose level. No other mortality was noted during the study.

Abnormal clinical signs evident during the 14-day observation period included slight to severe weakness, prostration, hypothermia, blood in the urine, staining (red and/or brown) of the inguinal hair, inguinal hair wet or stained yellow from urine, staining (brown) of the skin of the feet and/or tail, a reduced amount or lack of feces, dehydration, and porphyrin nasal and/or ocular discharges. Prostration was noted only in animals which died after exposure to the test material and severe weakness was either transient or seen only in moribund animals. Body weight losses were recorded for two of the four surviving males at the 500 mg/kg dose level during the first week of the study. During the second week of the study, all surviving animals gained weight.

Treatment-related observations recorded at necropsy included test material in the stomach and duodenum, incomplete collapse of the lungs upon thoracotomy, hemorrhage in the lungs, hemorrhage and necrosis in the glandular gastric mucosa, excessive mucus accumulation in the duodenum, brown fluid in the gastrointestinal tract, dark and/or small spleens, pale or dark livers, red discoloration of the hair of the face and the urine in the urinary bladder, and brown discoloration of the contents of the stomach, duodenum, and jejunum. In addition, the skin of the tail and feet or toes and the inguinal and abdominal hair were also discolored brown in many instances. Selected tissues were processed for microscopic examination. The cause of death of animals which died after exposure to the test material was not determined. However, the test material appeared to be a gastric irritant which caused leakage of the gastric contents into the abdominal cavity. The necrosis and hemorrhage observed in the glandular gastric mucosa may have contributed to the deaths.

**ABSTRACT, Cont.**

The acute oral LD<sub>50</sub> for this test material was calculated to be 574 mg/kg for male rats and 354 mg/kg for female rats. The acute oral LD<sub>50</sub> calculated by combining the male and female mortality data was 467 mg/kg. Based on the oral LD<sub>50</sub> calculated from the combined mortality data, the test material was classified as moderately toxic in rats according to the criteria set forth by Hodge and Sterner (1949) and classified as harmful if swallowed as defined in the 18th Adaptation on the EC Classification, Packaging, and Labelling of Dangerous Substances.

**PERFORMING LABORATORY**

Toxicological Sciences Laboratory  
Health and Environment Laboratories  
Eastman Kodak Company  
1100 Ridgeway Avenue  
B-320 Kodak Park  
Rochester, New York 14652-6272  
USA

**SPONSOR**

Eastman Kodak Company

**STUDY DATES**

Study Initiation: June 15, 1994  
Experiment Initiation: June 15, 1994  
Experiment Completion: February 10, 1995  
Study Completion: January 30, 1996

**STUDY DIRECTOR**

Kenneth P. Shepard, B.S.

**OTHER KEY PERSONNEL**

Leonard Sakal, B.S., Study Technician  
John W. Mosher, B.S., Principal Investigator  
Milan S. Vlaovic, D.V.M., Ph.D., Pathologist, Laboratory Animal Medicine

### PURPOSE/OBJECTIVE

The purpose of the study was to determine the estimated oral LD<sub>50</sub> of the test material in male and female rats and the clinical signs of toxicity associated with a single oral dose.

### TEST SUBSTANCE

Test Material Name: 4-Chlorobenzenesulphonamide

CAS Registry Number: 98-64-6

HAEL Laboratory Number: 94-0046

KAN: 002243

CIN: Not available

SRID or Lot I.D. Number: BB2673-182A

Physical State and Appearance: White powder

Received at Performing Laboratory: June 3, 1994

Composition: Refer to composition information included in the notification when applicable.

### TEST SYSTEM

Species: Rat

Strain: CD®(SD)BR VAF/Plus®

Source: Charles River Kingston, Stone Ridge, NY, USA

Number and Sex: Five males and five females per dose group

Number of Dose Groups: 4 (250, 500, 1000, and 2000 mg/kg)

Body Weight Range (grams):

2000 mg/kg                      Males = 201 - 234    Females = 178 - 191

500 & 1000 mg/kg              Males = 250 - 287    Females = 224 - 251

250 mg/kg                        Males = 250 - 261    Females = 188 - 222

Age at Study Initiation:              Males = 7-9 weeks    Females = 8-11 weeks

### HUSBANDRY AND ENVIRONMENTAL CONDITIONS

#### Environmental Conditions

A photoperiod of 12 hours light from 6 a.m. to 6 p.m. was maintained. Room temperature was maintained at 69-71 °F. Relative humidity was maintained at 49-74%.

## **HUSBANDRY AND ENVIRONMENTAL CONDITIONS, Cont.**

### **Housing**

All animals were individually housed in suspended, stainless-steel, mesh cages.

### **Diet and Water**

Agway® Prolab™ Animal Diet - RMH 3000 (certified) pellets and water (Monroe County (NY) Water Authority) were available ad libitum. No known contaminants which would interfere with the outcome of the study were expected to be present in feed or water from these sources. Analyses of feed and quarterly analyses of water are maintained on file within the testing laboratory.

### **Isolation**

Animals were isolated and monitored for at least five days after arrival and before release to the testing facility.

### **Animal Identification**

All animals were identified by cage numbers and uniquely-numbered metal ear tags.

## **TEST PROCEDURES AND CONDITIONS**

### **Test Procedure Guideline**

OECD Guideline for Testing of Chemicals: Guideline 401 (Annex V, test B.1).

### **Randomization**

A clinical examination was performed on each animal to ensure that only healthy animals were utilized. The procedure for including animals in the study was to randomly select and assign animals from the same shipment to the study. Randomization was done by computer-generated lists using the Automated Animal Toxicology System. After assignment of animals to the study, the body weights were determined to ensure that individual body weights did not exceed 20% of the mean weight for each sex.

**TEST PROCEDURES AND CONDITIONS, Cont.**

**Identification Numbers of Animals Used**

Dose Level	Males	Females
250 mg/kg	231-235	236-240
500 mg/kg	191-195	201-205
1000 mg/kg	196-200	206-210
2000 mg/kg	161-165	166-170

**Dose Levels**

Five animals of each sex were administered dose levels of 250, 500, 1000, or 2000 mg/kg of the test material.

**Dosing Regimen**

The test material was administered as a single dose to animals that had been fasted overnight. Variability in dosing test volume was minimized by adjusting the concentration to ensure a constant volume at all dose levels. The test material was administered by gavage as a 2.5, 5, 10, or 20% suspension in the vehicle.

**Vehicle and Control Substance**

The vehicle was a 0.5% aqueous suspension of guar gum (Jaguar®), Control Number: F-10-88-592-10. No control substance was used.

**Clinical Observations**

Animals were observed three times on the day of dosing (Day 0), and once each day thereafter for the duration of the experiment (a total of 14 calendar days). Observations included, but were not limited to, changes in the skin; fur; feces; urine; eyes; mucous membranes; respiratory, circulatory, autonomic, and central nervous systems; somatomotor activity; and behavior pattern.

**Body Weight Determinations**

Body weights were collected on Days 0 (prior to treatment), 7, and 14.

**TEST PROCEDURES AND CONDITIONS, Cont.**

**Necropsy**

Animals that died during the study were necropsied as soon as possible. Surviving animals were necropsied at the completion of the 14-day observation period.

**RESULTS**

**Mortality**

Mortality was 0% at 250 mg/kg, 20% at 500 mg/kg, and 100% at 1000 and 2000 mg/kg for male rats. For female rats, mortality was 0% at 250 mg/kg, and 100% at 500, 1000, and 2000 mg/kg.

**MORTALITY TABLE**

<b>DOSE (mg/kg)</b>	<b>NUMBER OF RATS EXPOSED (Male, Female)</b>	<b>NUMBER OF DEATHS (Male, Female)</b>	<b>TIME OF DEATH</b>
250	5,5	0,0	-----
500	5,5	1,5	Day 2 to Day 6
1000	5,5	5,5	Day 1 to Day 4
2000	5,5	5,5	Day 1

**RESULTS, Cont.**

**Clinical Observations**

Abnormal clinical signs evident during the 14-day observation period included slight to severe weakness, prostration, hypothermia, blood in the urine, staining (red and/or brown) of the inguinal hair, inguinal hair wet or stained yellow from urine, staining (brown) of the skin of the feet and/or tail, a reduced amount or lack of feces, dehydration, and porphyrin nasal and/or ocular discharge. Prostration was noted only in animals which died after exposure to the test material and severe weakness was either transient or seen only in moribund animals. The time of each observation and the number of animals involved at each dose level are listed in the following table.

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
250	Day 0	Slight Weakness Moderate Weakness	5/5 Males, 4/5 Females 1/5 Females
250	Day 1	Slight Weakness Moderate Weakness Staining (Red) of the Inguinal Hair Blood in Urine Reduced Amount of Feces	5/5 Males, 4/5 Females 1/5 Females 2/5 Males, 3/5 Females 5/5 Males, 5/5 Females 5/5 Males, 5/5 Females
250	Day 2	Slight Weakness Moderate Weakness Staining (Red) of the Inguinal Hair Staining (Brown and Wet) of the Inguinal Hair Blood in Urine Reduced Amount of Feces Staining (Brown) of the Skin of the Tail	4/5 Males, 4/5 Females 1/5 Females 2/5 Females 2/5 Males, 3/5 Females 4/5 Males, 3/5 Females 2/5 Males, 4/5 Females 2/5 Females
250	Day 3	Appeared Clinically Normal Slight Weakness Staining (Brown and Wet) of the Inguinal Hair Reduced Amount of Feces Staining (Brown) of the Skin of the Tail	3/5 Males, 2/5 Females 1/5 Males, 1/5 Females 2/5 Males, 3/5 Females 2/5 Females 1/5 Males, 3/5 Females

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
250	Day 4	Appeared Clinically Normal Slight Weakness Staining (Brown) of the Inguinal Hair Staining (Yellow) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	3/5 Males, 2/5 Females 1/5 Females 1/5 Males, 2/5 Females 1/5 Males 2/5 Females
250	Days 5-6	Appeared Clinically Normal Staining (Brown) of the Inguinal Hair Staining (Yellow) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	4/5 Males, 2/5 Females 1/5 Females 1/5 Males 3/5 Females
250	Days 7-8	Appeared Clinically Normal Staining (Brown) of the Inguinal Hair Staining (Yellow) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	4/5 Males, 3/5 Females 1/5 Females 1/5 Males 2/5 Females
250	Day 9	Appeared Clinically Normal Staining (Brown) of the Inguinal Hair Staining (Yellow) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	4/5 Males, 4/5 Females 1/5 Females 1/5 Males 1/5 Females
250	Days 10-14	Appeared Clinically Normal Staining (Brown) of the Inguinal Hair	5/5 Males, 4/5 Females 1/5 Females

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
500	Day 0	Slight to Moderate Weakness	5/5 Males, 5/5 Females
500	Day 1	Severe Weakness and Hypothermia Prostration Lack of Feces Blood in Urine Staining (Red) of the Inguinal Hair	5/5 Males, 5/5 Females 1/5 Males, 2/5 Females 5/5 Males, 5/5 Females 5/5 Males, 5/5 Females 4/5 Males, 3/5 Females
500	Day 2	Death Severe Weakness Hypothermia Lack of Feces Blood in Urine Staining (Red) of the Inguinal Hair Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet	1/5 Males, 4/5 Females 4/4 Males, 1/1 Females 1/4 Males, 1/1 Females 4/4 Males, 1/1 Females 4/4 Males, 1/1 Females 1/1 Females 4/4 Males 3/4 Males 3/4 Males
500	Day 3	Moderate Weakness Severe Weakness Hypothermia Lack of Feces Reduced Amount of Feces Blood in Urine Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Nasal and Ocular) Discharges	3/4 Males 1/4 Males, 1/1 Females 1/4 Males, 1/1 Females 1/4 Males, 1/1 Females 3/4 Males 3/4 Males, 1/1 Females 3/4 Males, 1/1 Females 4/4 Males, 1/1 Females 3/4 Males 3/4 Males 1/4 Males

