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August 28, 1992

(A)

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92 SEP -2 AM 7:54

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

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following reports pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). These reports describe various toxicity studies with UC 54229 (2,3-dihydro-2,3-dimethyl-7-benzofuranyl-N-(trimethylammonium-acetyl)-N-methylcarbamate chloride; CASRN [not available]).

(1) "A Seven Day Dietary Study with UC 54229 in Rats", Bio/dynamics, Project No. 83-2737, June 10, 1983.

(2) "Four-Week Dietary Study in Rats: UC 54229" Hazleton, Project No. 400-659, October 25, 1984.

(3) "Four-Week Dietary Study in Mice: UC 54229", Hazleton, Project No. 400-658, October 19, 1984.

Complete summaries of these reports are attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

Previous PMN submissions related to this substance are: (None)

83-2737

RECEIVED 1/31/95

(2)

In the attached reports the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of these reports. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,

William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summaries, and reports)

83-2737

SUMMARY

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 83-2737

A SEVEN DAY DIETARY STUDY

WITH UC54229 IN RATS

Final Report

Submitted to: Union Carbide Agricultural Products Company, Inc.

Date: June 10, 1983

SUMMARY

Bio/dynamics Inc.

PROJECT NO. 83-2737

A SEVEN DAY DIETARY STUDY

WITH UC54229 IN RATS

Abstract

This study, conducted for Union Carbide Agricultural Products Company, Inc., was designed to evaluate the cholinesterase inhibiting properties of UC54229 when administered, via the diet, to 10 male CD® rats at a dose level of 0.05% for seven days. Control animals (10 males) received untreated diets. Body weights were recorded pretest and on Day 7. Food consumption was measured over a six-day period. Plasma, erythrocyte and brain cholinesterase levels were evaluated for all animals at termination.

Mean body weight, body weight gain and food consumption values in the treated group were reduced 10.5%, 57.4% and 10.6%, respectively, after one week of treatment.

The mean erythrocyte, plasma and brain cholinesterase values of the animals receiving treated diets were reduced 8%, 50% and 55%, respectively, compared to the control. The observed decreases were attributed to the ingestion of UC54229 treated diets (0.05%).

Evaluations of mortality and physical observations did not reveal any effect attributable to the administration of UC54229 in the diet.

The mean erythrocyte, plasma and brain cholinesterase values of the animals receiving treated diets were reduced compared to the control. The observed decreases were attributed to the ingestion of UC54229 treated diets (0.05%).

Item 438

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 83-2737

A SEVEN DAY DIETARY STUDY

WITH UC54229 IN RATS

Final Report

Submitted to: Union Carbide Agricultural Products Company, Inc.

Date: June 10, 1983

Attn: Ronald L. Baron, Ph.D.

Bio/dynamics Inc.

PROJECT NO. 83-2737

A SEVEN DAY DIETARY STUDY

WITH UC54229 IN RATS

Abstract

This study, conducted for Union Carbide Agricultural Products Company, Inc., was designed to evaluate the cholinesterase inhibiting properties of UC54229 when administered, via the diet, to 10 male CD® rats at a dose level of 0.05% for seven days. Control animals (10 males) received untreated diets. Body weights were recorded pretest and on Day 7. Food consumption was measured over a six-day period. Plasma, erythrocyte and brain cholinesterase levels were evaluated for all animals at termination.

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Evaluations of mortality and physical observations did not reveal any effect attributable to the administration of UC54229 in the diet.

P.O. Box 43 • East Millstone, New Jersey 08873 • (201) 873-2550 • Telex: 844597 • Cable: BIO/DYN

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I. INTRODUCTION

This study, conducted for Union Carbide Agricultural Products Company, Inc., was designed to evaluate the cholinesterase inhibiting properties of UC54229 when administered, via the diet, to 10 male CD® rats at a dose level of 0.05% for seven days. Control animals (10 males) received untreated diets. Body weights were recorded pretest and on Day 7. Food consumption was measured over a six-day period. Plasma, erythrocyte and brain cholinesterase levels were evaluated for all animals at termination.

Species and strain of test animals, dose level and route of test substance administration were selected by the sponsor. This study was conducted at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey. All raw data and test substance samples are stored at this testing facility.

II. MATERIALS AND METHODS

A. Test Substance: UC54229 treated diet was provided by the sponsor.

Supplier:	Union Carbide Agricultural Products Company Research Triangle Park, North Carolina 27709
Date Received:	20 May 1983
Lot. No.:	5/18/83
Storage:	Refrigeration

B. Test Animals: Rats

Strain: CD®

Number of Animals:

Purchased: 25 Males

Placed on Test: 20 (10/group)

Supplier: Charles River Breeding Laboratories
Kingston, New York

Date Received: 19 May 1983

Age at Receipt: Approximately 6 weeks

Age at Initiation of Treatment: Approximately 7 weeks

Weight at Initiation of Treatment (grams):

	Mean	Range
Males:	211	198 - 218

C. Selection and Group Assignment: More animals than required for the study were purchased and equilibrated. Animals considered unsuitable for study on the basis of pretest physical examinations were eliminated prior to random selection for group assignment.