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
500	Day 4	Moderate Weakness Severe Weakness Hypothermia Lack of Feces Reduced Amount of Feces Blood in Urine Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Nasal and Ocular) Discharges	3/4 Males 1/4 Males, 1/1 Females 1/4 Males, 1/1 Females 1/4 Males, 1/1 Females 3/4 Males 2/4 Males, 1/1 Females 3/4 Males, 1/1 Females 3/4 Males, 1/1 Females 3/4 Males 3/4 Males 1/4 Males
500	Day 5	Moderate Weakness Severe Weakness Prostration Hypothermia Lack of Feces Reduced Amount of Feces Blood in Urine Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Nasal and Ocular) Discharges	2/4 Males 1/4 Males 1/1 Females 1/4 Males, 1/1 Females 1/4 Males, 1/1 Females 3/4 Males 1/4 Males, 1/1 Females 3/4 Males, 1/1 Females 3/4 Males, 1/1 Females 3/4 Males 3/4 Males 1/4 Males

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
500	Day 6	Death Appeared Clinically Normal Moderate Weakness Severe Weakness Hypothermia Reduced Amount of Feces Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Nasal and Ocular) Discharges	1/1 Females 1/4 Males 2/4 Males 1/4 Males 1/4 Males 2/4 Males 3/4 Males 3/4 Males 3/4 Males 3/4 Males 1/4 Males
500	Day 7	Appeared Clinically Normal Moderate Weakness Severe Weakness Reduced Amount of Feces Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Ocular) Discharges	1/4 Males 2/4 Males 1/4 Males 2/4 Males 3/4 Males 3/4 Males 3/4 Males 1/4 Males 1/4 Males
500	Day 8	Appeared Clinically Normal Moderate Weakness Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	1/4 Males 1/4 Males 1/4 Males 3/4 Males 3/4 Males
500	Days 9-10	Appeared Clinically Normal Slight Weakness Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	1/4 Males 1/4 Males 3/4 Males 3/4 Males

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
500	Days 11-13	Appeared Clinically Normal Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail	1/4 Males 3/4 Males 3/4 Males
500	Day 14	Appeared Clinically Normal Staining (Brown) of the Skin of the Tail	1/4 Males 3/4 Males

<b>DOSE (mg/kg)</b>	<b>TIME</b>	<b>CLINICAL SIGNS</b>	<b>NUMBER OF ANIMALS AFFECTED</b>
1000	Day 0	Moderate to Severe Weakness Prostration	5/5 Males, 5/5 Females 3/5 Males, 3/5 Females
1000	Day 1	Death (Prior to Examinations) Severe Weakness and Hypothermia Prostration Lack of Feces Blood in Urine Staining (Red) of the Inguinal Hair Death (After Examinations)	1/5 Females 5/5 Males, 4/4 Females 4/5 Males, 4/4 Females 5/5 Males, 4/4 Females 4/5 Males, 4/4 Females 2/5 Males, 1/4 Females 2/4 Females
1000	Day 2	Death Severe Weakness and Hypothermia Prostration Lack of Feces Blood in Urine Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet	4/5 Males, 2/2 Females 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males

Table continued on next page.

**RESULTS, Cont.**

**TABLE OF CLINICAL OBSERVATIONS, Cont.**

DOSE (mg/kg)	TIME	CLINICAL SIGNS	NUMBER OF ANIMALS AFFECTED
1000	Day 3	Severe Weakness and Hypothermia Prostration Lack of Feces Blood in Urine Dehydration Staining (Brown) of the Inguinal Hair Staining (Brown) of the Skin of the Tail Staining (Brown) of the Skin of the Feet Porphyrin (Nasal and Ocular) Discharges	1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males 1/1 Males
1000	Day 4	Death	1/1 Males

DOSE (mg/kg)	TIME	CLINICAL SIGNS	NUMBER OF ANIMALS AFFECTED
2000	Day 0	Severe Weakness and Prostration	5/5 Males, 5/5 Females
2000	Day 1	Death (Prior to Examinations) Severe Weakness and Prostration Hypothermia Death (During Examination)	5/5 Males, 4/5 Females 1/1 Females 1/1 Females 1/1 Females

**Body Weights**

Body weight losses (30 and 38 grams) were recorded for two of the four surviving males (Rats 194 and 195) at the 500 mg/kg dose level during the first week of the study. During the second week of the study, all surviving animals from all dose groups gained weight. The individual body weights for each animal are presented in the following tables.

**RESULTS, Cont.**

**Individual Body Weights, Cont.**

**TABLE OF INDIVIDUAL BODY WEIGHTS - MALES**

DOSE (mg/kg)	ANIMAL NUMBER	INDIVIDUAL BODY WEIGHTS (grams)		
		DAY 0	DAY 7	DAY 14 (Terminal)
250	231	252	321	372
250	232	255	312	366
250	233	250	322	387
250	234	261	326	369
250	235	252	308	360
500	191	265	Died Day 2	(247)
500	192	254	257	311
500	193	273	282	369
500	194	274	244	344
500	195	251	213	301
1000	196	250	Died Day 2	(226)
1000	197	268	Died Day 2	(246)
1000	198	269	Died Day 2	(248)
1000	199	287	Died Day 4	(241)
1000	200	270	Died Day 2	(253)

Table continued on next page.

**RESULTS, Cont.**

**Individual Body Weights, Cont.**

**TABLE OF INDIVIDUAL BODY WEIGHTS - FEMALES**

DOSE (mg/kg)	ANIMAL NUMBER	INDIVIDUAL BODY WEIGHTS (grams)		
		DAY 0	DAY 7	DAY 14 (Terminal)
250	236	213	255	273
250	237	188	213	220
250	238	196	231	241
250	239	215	246	254
250	240	222	261	279
500	201	239	Died Day 6	(185)
500	202	224	Died Day 2	(199)
500	203	238	Died Day 2	(214)
500	204	240	Died Day 2	(223)
500	205	239	Died Day 2	(212)
1000	206	242	Died Day 1	(225)
1000	207	251	Died Day 1	(236)
1000	208	241	Died Day 1	(226)
1000	209	240	Died Day 2	(219)
1000	210	229	Died Day 2	(212)

Table continued on next page.

**RESULTS, Cont.**

**Individual Body Weights, Cont.**

**TABLE OF INDIVIDUAL BODY WEIGHTS - MALES**

<b>DOSE (mg/kg)</b>	<b>ANIMAL NUMBER</b>	<b>INDIVIDUAL BODY WEIGHTS (grams)</b>		
		<b>DAY 0</b>	<b>DAY 7</b>	<b>DAY 14 (Terminal)</b>
2000	161	213	Died Day 1	(208)
2000	162	229	Died Day 1	(223)
2000	163	201	Died Day 1	(194)
2000	164	219	Died Day 1	(212)
2000	165	234	Died Day 1	(234)

**TABLE OF INDIVIDUAL BODY WEIGHTS - FEMALES**

<b>DOSE (mg/kg)</b>	<b>ANIMAL NUMBER</b>	<b>INDIVIDUAL BODY WEIGHTS (grams)</b>		
		<b>DAY 0</b>	<b>DAY 7</b>	<b>DAY 14 (Terminal)</b>
2000	166	179	Died Day 1	(171)
2000	167	189	Died Day 1	(175)
2000	168	191	Died Day 1	(182)
2000	169	179	Died Day 1	(172)
2000	170	178	Died Day 1	(174)

## **RESULTS, Cont.**

### **Necropsy and Histopathology Findings**

Treatment-related changes noted at necropsy of animals which died after exposure to the test material included incomplete collapse of the lungs upon thoracotomy; hemorrhage in the lungs; test material in the stomach and duodenum; hemorrhage and necrosis in the glandular gastric mucosa; a small spleen; dark spleens; pale or dark livers; gastrointestinal contents discolored brown; brown fluid in the gastrointestinal tract; excessive mucus accumulation in the duodenum; toes, skin of the paws, skin of the tail, and inguinal and abdominal hair discolored brown; and the hair of the face and urine in the urinary bladder discolored red.

Selected tissues were collected and processed for microscopic examination. Microscopic lesions that were determined to be associated with treatment of the test material were found in the stomach, liver, spleen, mesenteric lymphnodes, bone marrow, and lungs. A detailed record of the incidence and severity of all gross abnormalities and histological findings are presented in computer-generated tables which are included in the appended pathology report.

## **DATA ANALYSIS**

The LD<sub>50</sub> was obtained using the method of Weil (1952). The results were as follows:

LD <sub>50</sub> for male rats:	574 mg/kg (95% C.I. = 435 - 758 mg/kg)
LD <sub>50</sub> for female rats:	354 mg/kg (95% C.I. = 268 - 467 mg/kg)
LD <sub>50</sub> for both sexes combined:	467 mg/kg (95% C.I. = 372 - 585 mg/kg)

No dose/mortality curve was constructed since graphs become statistically useful only with the use of large numbers of animals and dose groups.

## **DISCUSSION AND INTERPRETATION**

The acute oral LD<sub>50</sub> for this test material was calculated to be 574 mg/kg for male rats and 354 mg/kg for female rats. The acute oral LD<sub>50</sub> calculated by combining the male and female mortality data was 467 mg/kg.

## **DISCUSSION AND INTERPRETATION, Cont.**

Mortality was first observed on the day following dosing and continued to Day 6 of the 14-day observation period. The majority of abnormal clinical signs noted during the study were agonal effects occurring prior to death, or were considered to be secondary to loss of body weight and/or stress. The cause of death for rats which died after exposure to the test material was not determined. Lesions observed at necropsy in rats on this study could be classified into four categories: lesions that are considered to be secondary to loss of body weight and/or stress, lesions that most likely represent agonal effects occurring just prior to death, lesions which were due to tissue coming in contact with the test material, and lesions which were determined to be incidental changes. The test material appears to be a gastric irritant as evidenced by necrosis and hemorrhage in the glandular gastric mucosa and hyperkeratosis and acanthosis in the non-glandular gastric mucosa. In addition, leakage of the test material or gastric juices through the stomach wall resulted in necrosis and hemorrhage in the liver adjacent to the stomach.

## **CONCLUSION**

Based on the oral LD<sub>50</sub> calculated from the combined mortality data, the test material was classified as moderately toxic to rats according to the criteria set forth by Hodge and Sterner (1949) and classified as harmful if swallowed as defined in the 18th Adaptation on the EC Classification, Packaging, and Labelling of Dangerous Substances.

## **DATA STORAGE**

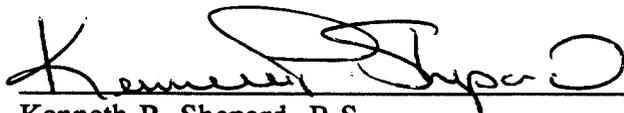
All test results presented in this report are supported by raw data which are maintained in the archives of the Health and Environment Laboratories, Eastman Kodak Company.

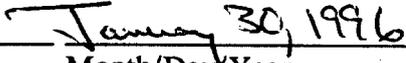
## **REFERENCES**

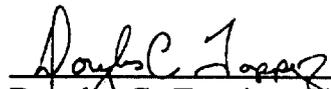
Hodge, H.C. and Sterner, J.H. (1949). Tabulation of toxicity classes. *Am. Indust. Hyg. Quart.*, 10:93-96.

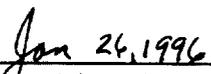
Weil, C.S. (1952). Tables of convenient calculations of medium-effective dose (LD<sub>50</sub> or ED<sub>50</sub>) and instructions in their use. *Biometrics*, 8:249-263.

SIGNATURE PAGE

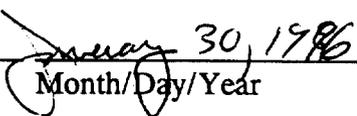
  
Kenneth P. Shepard, B.S.  
Study Director

  
Month/Day/Year

  
Douglas C. Topping, Ph.D.  
Unit Director, Mammalian Toxicology

  
Month/Day/Year

  
John L. O'Donoghue, V.M.D., Ph.D.  
Director, Health and Environment Laboratories

  
Month/Day/Year

## APPENDIX

## PATHOLOGY REPORT

Compound: 4-Chlorobenzenesulphonamide

Male and female rats given 2000, 1000, 500, or 250 mg/kg of the test material by gavage, as part of an acute oral toxicity study, were necropsied. Necropsy lesions are listed in computer-generated tables.

The cause of death for rats, which died after exposure to the test material, was not determined. However, necrosis and hemorrhage in the glandular gastric mucosa may have contributed to the deaths.

### GROSS PATHOLOGY

Male Rats - 2000 mg/kg dose group: Treatment-related changes consisted of the test material in the stomach (5/5). All rats died on Day 1. The carcasses of five rats showed minimal or moderate autolysis.

Male Rats - 1000 mg/kg dose group: Treatment-related changes included incomplete collapse of the lungs upon thoracotomy (5/5), minor hemorrhage in the lungs (1/5), minor to moderate hemorrhage (5/5) and minimal to moderate necrosis (4/5) in the glandular gastric mucosa, a small spleen (1/5), and a pale liver (1/5). In addition, gastric (3/5), duodenal (3/5), and jejunal (3/5) contents were discolored brown as were the skin of the tail (1/5) and toes (1/5), and inguinal (3/5) and abdominal (1/5) hair. The hair of the face (1/5), and urine in the urinary bladder (4/5) were discolored red. The carcass of a single rat showed minimal autolysis (1/5). Four rats died on Day 2 and the remaining rat died on Day 4.

Male Rats - 500 mg/kg dose group: Treatment-related changes in a single rat, which died on Day 2, included incomplete collapse of the lungs upon thoracotomy, moderate hemorrhage in the glandular gastric mucosa, and red discolored urine in the urinary bladder. In addition, the gastric, duodenal, and jejunal contents and inguinal hair were discolored brown. Treatment-related changes in the remaining four rats, which survived the 14-day observation period, consisted of brown discoloration of the skin of the tail (3/4). The carcass of a single rat showed minor autolysis.

Male Rats - 250 mg/kg dose group: No treatment-related changes were observed. All rats survived the 14-day observation period.

Female Rats - 2000 mg/kg dose group: Treatment-related changes included the test material in the stomach (5/5) and duodenum (1/5), and minor hemorrhage in the glandular gastric mucosa (2/5). All rats died on Day 1. The carcasses of four rats showed minor or moderate autolysis.

Female Rats - 1000 mg/kg dose group: Treatment-related changes included incomplete collapse of the lungs upon thoracotomy (4/5), minimal to moderate hemorrhage (5/5) and necrosis (4/5) in the glandular gastric mucosa, red urine (1/5) in the urinary bladder, and dark spleens (2/5). Brown fluid was observed in the duodenum (1/5) and jejunum (1/5). In addition, the inguinal hair was discolored brown (1/5), and there was excessive mucus accumulation in the duodenum (2/5). Three rats died on Day 1 and the remaining two rats died on Day 2.

Female Rats - 500 mg/kg dose group: Treatment-related changes included incomplete collapse of the lungs upon thoracotomy (5/5), minor or moderate hemorrhage (5/5) and necrosis (5/5) in the glandular gastric mucosa, a dark liver (1/5), dark (5/5) and small (1/5) spleens, and red urine (1/5) in the urinary bladder. In Rat 201, brown fluid was observed in the stomach, and small and large intestines (1/5). In addition, the skin of the forepaws (1/5), and inguinal hair (5/5) were discolored brown. Four rats died on Day 2 and the remaining rat died on Day 6. The carcass of a single rat showed minor autolysis.

Female Rats - 250 mg/kg dose group: Treatment-related changes consisted of brown discoloration of the inguinal hair in one rat (1/5). No signs of organ toxicity were observed. All rats survived the 14-day observation period.

## HISTOPATHOLOGY

Gross lesions and target organs were processed for microscopic examination.

Microscopic lesions which may be associated with the treatment were found in the stomach, liver, spleen, mesenteric lymph nodes, bone marrow, and lungs. Microscopic lesions were graded on a scale of minimal (1), minor (2), moderate (3), and severe (4).

Gastric lesions included hyperkeratosis and acanthosis of the non-glandular mucosa, and focal necrosis and hemorrhage of the glandular mucosa. The incidences of minimal to minor hyperkeratosis and acanthosis were 0, 4, 0 for male rats, and 1, 0, 0 for female rats from the 250, 500, and 1000 mg/kg dose group, respectively. Lesions in the non-glandular gastric mucosa were characterized by a thickened keratin layer, which was otherwise normal, and acanthosis, or increased thickness of stratum spinosum (prickle cell layer). Hyperplasia of the non-glandular gastric mucosa (hyperkeratosis and acanthosis) is a common reactive change to irritation.

Minimal to minor focal necrosis of the glandular gastric mucosa was only observed in three male rats from the 1000 mg/kg dose group. The affected mucosa contained small, superficial foci of necrosis which did not involve the full thickness of the mucus membrane. Minimal to moderate hemorrhage of the glandular gastric mucosa was observed in four male rats from the 1000 mg/kg dose group, and two female rats from the 500 mg/kg dose group.

Hepatic lesions included minimal to minor diffuse necrosis and hemorrhage of the hepatic capsule and adjacent parenchyma of two male rats from the 1000 mg/kg dose group. The affected livers showed a band of necrosis involving the hepatic capsule and the adjoining liver parenchyma. Similar hepatic lesions were observed with leakage through the stomach wall.

Splenic lesions included atrophy of the lymphatic follicles and the red pulp and congestion of the red pulp. The incidences of minor to moderate lymphatic follicle atrophy were 0, 0, 1 for male rats, and 0, 4, 2 for female rats from the 250, 500, and 1000 mg/kg dose groups, respectively. A typical lesion was characterized by lymphocyte depletion in the periarteriolar lymphoid sheaths and marginal zones. Moderate to severe atrophy and congestion of the splenic red pulp was observed in the 0, 4, 2 female rats from the 250, 500 and 1000 mg/kg dose groups, respectively.

Minor to moderate atrophy and congestion were observed in the bone marrow of single male and female rats from the 1000 and 500 mg/kg dose groups, respectively. The affected bone marrows contained an increased number of vacuoles and red blood cells. Hematopoietic tissue was reduced in size, and the bone marrow sinusoids were congested.

Changes in the lungs included congestion, hemorrhage, and edema of the alveolar wall. Minor to moderate congestion of the lungs was observed in 0, 1, and 5 male rats, and 0, 5, and 2 female rats from the 250, 500, and 1000 mg/kg dose groups, respectively. Congestion involved not only the larger blood vessels, but also the vasculature of the alveolar septa. Minor hemorrhages were observed in 0, 1, and 3 male rats from the 250, 500, and 1000 mg/kg dose groups, respectively. Minimal edema was observed in the lungs of male Rat 191 (500 mg/kg).

The following lesions and all other lesions listed in the attached tables were not considered treatment-related.

Minimal to minor cytoplasmic vacuolation in the proximal convoluted tubules was observed in the kidneys of three male rats from the 500 mg/kg dose group, and five female rats from the 250 mg/kg dose group. Affected tubular epithelial cells contained large, irregularly shaped vacuoles localized between the normally appearing nucleus and the basement membrane. This cellular change lacked a dose-response relationship, similar vacuoles are occasionally observed in untreated rats, therefore, this lesion was not considered treatment-related.

Several additional spontaneous lesions or incidental findings were observed in the lungs, liver, and kidneys. These findings included the presence of alveolar macrophages, peribronchial lymphocytic accumulations, and focal and diffuse chronic inflammation of the alveolar wall in the lungs; cytoplasmic vacuolation of hepatocytes and chronic focal inflammation in the liver; hyperplasia and hypertrophy of urinary bladder mucosa, and

hydronephrosis and focal tubular mineralization in the kidneys.

Comments: No concurrent control group was available for examination, therefore, the conclusions in this study were based on the experience of the pathologist with control animals from other studies.

The treatment-related stomach and liver lesions were due to contact with the test material. The test material induced necrosis and hemorrhage in the glandular mucosa and hyperkeratosis and acanthosis in the non-glandular mucosa due to irritation. Leakage of the test material or gastric juices through the stomach wall resulted in necrosis and hemorrhage in the liver adjacent to the stomach.

The lung lesions (congestion, hemorrhage, and edema) were only observed in animals dying spontaneously, and most likely represent agonal effects occurring shortly prior to death.

Lymphocyte depletion in the periarteriolar lymphoid sheaths and marginal zones of the spleen was probably secondary to stress. It has been reported that stress, mediated by steroid release from the adrenal cortex, is associated with lymphoid tissue involution in the spleen (Zbinden, 1963). Atrophy and congestion observed in the hematopoietic tissue of the spleen and bone marrow were also considered to be related to stress and/or gastric hemorrhage.

Overall, the test material appeared to be a gastric irritant. All other effects appear to represent secondary changes.

REFERENCES:

Zbinden, G.: Experimental and clinical aspects of drug toxicity. In: Garattini, S. and Shore, P. A. (eds): Advances in Pharmacology, Academic Press, New York, 1963, pp 1-112.

  
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Milan S. Vlaovic, D.V.M., Ph.D.

  
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Reviewed by  
John L. O'Donoghue, V.M.D., Ph.D.

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000 MG/KG M	500.000 MG/KG M	1000.000 MG/KG M	2000.000 MG/KG M
TRACHEA	5	5	5	5
LUNGS	5	5	5	5
COLLAPSE INCOMPLETE ON THORACOTOMY	0	1	5	0
HEMORRHAGE	0	0	1	0
THYMUS	5	5	5	5
HEMORRHAGE	0	1	1	1
HEART	5	5	5	5
ESOPHAGUS	5	5	5	5
STOMACH	5	5	5	5
STOMACH CONTENTS-TEST ARTICLE PRESENT	0	0	0	5
STOMACH, GLANDULAR				
HEMORRHAGE	0	1	5	0
NECROSIS	0	0	4	0
STOMACH CONTENTS				
DISCOLORATION, BROWN	0	1	3	0
DUODENUM	5	5	5	5
AUTOLYSIS	0	0	1	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	3	0
JEJUNUM	5	5	5	5
AUTOLYSIS	0	0	1	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	3	0
ILEUM	5	5	5	5
AUTOLYSIS	0	0	1	0
CECUM	5	5	5	5
AUTOLYSIS	0	0	1	0
COLON	5	5	5	5
AUTOLYSIS	0	0	1	0
RECTUM	5	5	5	5
AUTOLYSIS	0	0	1	0
LIVER	5	5	5	5
PALLOR	0	0	1	0
KIDNEYS	5	5	5	5
URINARY BLADDER	5	5	5	5
URINE				
DISCOLORATION, RED	0	1	4	0
PITUITARY GLAND	5	5	5	5
ADRENALS	5	5	5	5
PANCREAS, NOS	5	5	5	5
THYROID GLANDS	5	5	5	5

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY:

*J. M. [Signature]*

DATE: 9-19-91

ACCEPTED BY:

*[Signature]*

DATE:

10/24/91

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000	500.000	1000.000	2000.000
	MG/KG M	MG/KG M	MG/KG M	MG/KG M
PARATHYROID GLANDS	5	5	5	5
SPLEEN	5	5	5	5
SMALL	0	0	1	0
MESENTERIC LYMPH NODES	5	5	5	5
BONE MARROW	5	5	5	5
BRAIN	5	5	5	5
EYES	5	5	5	5
SALIVARY GLANDS	5	5	5	5
ADIPOSE TISSUE	5	5	5	5
SKIN, NOS	5	4	5	5
SKIN OF TAIL				
DISCOLORATION, BROWN	0	3	1	0
SKIN OF FOOT AND TOE				
DISCOLORATION, BROWN	0	0	1	0
HAIR	5	5	5	5
HAIR OF INGUINAL REGION				
DISCOLORATION, BROWN	0	1	3	0
HAIR OF ABDOMEN				
DISCOLORATION, BROWN	0	0	1	0
HAIR OF FACE				
DISCOLORATION, RED	0	0	1	0
ACCESSORY SEX ORGANS (MALE)	5	5	5	5
EPIDIDYMIDES	5	5	5	5
TESTES	5	5	5	5
BODY AS A WHOLE, NOS	0	1	1	5
AUTOLYSIS	0	1	1	5

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY: John Mosher DATE: 9-19-91 ACCEPTED BY: Janet S. Vanni DATE: 10/5/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	250.000 MG/KG				
	GROUP - M				
	231	232	233	234	235
DAYS ON TEST	14	14	14	14	14
TRACHEA	X	X	X	X	X
LUNGS	N	N	N	N	N
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
STOMACH	N	N	N	N	N
DUODENUM	X	X	X	X	X
JEJUNUM	X	X	X	X	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	N	N	N	N	N
KIDNEYS	N	N	N	N	N
URINARY BLADDER	N	N	N	N	N
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	N	N	N	N	N
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	N	N	N	N	N
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
HAIR	X	X	X	X	X
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X
EPIDIDYMIDES	X	X	X	X	X
TESTES	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \* - SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John Moker DATE: 9-19-94 ACCEPTED BY: Anthony V. Vroom DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG GROUP - M				
	191	192	193	194	195
DAYS ON TEST	2	14	14	14	14
TRACHEA	X	X	X	X	X
LUNGS COLLAPSE INCOMPLETE ON THORACOTOMY	P	N	N	N	N
THYMUS HEMORRHAGE	2	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH STOMACH, GLANDULAR HEMORRHAGE STOMACH CONTENTS DISCOLORATION, BROWN	3 P	N	N	N	N
*DUODENUM INTESTINAL CONTENTS DISCOLORATION, BROWN	P	X	X	X	X
*JEJUNUM INTESTINAL CONTENTS DISCOLORATION, BROWN	P	X	X	X	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	N	N	N	N	N
KIDNEYS	N	N	N	N	N
URINARY BLADDER URINE DISCOLORATION, RED	P	N	N	N	N
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	N	N	N	N	N
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	N	N	N	N	N
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS SKIN OF TAIL DISCOLORATION, BROWN	X		X	P	P
HAIR HAIR OF INGUINAL REGION DISCOLORATION, BROWN	1	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: J. M. Moler

DATE: 9-19-94

ACCEPTED BY: Michael J. Mamm

DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
 SOFTWARE VERS # 3.0  
 ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG					GROUP - M				
	191	192	193	194	195	191	192	193	194	195
DAYS ON TEST	2	14	14	14	14					
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X					
EPIDIDYIMIDES	X	X	X	X	X					
TESTES	X	X	X	X	X					
BODY AS A WHOLE, NOS AUTOLYSIS	2									

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
 P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. Mader DATE: 9-19-91 ACCEPTED BY: Jonathan J. Mason DATE: 10/24/91

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG GROUP - M				
	196	197	198	199	200
DAYS ON TEST	2	2	2	4	2
TRACHEA	X	X	X	X	X
LUNGS COLLAPSE INCOMPLETE ON THORACOTOMY HEMORRHAGE	P	P	P	P	P 2
THYMUS HEMORRHAGE	X	3	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH STOMACH, GLANDULAR HEMORRHAGE NECROSIS STOMACH CONTENTS DISCOLORATION, BROWN	3 2 P	3 1 P	2 P	3 3	3 3
*DUODENUM AUTOLYSIS INTESTINAL CONTENTS DISCOLORATION, BROWN	P	P	P	3	X
*JEJUNUM AUTOLYSIS INTESTINAL CONTENTS DISCOLORATION, BROWN	P	P	P	3	X
ILEUM AUTOLYSIS	X	X	X	3	X
CECUM AUTOLYSIS	X	X	X	3	X
COLON AUTOLYSIS	X	X	X	3	X
RECTUM AUTOLYSIS	X	X	X	3	X
*LIVER PALLOR	N	N	N	3	N
KIDNEYS	N	N	N	N	N
URINARY BLADDER URINE DISCOLORATION, RED	P	P	P	P	X
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN SMALL	N	N	N	4	N
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	N	N	N	N	N
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. Moke

DATE: 9-19-94 ACCEPTED BY: Amber J. V. Brown

DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG				
	196	197	198	199	200
DAYS ON TEST	2	2	2	4	2
ADIPOSE TISSUE	X	X	X	X	X
*SKIN, NOS	X	X	X		X
SKIN OF TAIL					
DISCOLORATION, BROWN				2	
SKIN OF FOOT AND TOE					
DISCOLORATION, BROWN				2	
*HAIR			X		X
HAIR OF INGUINAL REGION					
DISCOLORATION, BROWN	1	1		3	
HAIR OF ABDOMEN					
DISCOLORATION, BROWN				3	
HAIR OF FACE					
DISCOLORATION, RED				3	
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X
EPIDIDYMIDES	X	X	X	X	X
TESTES	X	X	X	X	X
BODY AS A WHOLE, NOS					
AUTOLYSIS	1				

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*-SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John Moter DATE: 9-19-94 ACCEPTED BY: William J. Vlammi DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	2000.000 MG/KG					GROUP - M				
	161	162	163	164	165	161	162	163	164	165
DAYS ON TEST	1	1	1	1	1					
TRACHEA	X	X	X	X	X					
LUNGS	X	X	X	X	X					
THYMUS HEMORRHAGE	X	X	X		X				2	
HEART	X	X	X	X	X					
ESOPHAGUS	X	X	X	X	X					
STOMACH STOMACH CONTENTS-TEST ARTICLE PRESENT	P	P	P	P	P					
DUODENUM	X	X	X	X	X					
JEJUNUM	X	X	X	X	X					
ILEUM	X	X	X	X	X					
CECUM	X	X	X	X	X					
COLON	X	X	X	X	X					
RECTUM	X	X	X	X	X					
LIVER	X	X	X	X	X					
KIDNEYS	X	X	X	X	X					
URINARY BLADDER	X	X	X	X	X					
PITUITARY GLAND	X	X	X	X	X					
ADRENALS	X	X	X	X	X					
PANCREAS, NOS	X	X	X	X	X					
THYROID GLANDS	X	X	X	X	X					
PARATHYROID GLANDS	X	X	X	X	X					
SPLEEN	X	X	X	X	X					
MESENTERIC LYMPH NODES	X	X	X	X	X					
BONE MARROW	X	X	X	X	X					
BRAIN	X	X	X	X	X					
EYES	X	X	X	X	X					
SALIVARY GLANDS	X	X	X	X	X					
ADIPOSE TISSUE	X	X	X	X	X					
SKIN, NOS	X	X	X	X	X					
HAIR	X	X	X	X	X					
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X					
EPIDIDYMIDES	X	X	X	X	X					
TESTES	X	X	X	X	X					
BODY AS A WHOLE, NOS AUTOLYSIS	1	1	1	1	3					

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \* - SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY:

*John M. O'Dell*

DATE: 9-19-91

ACCEPTED BY:

*William J. O'Brien* DATE: 10/24/91

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000	500.000	1000.000	2000.000
	MG/KG F	MG/KG F	MG/KG F	MG/KG F
TRACHEA	5	5	5	5
LUNGS	5	5	5	5
COLLAPSE INCOMPLETE ON THORACOTOMY	0	5	4	0
THYMUS	5	5	5	5
HEART	5	5	5	5
ESOPHAGUS	5	5	5	5
STOMACH	5	5	5	5
STOMACH CONTENTS--TEST ARTICLE PRESENT	0	0	0	5
STOMACH, GLANDULAR				
HEMORRHAGE	0	5	5	2
NECROSIS	0	5	4	0
STOMACH CONTENTS				
DISCOLORATION, BROWN	0	1	0	0
DUODENUM	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS--TEST ARTICLE PRESENT	0	0	0	1
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	1	0
INCREASED	0	0	2	0
JEJUNUM	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	1	0
ILEUM	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	0	0
CECUM	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	0	0
COLON	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	0	0
RECTUM	5	5	5	5
AUTOLYSIS	0	1	0	0
INTESTINAL CONTENTS				
DISCOLORATION, BROWN	0	1	0	0
LIVER	5	5	5	5
COLOR--DARKER THAN NORMAL	0	1	0	0
KIDNEYS	5	5	5	5
URINARY BLADDER	5	5	5	5
URINE				
DISCOLORATION, RED	0	1	1	0

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY:

*John M. Oker*

DATE: 9-19-94

ACCEPTED BY:

*Julia S. Ulasov*

DATE: 10/24/94

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000	500.000	1000.000	2000.000
	MG/KG F	MG/KG F	MG/KG F	MG/KG F
PITUITARY GLAND	5	5	5	5
ADRENALS	5	5	5	5
PANCREAS, NOS	5	5	5	5
THYROID GLANDS	5	5	5	5
PARATHYROID GLANDS	5	5	5	5
SPLEEN	5	5	5	5
COLOR-DARKER THAN NORMAL	0	5	2	0
SMALL	0	1	0	0
MESENTERIC LYMPH NODES	5	5	5	5
BONE MARROW	5	5	5	5
BRAIN	5	5	5	5
EYES	5	5	5	5
SALIVARY GLANDS	5	5	5	5
ADIPOSE TISSUE	5	5	5	5
SKIN, NOS	5	5	5	5
FOREPAW				
DISCOLORATION, BROWN	0	1	0	0
HAIR	5	5	5	5
HAIR OF INGUINAL REGION				
DISCOLORATION, BROWN	1	5	1	0
FALLOPIAN TUBES	5	5	5	5
VAGINA	5	5	5	5
UTERUS	5	5	5	5
HYDROMETRA	1	0	1	1
OVARIES	5	5	5	5
CERVIX UTERI	5	5	5	5
BODY AS A WHOLE, NOS	0	1	0	4
AUTOLYSIS	0	1	0	4

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY: Joh. Mester DATE: 9-19-91 ACCEPTED BY: Stanley S. Varni DATE: 10/24/91

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	250.000 MG/KG GROUP - F				
	236	237	238	239	240
DAYS ON TEST	14	14	14	14	14
TRACHEA	X	X	X	X	X
LUNGS	N	N	N	N	N
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
STOMACH	N	N	N	N	N
DUODENUM	X	X	X	X	X
JEJUNUM	X	X	X	X	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	N	N	N	N	N
KIDNEYS	N	N	N	N	N
URINARY BLADDER	N	N	N	N	N
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	N	N	N	N	N
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	N	N	N	N	N
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
HAIR	X	X	X	X	
HAIR OF INGUINAL REGION DISCOLORATION, BROWN					P
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS		X	X	X	X
HYDROMETRA	1				
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X=NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. Oster DATE: 9/9/94 ACCEPTED BY: Anderson J. Ullman DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG GROUP - F				
	201	202	203	204	205
DAYS ON TEST	6	2	2	2	2
TRACHEA	X	X	X	X	X
LUNGS COLLAPSE INCOMPLETE ON THORACOTOMY	P	P	P	P	P
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
STOMACH STOMACH, GLANDULAR HEMORRHAGE	2	2	3	2	3
NECROSIS	3	2	3	3	3
STOMACH CONTENTS DISCOLORATION, BROWN	P				
*DUODENUM AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
*JEJUNUM AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
*ILEUM AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
*CECUM AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
*COLON AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
*RECTUM AUTOLYSIS	4	X	X	X	X
INTESTINAL CONTENTS DISCOLORATION, BROWN	P				
LIVER COLOR-DARKER THAN NORMAL	3	N	N	N	N
KIDNEYS	N	N	N	N	N
URINARY BLADDER URINE DISCOLORATION, RED	X	X	X		X
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN COLOR-DARKER THAN NORMAL SMALL	3 3	3	2	3	2
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	N	N	X	N	N

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. ...