D. Animal Identification: Each rat was identified with a metal ear tag bearing its animal number. If the tag was lost, it was replaced and/or rat was toe-clipped for identification.

E. Experimental Outline:

Group	Test Substance	Dose Level	Number of Males	
			Initial	Cholinesterase Termination
I	Control	0.0%	10	10
II	UC54229 Treated Diet	0.05%	10	10

F. Husbandry:

Acclimation Period:	7 days (19 - 25 May 1983)
Housing:	Individually in elevated stainless steel cages.
Food:	Standard laboratory diet (Purina Lab Chow® - 5002) ad libitum during the acclimation and treatment periods. Control and treated diets presented during the study were provided by the sponsor.
Water:	ad libitum. By automated water system (Elizabethtown Water Company).
Environmental Conditions:	12 hour light/dark cycle
	Temperature monitored twice daily.

G. Test Substance Administration:

Route:	Oral via dietary admixture.
Frequency:	Continuously
Dates of Treatment:	26 May through 2 June 1983

H. Observations:

For Mortality and Gross Signs of Toxicologic or Pharmacologic Effects:	Twice daily
Detailed Physical Examination for Signs of Local or Systemic Toxicity, Pharmacologic Effects and Palpation for Tissue Masses:	Weekly

I. Body Weight:	(Meth. and Ref., Appendix A)
	Pretest and on Day 7.
J. Food Consumption:	(Meth. and Ref., Appendix A)
	Measured over the first six days of treatment.

K. Laboratory Studies: (Meth. and Ref., Appendix A)

Blood was obtained via venipuncture of the orbital sinus (retrobulbar venous plexus) under light ether anesthesia.

Number of Animals: All survivors - 20 males (10/group)

Time Interval: Termination - 2 June 1983

Parameter Evaluated

Clinical Chemistry:

cholinesterase
brain
erythrocyte
plasma

L. Postmortem:

Sacrifice Method: Exsanguination under ether anesthesia.

Date: 2 June 1983

Disposition: All animals were discarded after sacrifice.

M. Statistical Analysis: (Meth. and Ref., Appendix A)

Body weight, body weight gain, food consumption and cholinesterase values were analyzed. Mean values of the dose group were compared to control. Statistically significant differences from control are indicated in appendices.

III. RESULTS AND DISCUSSION

A. Mortality (Animal Termination History - Appendix B):

All control and treated animals survived the one-week duration of the study.

B. Physical Observations:

Physical observations noted during the one week of study were unremarkable.

C. Body Weight and Food Consumption (Appendix C):

The mean body weight, body weight gain and food consumption data of the animals receiving UC54229 treated diets (0.05%) were significantly reduced compared to the controls after one week of treatment.

Mean body weight, body weight gain and food consumption were reduced 10.5, 57.4 and 10.6%, respectively.

D. Cholinesterase Evaluation (Appendix D):

The mean erythrocyte, plasma and brain cholinesterase values of the animals receiving treated diets were reduced compared to the control. The observed decreases were attributed to the ingestion of UC54229 treated diets (0.05%).

	Plasma μM/ml/min	RBC μM/ml/min	Brain μM/g/min
Control	0.4	8.3	3.1
Treated	0.2[a]	7.6**	1.4**
% Decrease	50	8	55

**$p \leq 0.01$
[a]Statistical analysis not performed due to standard deviation of 0.0.

Ira W. Daly, Ph.D., D.A.B.T.
Director of Toxicology
Study Director

6/18/83
Date

Appendix A
A Seven Day Dietary Study
with UC54229 in Rats

Methodology and References - General

Parameter	Reference or Description
Physical Examination	Behavior: aggressiveness, increased or decreased activity. Respiration: nasal discharge and rales. Ocular: chromodacryorrhea, excessive lacrimation and percent opacity. Appearance: alopecia, ano-genital staining and general condition. Gastrointestinal: abdominal shape and fecal consistency. Palpation for tissue masses. Other: includes any unusual observation not included above.
Body Weight	INTEC Automatic Data Acquisition System.
Food Consumption	INTEC Automatic Data Acquisition System. Animals were presented with full feeders weighing 520 grams (includes weight of feed, jar and lid). After 6 days feeders were reweighed and resulting weight was subtracted from the full feeder weight. Resulting value = g/6 days. When body weights were taken weekly: $g/kg/day = \frac{g/interval}{average\ body\ weight\ (kg)} \div 6Days.$ $Average\ BW = \frac{Previous\ BW + Current\ BW}{2}$
Statistical Analysis	Test substance treated groups were compared to control by the F-test and Student's t-test. When variances differed significantly (F-test), Student's t-test was appropriately modified using Cochran's approximation (t'). Snedecor, G.W. and Cochran, W.G. Statistical Methods. 6th ed., Iowa State University Press, Ames (1967), pp. 104-106, 114-119.