DATE: 9-19-94

ACCEPTED BY: Melvin J. ...

DATE: 10/14/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG		GROUP - F		
	201	202	203	204	205
DAYS ON TEST	6	2	2	2	2
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
*SKIN, NOS FOREPAW DISCOLORATION, BROWN		X	X	X	X
HAIR HAIR OF INGUINAL REGION DISCOLORATION, BROWN	2	3	3	1	3
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS	X	X	X	X	X
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X
BODY AS A WHOLE, NOS AUTOLYSIS	2				

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY:

*Joh Mosler*

DATE: 9-19-94

ACCEPTED BY:

*Walter J. Vroman*

DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG				
	206	207	208	209	210
DAYS ON TEST	1	1	1	2	2
TRACHEA	X	X	X	X	X
LUNGS COLLAPSE INCOMPLETE ON THORACOTOMY	X	P	P	P	P
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
STOMACH STOMACH, GLANDULAR HEMORRHAGE NECROSIS	1	1	2	3	3
*DUODENUM INTESTINAL CONTENTS INCREASED DISCOLORATION, BROWN	X		2	P	X
*JEJUNUM INTESTINAL CONTENTS DISCOLORATION, BROWN	X	X	X	P	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	N	N
KIDNEYS	X	X	X	N	N
URINARY BLADDER URINE DISCOLORATION, RED	X	X	X	X	P
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN COLOR-DARKER THAN NORMAL	X	X	X	3	3
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	N	N
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
HAIR HAIR OF INGUINAL REGION DISCOLORATION, BROWN	X	X	X	1	
FALLOPIAN TUBES	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. M...

DATE: 9-19-64

ACCEPTED BY: Robert J. V...

DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
 SOFTWARE VERS # 3.0  
 ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG GROUP - F				
	206	207	208	209	210
DAYS ON TEST	1	1	1	2	2
VAGINA	X	X	X	X	X
UTERUS HYDROMETRA	X	2	X	X	X
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
 P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: Joh Moller DATE: 9-19-94 ACCEPTED BY: William J. Vlasov DATE: 10/24/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	2000.000 MG/KG				
	166	167	168	169	170
DAYS ON TEST	1	1	1	1	1
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
STOMACH					
STOMACH CONTENTS-TEST ARTICLE PRESENT	P	P	P	P	P
STOMACH, GLANDULAR HEMORRHAGE		2	2		
DUODENUM					
INTESTINAL CONTENTS-TEST ARTICLE PRESENT	P	X	X	X	X
JEJUNUM	X	X	X	X	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
URINARY BLADDER	X	X	X	X	X
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	X	X	X	X	X
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
HAIR	X	X	X	X	X
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS	X		X	X	X
HYDROMETRA		1			
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
P-PRESENT, A-ABSENT, \*--SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY:

*Joh Mader*

DATE: 9-19-94

ACCEPTED BY:

*Anthony V. V. V.*

DATE: 10/14/94

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
 SOFTWARE VERS # 3.0  
 ACCESSION NUMBER 002243

ANIMAL #	2000.000 MG/KG					GROUP - F
	166	167	168	169	170	
DAYS ON TEST	1	1	1	1	1	
BODY AS A WHOLE, NOS AUTOLYSIS	2		2	3	3	

KEY: N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
 P-PRESENT, A-ABSENT, \* -SEE COMMENT REPORT (FORM #2), X-NORMAL BUT NOT COLLECTED

REVIEWED BY: John M. Moler DATE: 9-17-94 ACCEPTED BY: Melanie J. Vassini DATE: 10/24/94

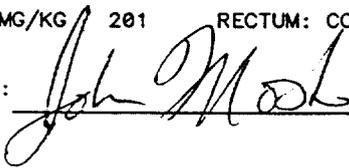
## GROSS PATHOLOGY COMMENT REPORT

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

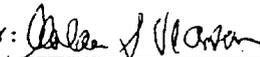
DAY	DOSE LEVEL	ANIMAL #	COMMENT
50	1000.000 MG/KG	207	DUODENUM: CONTAINED MUCUS.
50	1000.000 MG/KG	208	DUODENUM: CONTAINED MUCUS.
51	1000.000 MG/KG	197	STOMACH: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	197	DUODENUM: CONTAINED BROWN MUCUS.
51	500.000 MG/KG	191	DUODENUM: CONTAINED BROWN FLUID.
51	500.000 MG/KG	191	JEJUNUM: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	209	DUODENUM: CONTAINED BROWN MUCUS.
51	1000.000 MG/KG	196	STOMACH: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	196	DUODENUM: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	196	JEJUNUM: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	197	JEJUNUM: CONTAINED BROWN MUCUS.
51	500.000 MG/KG	191	DUODENUM: CONTAINED BROWN MUCUS.
51	500.000 MG/KG	191	JEJUNUM: CONTAINED BROWN MUCUS.
51	500.000 MG/KG	191	STOMACH: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	198	STOMACH: CONTAINED BROWN FLUID.
51	1000.000 MG/KG	198	DUODENUM: CONTAINED BROWN MUCUS.
51	1000.000 MG/KG	198	JEJUNUM: CONTAINED BROWN MUCUS.
54	1000.000 MG/KG	209	JEJUNUM: CONTAINED BROWN MUCUS.
54	1000.000 MG/KG	199	HAIR OF FACE: PORPHYRIN STAIN.
54	1000.000 MG/KG	199	SKIN OF FEET: STAINED BROWN.
54	1000.000 MG/KG	199	LIVER: PORTION OF LIVER ADJACENT TO STOMACH WAS PALE.
55	500.000 MG/KG	201	SKIN OF FOREPAWS: LEFT AND RIGHT FOREPAWS STAINED BROWN.
55	500.000 MG/KG	201	DUODENUM: CONTAINED BROWN FLUID.
55	500.000 MG/KG	201	JEJUNUM: CONTAINED BROWN FLUID.
55	500.000 MG/KG	201	ILEUM: CONTAINED BROWN FLUID.
55	500.000 MG/KG	201	CECUM: CONTAINED BROWN FLUID.
55	500.000 MG/KG	201	COLON: CONTAINED BROWN FLUID.
55	500.000 MG/KG	201	RECTUM: CONTAINED BROWN FLUID.

REVIEWED BY:



DATE: 11-2-94

ACCEPTED BY:



DATE: 1/2/94

SUMMARY HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000	500.000	1000.000	2000.000
	MG/KG M	MG/KG M	MG/KG M	MG/KG M
LUNGS	5	5	5	0
ALVEOLAR MACROPHAGES	5	5	5	0
PERIVASCULAR CUFFING	1	0	0	0
CONGESTION	0	1	5	0
EDEMA	0	1	0	0
HEMORRHAGE	0	1	3	0
BRONCHUS				
LYMPHOCYTIC INFLAMMATORY INFILTRATE	5	5	5	0
ALVEOLAR WALL				
INFLAMMATION, CHRONIC FOCAL	2	0	3	0
INFLAMMATION, CHRONIC DIFFUSE	0	1	1	0
STOMACH	5	4	5	0
AUTOLYSIS	0	0	1	0
STOMACH, NON-GLANDULAR				
HYPERKERATOSIS	0	4	0	0
ACANTHOSIS	0	4	0	0
STOMACH, GLANDULAR				
NECROSIS, FOCAL	0	0	3	0
HEMORRHAGE	0	0	4	0
LIVER	5	5	5	0
INFLAMMATION, CHRONIC FOCAL	2	1	0	0
AUTOLYSIS	0	0	1	0
HEPATOCTE				
CYTOPLASMIC VACUOLIZATION	5	5	2	0
HEPATIC CAPSULE				
NECROSIS, DIFFUSE	0	0	2	0
HEMORRHAGE	0	0	2	0
KIDNEYS	5	5	5	0
HYDRONEPHROSIS, BILATERAL	1	0	0	0
HYDRONEPHROSIS, UNILATERAL	1	2	0	0
AUTOLYSIS	0	1	5	0
PROXIMAL CONVOLUTED RENAL TUBULE				
DEGENERATION, HYALIN	4	1	0	0
CYTOPLASMIC VACUOLIZATION	0	3	0	0
REGENERATION	0	1	0	0
RENAL PELVIS				
INFLAMMATION, CHRONIC FOCAL	0	1	0	0
URINARY BLADDER	5	4	5	0
MUCOSA				
HYPERPLASIA	0	1	0	0
HYPERTROPHY	0	1	0	0
SPLEEN	5	5	5	0
SPLENIC LYMPHATIC FOLLICLE				
ATROPHY	0	0	1	0
BONE MARROW	5	5	5	0
ATROPHY	0	0	1	0
CONGESTION	0	0	1	0

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY: London J. Mani DATE: 05/21/94 ACCEPTED BY: [Signature] DATE: 2/14/95

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	250.000 MG/KG					GROUP - M				
	231	232	233	234	235	231	232	233	234	235
DAYS ON TEST	14	14	14	14	14					
LUNGS										
ALVEOLAR MACROPHAGES	1	1	1	1	1					
PERIVASCULAR CUFFING										1
BRONCHUS										
LYMPHOCYTTIC INFLAMMATORY INFILTRATE	1	1	1	1	1					
ALVEOLAR WALL										
INFLAMMATION, CHRONIC FOCAL	1	1								
STOMACH	N	N	N	N	N					
LIVER										
INFLAMMATION, CHRONIC FOCAL				1						1
HEPATOCTYTE										
CYTOPLASMIC VACUOLIZATION	2	2	2	2	2					
KIDNEYS	N									
HYDRONEPHROSIS, BILATERAL				2						
HYDRONEPHROSIS, UNILATERAL										2
PROXIMAL CONVOLUTED RENAL TUBULE										
DEGENERATION, HYALIN			1	1	1	1				
URINARY BLADDER	N	N	N	N	N					
SPLEEN	N	N	N	N	N					
BONE MARROW	N	N	N	N	N					

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY: *A. S. Shami* DATE: *6/2/95* ACCEPTED BY: *J. L. Oyle* DATE: *2/10/95*

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG					GROUP - M
	191	192	193	194	195	
DAYS ON TEST	2	14	14	14	14	
LUNGS						
ALVEOLAR MACROPHAGES	1	1	1	1	1	
CONGESTION	3					
EDEMA	1					
HEMORRHAGE	2					
BRONCHUS						
LYMPHOCYTIC INFLAMMATORY INFILTRATE	1	1	1	1	1	
ALVEOLAR WALL						
INFLAMMATION, CHRONIC DIFFUSE	2					
STOMACH	A					
STOMACH, NON-GLANDULAR						
HYPERKERATOSIS		1	1	1	1	
ACANTHOSIS		1	1	1	1	
LIVER						
INFLAMMATION, CHRONIC FOCAL			1			
HEPATOCTE						
CYTOPLASMIC VACUOLIZATION	2	2	2	2	2	
*KIDNEYS						
AUTOLYSIS	2					
HYDRONEPHROSIS, UNILATERAL				1	1	
PROXIMAL CONVOLUTED RENAL TUBULE						
CYTOPLASMIC VACUOLIZATION		1	1		2	
REGENERATION			2			
DEGENERATION, HYALIN				2		
RENAL PELVIS						
INFLAMMATION, CHRONIC FOCAL			1			
URINARY BLADDER	N	N	N	A		
MUCOSA						
HYPERPLASIA					2	
HYPERTROPHY					2	
SPLEEN	N	N	N	N	N	
BONE MARROW	N	N	N	N	N	

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE

\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY: John J. Mason DATE: 4/28/95 ACCEPTED BY: [Signature] DATE: 2/10/95

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG					GROUP - M
	196	197	198	199	200	
DAYS ON TEST	2	2	2	4	2	
LUNGS						
ALVEOLAR MACROPHAGES	1	1	1	1	1	
CONGESTION	2	2	2	3	3	
HEMORRHAGE		2		2	2	
BRONCHUS						
LYMPHOCYTIC INFLAMMATORY INFILTRATE	1	1	1	1	1	
ALVEOLAR WALL						
INFLAMMATION, CHRONIC DIFFUSE	2					
INFLAMMATION, CHRONIC FOCAL		2	2	1		
STOMACH						
AUTOLYSIS				3		
STOMACH, GLANDULAR						
NECROSIS, FOCAL	2	1			2	
HEMORRHAGE	2	3	2		1	
*LIVER						
AUTOLYSIS				3		
HEPATOCTE						
CYTOPLASMIC VACUOLIZATION	1	3				
HEPATIC CAPSULE						
NECROSIS, DIFFUSE			2		1	
HEMORRHAGE			2		1	
KIDNEYS						
AUTOLYSIS	2	2	2	3	3	
URINARY BLADDER	N	N	N	N	N	
SPLEEN						
SPLENIC LYMPHATIC FOLLICLE						
ATROPHY				3		
BONE MARROW						
ATROPHY	N	N	N		N	
CONGESTION				2	2	

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY:

*Audrey J. Vanni*

DATE: *6/25/99*

ACCEPTED BY:

*John P. ...*

DATE: *2/10/95*

SUMMARY HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

GROUP	250.000	500.000	1000.000	2000.000
	MG/KG F	MG/KG F	MG/KG F	MG/KG F
LUNGS	5	5	2	0
ALVEOLAR MACROPHAGES	5	5	2	0
CONGESTION	0	5	2	0
BRONCHUS				
LYMPHOCYTIC INFLAMMATORY INFILTRATE	5	5	2	0
ALVEOLAR WALL				
INFLAMMATION, CHRONIC FOCAL	4	4	2	0
STOMACH	5	5	1	0
AUTOLYSIS	0	3	1	0
STOMACH, NON-GLANDULAR				
HYPERKERATOSIS	1	0	0	0
ACANTHOSIS	1	0	0	0
STOMACH, GLANDULAR				
HEMORRHAGE	0	2	0	0
LIVER	5	5	2	0
INFLAMMATION, CHRONIC FOCAL	3	0	0	0
AUTOLYSIS	0	3	2	0
HEPATOCTE				
CYTOPLASMIC VACUOLIZATION	4	0	0	0
KIDNEYS	5	5	2	0
HYDRONEPHROSIS, BILATERAL	1	1	0	0
AUTOLYSIS	0	3	2	0
RENAL TUBULE				
MINERALIZATION	2	0	0	0
PROXIMAL CONVOLUTED RENAL TUBULE				
CYTOPLASMIC VACUOLIZATION	5	0	0	0
URINARY BLADDER	5	2	2	0
AUTOLYSIS	0	1	1	0
SPLEEN	5	5	2	0
SPLENIC LYMPHATIC FOLLICLE				
ATROPHY	0	4	2	0
SPLENIC RED PULP				
ATROPHY	0	4	2	0
CONGESTION	0	4	2	0
BONE MARROW	5	5	2	0
ATROPHY	0	1	0	0
CONGESTION	0	1	0	0

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

REVIEWED BY: *John S. Mason* DATE: *1/28/95* ACCEPTED BY: *John P. O'Connell* DATE: *2/1/95*

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	250.000 MG/KG GROUP - F				
	236	237	238	239	240
DAYS ON TEST	14	14	14	14	14
LUNGS					
ALVEOLAR MACROPHAGES	1	1	1	1	1
BRONCHUS					
LYMPHOCYTIC INFLAMMATORY INFILTRATE	1	1	1	1	1
ALVEOLAR WALL					
INFLAMMATION, CHRONIC FOCAL	1	1	1	1	
STOMACH		N	N	N	N
STOMACH, NON-GLANDULAR					
HYPERKERATOSIS	1				
ACANTHOSIS	1				
LIVER		N			
INFLAMMATION, CHRONIC FOCAL	1			1	1
HEPATOCTE					
CYTOPLASMIC VACUOLIZATION	1		3	1	1
KIDNEYS					
HYDRONEPHROSIS, BILATERAL		1			
RENAL TUBULE					
MINERALIZATION	1			1	
PROXIMAL CONVOLUTED RENAL TUBULE					
CYTOPLASMIC VACUOLIZATION	2	2	2	2	2
URINARY BLADDER	N	N	N	N	N
SPLEEN	N	N	N	N	N
BONE MARROW	N	N	N	N	N

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY: John J. Vaam DATE: 6/15/95 ACCEPTED BY: John P. O'Neil DATE: 2/16/95

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	500.000 MG/KG GROUP - F				
	201	202	203	204	205
DAYS ON TEST	6	2	2	2	2
LUNGS					
ALVEOLAR MACROPHAGES	1	1	1	1	1
CONGESTION	2	2	2	2	3
BRONCHUS					
LYMPHOCYTIC INFLAMMATORY INFILTRATE	1	1	1	1	1
ALVEOLAR WALL INFLAMMATION, CHRONIC FOCAL	2		2	1	1
STOMACH					
AUTOLYSIS	3			3	3
STOMACH, GLANDULAR HEMORRHAGE		2	2		
LIVER					
AUTOLYSIS	3	N	N	3	3
KIDNEYS					
AUTOLYSIS	3		N	3	3
HYDRONEPHROSIS, BILATERAL		1			
URINARY BLADDER					
AUTOLYSIS	A	A	N	3	A
SPLEEN					
SPLENIC LYMPHATIC FOLLICLE ATROPHY	2	3	2	2	
SPLENIC RED PULP					
ATROPHY		4	3	3	3
CONGESTION		4	3	3	3
BONE MARROW					
ATROPHY	3		N	N	N
CONGESTION	3				

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY: *Jason J. Waom* DATE: *6/1/95* ACCEPTED BY: *John Ogle* DATE: *2/10/95*

INDIVIDUAL ANIMAL HISTOPATHOLOGY INCIDENCE TABLE

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

ANIMAL #	1000.000 MG/KG		GROUP - F		
	206	207	208	209	210
DAYS ON TEST	1	1	1	2	2
LUNGS					
ALVEOLAR MACROPHAGES				1	1
CONGESTION				3	3
BRONCHUS					
LYMPHOCYTIC INFLAMMATORY INFILTRATE				1	1
ALVEOLAR WALL					
INFLAMMATION, CHRONIC FOCAL				1	1
LIVER					
AUTOLYSIS				3	3
KIDNEYS					
AUTOLYSIS				3	3
SPLEEN					
SPLENIC LYMPHATIC FOLLICLE					
ATROPHY				2	2
SPLENIC RED PULP					
ATROPHY				4	4
CONGESTION				4	4
URINARY BLADDER					
AUTOLYSIS				N	3
BONE MARROW					
AUTOLYSIS				N	N
STOMACH					
AUTOLYSIS				N	3

KEY: P-PRESENT, A-ABSENT, N-NORMAL, 1-MINIMAL, 2-MINOR, 3-MODERATE, 4-SEVERE  
\* - SEE COMMENT REPORT (FORM #3)

REVIEWED BY: *Jordan J. Mann* DATE: *6/18/95* ACCEPTED BY: *[Signature]* DATE: *2/10/95*

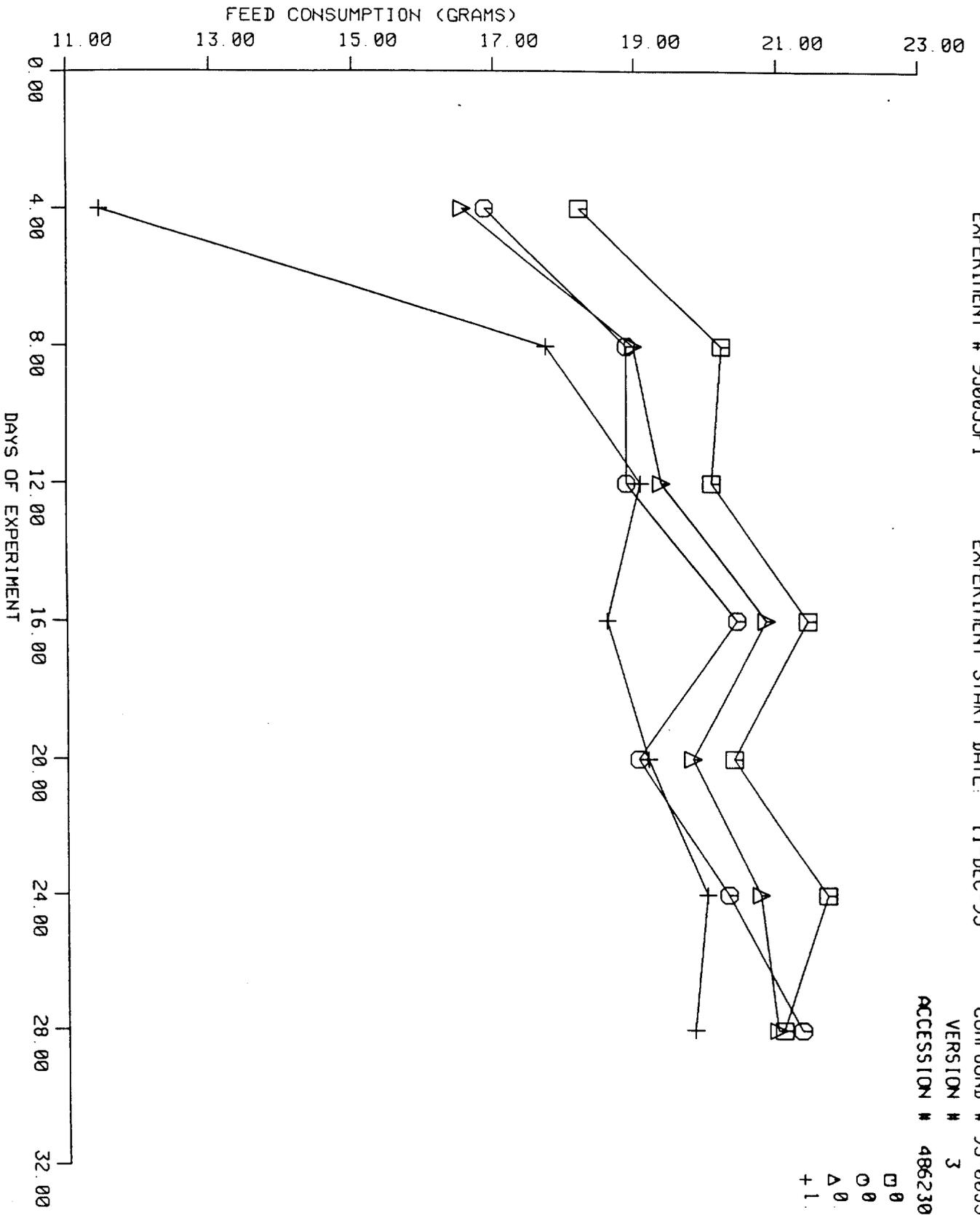
HISTOPATHOLOGY COMMENT REPORT

EXPERIMENT # 940046A0

COMPOUND # 94-0046  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 002243

DAY	DOSE LEVEL	ANIMAL#	COMMENT
131	1000.000 MG/KG	198	LIVER-SUBCAPSULAR NECROSIS AND HEMORRHAGE
131	1000.000 MG/KG	200	LIVER-SUBCAPSULAR NECROSIS AND HEMORRHAGE
131	500.000 MG/KG	193	KIDNEYS-PELVIS:UNILATERAL SUBMUCOSAL ACCUM. OF MONONUCLEAR CELLS.

REVIEWED BY: *John S. Moran* DATE: 6/28/95 ACCEPTED BY: *John P. ...* DATE: 2/10/95



EXPERIMENT # 950055F1

EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055

VERSION # 3

ACCESSION # 486230

□ 0.000	%	F
○ 0.150	%	F
△ 0.450	%	F
+ 1.500	%	F

## STUDY MEAN FOR FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

EXPERIMENT # 950055F1

EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 486230

				MEAN	DOSE(MG/KG/DY)
GROUP #	1	0.000 %	F	20.5	0.0
GROUP #	2	0.150 %	F	19.4	132.5
GROUP #	3	0.450 %	F	19.6	381.4
GROUP #	4	1.500 %	F	18.0	1274.5

NOTE: FOR GROUP HOUSED ANIMALS, FEED CONSUMPTION IS DERIVED FROM A COMMON CONTAINER

REVIEWED BY: Alicia M. Warthling DATE: 1/10/96 ACCEPTED BY: William J. Jones DATE: 1/11/96

MEAN FOR FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

EXPERIMENT # 950055F1

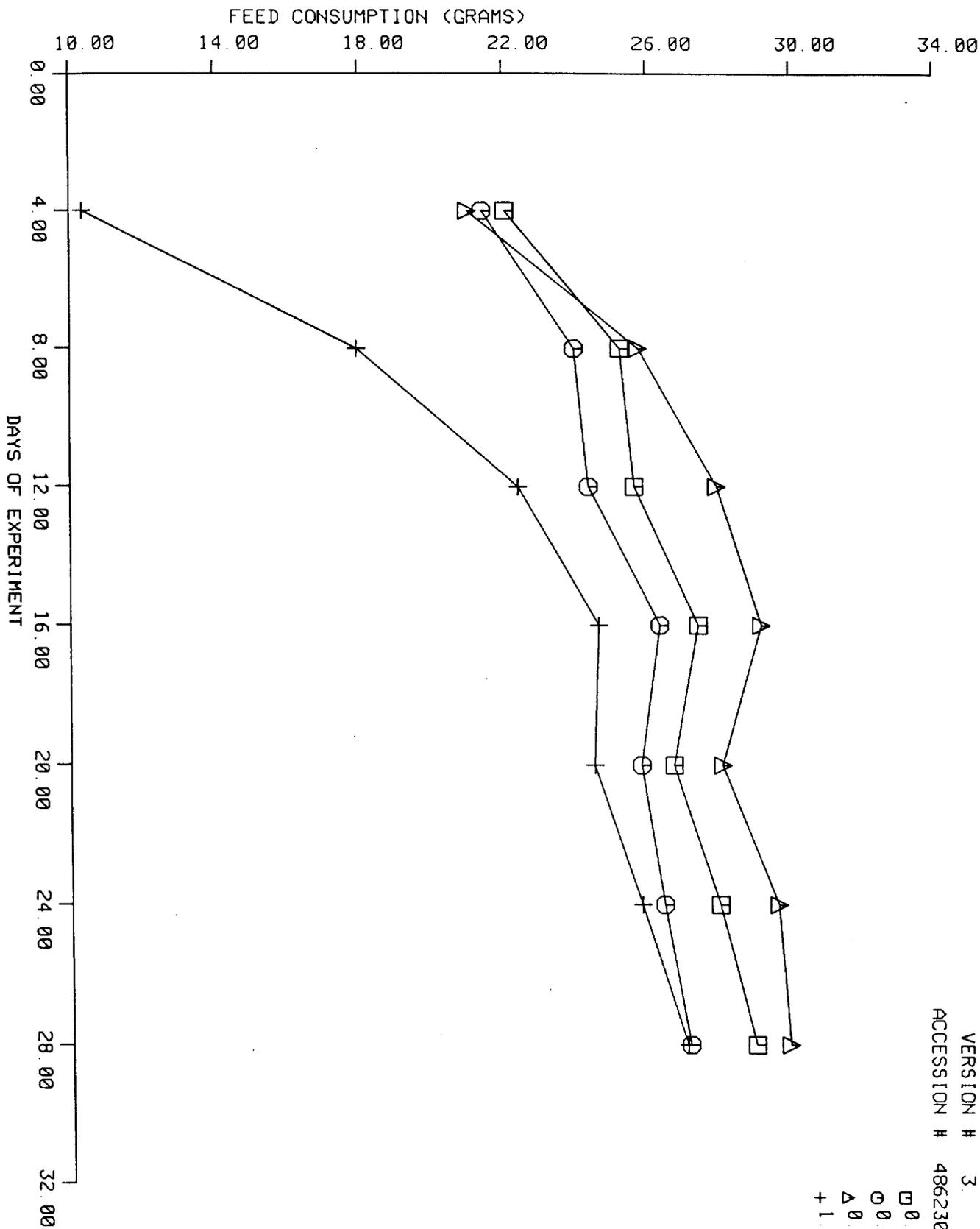
EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 486230

		0.000	0.150	0.450	1.500
		%	%	%	%
		GROUP-F	GROUP-F	GROUP-F	GROUP-F
WEEK #	1				
*DAY	4	18.2 A 0.9	16.9 1.1	16.6 1.5	11.4 1.8
		0.0 B 0.0	139.0 9.2	394.7 31.0	985.7 110.9
		5 C	5	5	5
WEEK #	2				
DAY	8	20.2 0.6	18.9 1.3	19.0 1.8	17.8 1.1
		0.0 0.0	155.6 16.7	452.7 9.4	1528.9 134.5
		5	5	5	5
DAY	12	20.1 1.5	18.9 0.9	19.4 0.7	19.1 1.7
		0.0 0.0	130.8 10.8	389.8 16.9	1380.7 75.1
		5	5	5	5
WEEK #	3				
DAY	16	21.4 1.5	20.4 1.1	20.9 1.3	18.6 2.2
		0.0 0.0	135.8 10.3	395.3 18.0	1279.0 105.7
		5	5	5	5
DAY	20	20.4 1.0	19.1 1.7	19.8 1.2	19.2 1.6
		0.0 0.0	121.8 9.1	355.3 31.7	1251.7 52.9
		5	5	5	5
WEEK #	4				
DAY	24	21.7 1.7	20.3 0.3	20.8 1.0	20.0 1.8
		0.0 0.0	125.8 7.4	357.6 26.0	1279.1 78.7
		5	5	5	5
DAY	28	21.1 3.6	21.4 1.0	21.0 1.8	19.9 2.0
		0.0 0.0	125.9 9.7	350.2 19.3	1222.2 73.4
		5	5	5	5

KEY: \* - STATISTICAL DIFFERENCE (P<=0.05) AMONG GROUPS, ONE WAY ANOVA, SEE STATISTICAL REPORT  
BARTLETT'S TEST USED

REVIEWED BY: Alison M. WauHling DATE: 1/10/96 ACCEPTED BY: William J. Baker DATE: 1/11/96



EXPERIMENT # 950055F1

EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055

VERSION # 3  
 ACCESSION # 486230

□ 0.000	%	M
○ 0.150	%	M
△ 0.450	%	M
+ 1.500	%	M

## STUDY MEAN FOR FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

EXPERIMENT # 950055F1

EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 486230

			MEAN	DOSE(MG/KG/DY)	
GROUP #	1	0.000 %	M	26.3	0.0
GROUP #	2	0.150 %	M	25.1	123.2
GROUP #	3	0.450 %	M	27.4	381.0
GROUP #	4	1.500 %	M	21.8	1234.7

NOTE: FOR GROUP HOUSED ANIMALS, FEED CONSUMPTION IS DERIVED FROM A COMMON CONTAINER

REVIEWED BY:

Alison M. Warthling

DATE:

1/10/96

ACCEPTED BY:

William J. Bates

DATE:

1/11/96

MEAN FOR FEED CONSUMPTION (GRAMS/ANIMAL/DAY)

EXPERIMENT # 950055F1

EXPERIMENT START DATE: 11-DEC-95

COMPOUND # 95-0055  
SOFTWARE VERS # 3.0  
ACCESSION NUMBER 486230

		0.000	0.150	0.450	1.500
		%	%	%	%
		GROUP-M	GROUP-M	GROUP-M	GROUP-M
WEEK #	1				
*DAY	4	22.0 A 2.1	21.4 1.1	21.0 1.3	10.3 1.2
		0.0 B 0.0	145.5 1.9	417.4 7.9	839.2 37.8
		5 C	5	5	5
WEEK #	2				
*DAY	8	25.2 2.3	24.0 1.7	25.8 1.3	17.9 3.1
		0.0 0.0	162.8 7.3	512.1 24.3	1455.2 205.2
		5	5	5	5
*DAY	12	25.7 2.3	24.4 1.5	28.0 1.3	22.4 2.4
		0.0 0.0	125.9 1.6	407.6 19.0	1362.5 53.2
		5	5	5	5
WEEK #	3				
*DAY	16	27.5 3.0	26.4 2.2	29.2 1.7	24.7 2.1
		0.0 0.0	125.7 3.7	390.4 5.9	1348.3 35.1
		5	5	5	5
DAY	20	26.8 2.7	25.9 1.8	28.1 1.2	24.5 2.0
		0.0 0.0	113.0 4.0	346.0 16.9	1222.7 40.6
		5	5	5	5
WEEK #	4				
DAY	24	28.1 2.9	26.5 2.2	29.7 2.4	25.8 2.1
		0.0 0.0	109.5 4.6	343.4 13.5	1205.3 49.1
		5	5	5	5
DAY	28	29.0 3.5	27.2 2.7	30.0 2.6	27.2 2.6
		0.0 0.0	105.7 5.0	327.6 7.8	1184.1 32.5
		5	5	5	5

KEY: \* - STATISTICAL DIFFERENCE (P<=0.05) AMONG GROUPS, ONE WAY ANOVA, SEE STATISTICAL REPORT  
BARTLETT'S TEST USED

REVIEWED BY:

*Alison M. Waithling*

DATE: 1/10/96

ACCEPTED BY:

*William J. ...*

DATE: 1/11/96

51 FEB 22 AM 11:12

STUDY TITLE

**4-CHLOROBENZENESULPHONAMIDE  
ACUTE DERMAL IRRITATION STUDY IN THE RABBIT**

**HAEL NUMBER: 94-0046 KAN: 002243  
CAS REGISTRY NUMBER: 98-64-6**

**FINAL REPORT**

AUTHOR

Kenneth P. Shepard, B.S.

PERFORMING LABORATORY

Toxicological Sciences Laboratory  
Corporate Health and Environment Laboratories  
Eastman Kodak Company  
1100 Ridgeway Avenue  
B-320 Kodak Park  
Rochester, New York 14652-6272  
USA

LABORATORY PROJECT ID

HAEL Number: 94-0046

STUDY SPONSOR

Eastman Kodak Company

STUDY COMPLETION DATE

August 3, 1994

**QUALITY ASSURANCE INSPECTION STATEMENT**

[21 CFR 58.35(B)(7), 40 CFR 792.35(B)(7), and 40 CFR 160.35(B)(7)]

STUDY: 94-0046-1 STUDY DIRECTOR: SHEPARD, K.P.  
ACCESSION NUMBER: 002243

PAGE 1  
07/28/94

STUDY TYPE: ACUTE DERMAL IRRITATION TEST

*Janice M. Bealinger / MSJ*  
(AUDITOR, QUALITY ASSURANCE UNIT)

*7/28/94*  
DATE

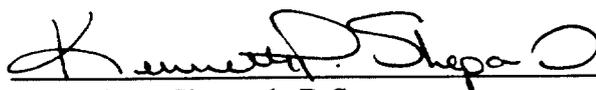
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TO THE BEST OF MY KNOWLEDGE, THIS FINAL REPORT ACCURATELY DESCRIBES THE METHODS AND STANDARD OPERATING PROCEDURES, AND THE REPORTED RESULTS ACCURATELY REFLECT THE RAW DATA. THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY ASSURANCE UNIT OF HAEL, EASTMAN KODAK COMPANY ROCHESTER, N.Y. AND WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES:  
-----

INSPECTION DATES -----	PHASE(S) INSPECTED -----	STATUS REPORT DATES -----
06/28/94	PROTOCOL APPENDIX/AMENDMENT SUBMISSION	
06/30/94	CLINICAL SIGNS AT 48 HRS.	07/29/94
07/28/94	FINAL REPORT REVIEW	07/29/94

**COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS**

The study described by this report was conducted in compliance with the following Good Laboratory Practice Standards:

Annex 2 of the Organization for Economic Cooperation and Development  
Guidelines for Testing of Chemicals C(81)30 (Final).

  
\_\_\_\_\_  
Kenneth P. Shepard, B.S.  
Study Director

8 / 3 / 94  
\_\_\_\_\_  
Month/Day/Year

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**ABSTRACT**

**4-CHLOROBENZENESULPHONAMIDE**

**ACUTE DERMAL IRRITATION STUDY IN THE RABBIT**

**HAEL NUMBER: 94-0046 KAN: 002243**

**CAS REGISTRY NUMBER: 98-64-6**

A dermal irritation study was conducted by administering single topical doses of 0.5 gram of the test material to rabbits. The test material was left in contact with the skin under an occlusive wrap for four hours. No signs of irritation were evident at any time during the 72-hour observation period. Based on the lack of an irritant response, the test material requires no skin irritation classification as defined in the 18th Adaptation on the EC Classification, Packaging, and Labelling of Dangerous Substances.

**PERFORMING LABORATORY**

Toxicological Sciences Laboratory  
Corporate Health and Environment Laboratories  
Eastman Kodak Company  
1100 Ridgeway Avenue  
B-320 Kodak Park  
Rochester, New York 14652-6272  
USA

**SPONSOR**

Eastman Kodak Company

**STUDY DATES**

Study Initiation: June 28, 1994  
Experiment Initiation: June 28, 1994  
Experiment Completion: July 1, 1994  
Study Completion: August 3, 1994

**STUDY DIRECTOR**

Kenneth P. Shepard, B.S.

**OTHER KEY PERSONNEL**

Len Sakal, B.S., Study Technician  
John W. Mosher, B.S., Principal Investigator  
Milan S. Vlaovic, D.V.M., Ph.D., Laboratory Animal Medicine

### **PURPOSE/OBJECTIVE**

The purpose of the study was to determine the potential of the test material to cause primary irritation of mammalian skin.

### **TEST SUBSTANCE**

Test Material Name: 4-Chlorobenzenesulphonamide  
CAS Registry Number: 98-64-6  
HAEL Laboratory Number: 94-0046  
KAN: 002243  
CIN: Not available  
SRID or Lot I.D. Number: BB2673-182A  
Physical State and Appearance: White powder  
Received at Performing Laboratory: June 3, 1994  
Composition: Refer to composition information included in the notification when applicable.

### **TEST SYSTEM**

Species: Rabbit  
Strain: Hra:(NZW)SPF  
Source: Hazleton Research Laboratories, Denver, PA, USA  
No. of Animals: 3  
Sex: Not Determined  
Body Weight Range at Dosing (grams): 2664 - 3085  
Age: Young Adults (At least three months old)

### **HUSBANDRY AND ENVIRONMENTAL CONDITIONS**

#### **Housing**

All animals were individually housed in suspended, stainless-steel, mesh cages.

## **HUSBANDRY AND ENVIRONMENTAL CONDITIONS, Cont.**

### **Environmental Conditions**

A photoperiod of 12 hours light from 6 a.m. to 6 p.m. was maintained. Room temperature was maintained at 65-67°F. Relative humidity was maintained at 70-71%.

### **Diet and Water**

Agway® Prolab™ High Fiber Rabbit Diet certified pellets and water (Monroe County (NY) Water Authority) were available ad libitum. No known contaminants which would interfere with the outcome of the study were expected to be present in feed or water from these sources. Analyses of feed and quarterly analyses of water are maintained on file within the testing laboratory.

### **Isolation**

Rabbits were isolated and monitored for at least five days after arrival and before release to the testing facility.

### **Animal Identification**

All rabbits were identified by cage numbers and uniquely-numbered, metal ear tags.

## **TEST PROCEDURES AND CONDITIONS**

### **Test Procedure Guideline**

OECD Guideline for Testing of Chemicals: Guideline 404, Dated 17 July, 1992; (Annex V, test B.4).

### **Dose Level**

0.5 gram/animal

## TEST PROCEDURES AND CONDITIONS, Cont.

### Identification Numbers of Animals Used

28, 29, and 30

### Dosing Regimen

The hair was removed from an area of the dorsal skin with an electric clipper. A single dose of the material was placed in contact with the skin using a fiber pad and an occlusive wrap to hold the test material in place for four hours. At the end of the exposure period, the application site was rinsed with running water.

### Control Substance

No control substance was used. Adjacent areas of untreated skin of each animal served as control sites for the test areas.

### Vehicle

No vehicle was used. The test material was administered as a solid moistened thoroughly with water.

### Clinical Observations

The site of application was examined at 1, 24, 48, and 72 hours after removal of the occlusive patch. Observations included estimation of erythema, edema, necrosis, eschar formation, scarring, erosion, and staining caused by the material as well as general systemic effects.

### Necropsy

No necropsies were conducted at the conclusion of the 72-hour observation period.

## **RESULTS**

### **Clinical Observations**

Graded as described in OECD Guideline 404 (Annex V test B.4) (erythema, edema)

<b>ANIMAL NUMBER</b>	<b>DOSE (gram)</b>	<b>RESPONSE AT THE SITE OF APPLICATION</b>			
		<b>1 HOUR</b>	<b>24 HOURS</b>	<b>48 HOURS</b>	<b>72 HOURS</b>
28	0.5	0,0	0,0	0,0	0,0
29	0.5	0,0	0,0	0,0	0,0
30	0.5	0,0	0,0	0,0	0,0

### **Description of Serious Lesions and Irritation Other Than Erythema and Edema**

No irritant response or serious lesion was noted during the 72-hour observation period.

### **Toxic Effects Other Than Irritation**

No toxic effects were noted during the study.

## **DATA ANALYSIS**

Not applicable

## **DISCUSSION AND INTERPRETATION**

Since no signs of irritation were evident at any time during the study, the test material was not considered a dermal irritant.

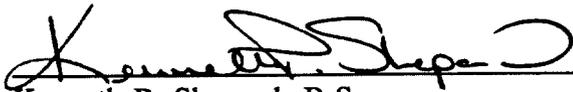
## **CONCLUSION**

Based on the lack of an irritant response, the test material requires no skin irritation classification as defined in the 18th Adaptation on the EC Classification, Packaging, and Labelling of Dangerous Substances.

## **DATA STORAGE**

All test results presented in this report are supported by raw data which are maintained in the archives of the Corporate Health and Environment Laboratories, Eastman Kodak Company.

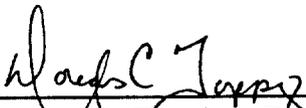
**SIGNATURE PAGE**



Kenneth P. Shepard, B.S.  
Study Director

8/3/94

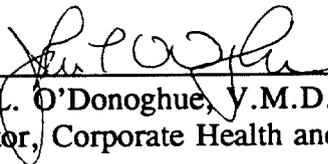
Month/Day/Year



Douglas C. Topping, Ph.D.  
Unit Director, Mammalian Toxicology Section

August 1, 1994

Month/Day/Year



John L. O'Donoghue, V.M.D., Ph.D.  
Director, Corporate Health and Environment Laboratories

8/2/94

Month/Day/Year

## Triage of 8(e) Submissions

Date sent to triage: \_\_\_\_\_

**NON-CAP**

**CAP**

Submission number: 13588A

TSCA Inventory: **(Y)**    N    D

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO            AQUATO

Group 2 - Ernie Falke (1 copy total)

**(ATOX)**    SBTOX    SEN            w/NEUR

Group 3 -HERD (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; refile after triage evaluation.
- This **original** submission has been **split**; rejoin after triage evaluation.
- Other:

### Photocopies Needed for Triage Evaluation

entire document: **(0)**    1    2    3

front section and CECATS: **(0)**    1    2    3

Initials: JW

Date: 6/26/96

CREATS DATA: Submission # REIO: 0296-13588 SIO: A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Eastman Kodak

Compound

SUB DATE: 02/15/96 OTS DATE: 02/23/96

CSRAD DATE: 04/03/96

CHEMICAL NAME:

CAS# 98-64-6

CREATS SURVIVE: IRACKING DRAISE ENTRY FORM

**INFORMATION REQUESTED, FLWP DATE:**

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONALE)
- DISPOSITION: (63) REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

**VOLUNTARY ACTIONS:**

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/UNDERWAY
- (0403) NOTIFICATION OF WORKER/OTHERS
- 0404 LABEL/MSDS CHANGES
- 0405 PROCESS/HANDLING CHANGES
- 0406 APPL USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/REL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 ACUTE TOX. (ANIMAL)	01 02 04	0226 CONFIDENTIAL	01 02 04		
<u>0212</u> ACUTE TOX. (ANIMAL)	01 <u>02</u> 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIALGE DATA: NON-CBI INVENTORY Ongoing Review SPECIES TOXICOLOGICAL CONCERN: USE: PRODUCTION:

YES (CONTINUE)

YES (DROP/REFER)

RAT

LOW

Site - limited intermediate

NO (DROP)

NO (CONTINUE)

RST

MED

Ac. oral

DETERMINE

REFER:

HIGH

COMMENTS:

13588A

M

Acute oral toxicity in the rat is of moderate concern based on an LD<sub>50</sub> value of 467 mg/kg (574 mg/kg males and 354 mg/kg females). CD(SD)BR rats (5/sex/dose) received single gavage doses of 250, 500, 1000 or 2000 mg/kg. Deaths were as follows: 0/10, 6/10, 10/10, and 10/10. Clinical signs at all doses included weakness, staining of inguinal hair and skin of tail, blood in urine, and reduced feces. At 500 mg/kg and above, prostration, hypothermia, dehydration, porphyrin discharge of the nose and eye, and staining of feet were also seen. At necropsy, treatment-related changes were in the lung (incomplete collapse, hemorrhage), gastrointestinal tract (hemorrhage and necrosis of gastric mucosa, mucus accumulation), spleen (small, dark), and liver (pale or dark). Histopathologic changes included hyperkeratosis and acanthosis of gastric mucosa, hepatic necrosis and hemorrhage, splenic atrophy and congestion, atrophy and congestion of the bone marrow, and congestion, hemorrhage and edema.