Appendix A (cont.)
A Seven Day Dietary Study
with UC54229 in Rats

Methodology and References - Clinical Chemistry (cont.)

Abbreviation	Parameter	Specimen	Reporting Units	Reference or Description
	Cholinesterase	Erythro-cyte	µM/ml/min	CentrifiChem System 500®; Modified Ellman and Kinetic Method.
		Plasma	µM/ml/min	
		Brain	µM/g/min	

Appendix B
A Seven Day Dietary Study
with UC54229 in Rats

Animal Termination History

Group %	Males An. No.	Type of Death[a]	Date of Death	Days on Test	Group %	Males An. No.	Type of Death[a]	Date of Death	Days on Test
I 0.0	1001	T	6/2/83	8	II 0.05	2001	T	6/2/83	8
	1002	T	6/2/83	8		2002	T	6/2/83	8
	1003	T	6/2/83	8		2003	T	6/2/83	8
	1004	T	6/2/83	8		2004	T	6/2/83	8
	1005	T	6/2/83	8		2005	T	6/2/83	8
	1006	T	6/2/83	8		2006	T	6/2/83	8
	1007	T	6/2/83	8		2007	T	6/2/83	8
	1008	T	6/2/83	8		2008	T	6/2/83	8
	1009	T	6/2/83	8		2009	T	6/2/83	8
	1010	T	6/2/83	8		2010	T	6/2/83	8

[a]T = Terminal.

Appendix C
A Seven Day Dietary Study
with UC54229 in Rats

Body Weight, Body Weight Gain and Food Consumption Values

Group %	An.No.	Week 0 grams	Week 1 grams	Weight Gain Week 0-1 grams	Food Consumption g/kg/day	Test Substance Intake mg/kg/day
I	1001	216	256	40	100.3	0.0
0.0	1002	211	253	42	104.9	0.0
	1003	198	273	75	121.0	0.0
	1004	215	265	50	118.1	0.0
	1005	213	250	37	103.0	0.0
	1006	212	254	42	111.6	0.0
	1007	210	266	56	113.4	0.0
	1008	208	245	37	108.9	0.0
	1009	207	249	42	111.8	0.0
	1010	212	264	52	112.7	0.0
	Mean	210	258	47	110.6	0.0
	S.D.	5	9	12	6.5	0.0
	N	10	10	10	10	10
II	2001	205	225	20	a	-
0.05	2002	215	241	26	102.3	51.2
	2003	218	231	13	90.6	45.3
	2004	217	239	22	99.4	49.7
	2005	213	234	21	105.1	52.6
	2006	209	224	15	95.5	47.8
	2007	211	226	15	a	-
	2008	202	230	28	103.4	51.7
	2009	214	231	17	95.9	48.0
	2010	211	230	19	99.0	49.5
	Mean	212	231**	20**	98.9**	49.5
	S.D.	5	6	5	4.8	2.4
	N	10	10	10	8	8

Significantly different from control: $**p \leq 0.01$.
[a]Food Consumption not recorded due to excess feed spillage.

Appendix D
A Seven Day Dietary Study
with UC54229 in Rats

Plasma, Erythrocyte and Brain Cholinesterase Values

Group %	An.No.	Plasma µM/ml/min	RBC µM/ml/min	Brain µM/g/min
I	1001	0.5	8.1	3.0
0.0	1002	0.4	8.6	3.5
	1003	0.4	8.8	2.7
	1004	0.5	8.3	3.3
	1005	0.4	8.0	3.5
	1006	0.4	7.7	3.0
	1007	0.4	8.4	3.0
	1008	0.4	7.3	2.5
	1009	0.5	8.9	3.1
	1010	0.5	8.4	3.4
	Mean	0.4	8.3	3.1
	S.D.	0.1	0.5	0.3
	N	10	10	10
II	2001	0.2	7.7	1.2
0.05	2002	0.2	7.3	1.5
	2003	0.2	8.1	1.5
	2004	0.2	7.7	1.3
	2005	0.2	7.5	1.7
	2006	0.2	7.0	1.5
	2007	0.2	7.2	1.2
	2008	0.2	8.1	1.2
	2009	0.2	7.3	1.6
	2010	0.2	8.1	1.4
	Mean	0.2[a]	7.6**	1.4**
	S.D.	0.0	0.4	0.2
	N	10	10	10

Significantly different from control: ** $p \leq 0.01$.
[a]Statistical analysis not performed due to standard deviation of 0.0.

Appendix E
A Seven Day Dietary Study
with UC54229 in Rats

PERSONNEL

DEPARTMENT/TITLE	NAME	DEGREE
PRESIDENT	Geoffrey K. Hogan	Ph.D., D.A.B.T.
DIRECTOR OF TOXICOLOGY AND STUDY DIRECTOR	Ira W. Daly	Ph.D., D.A.B.T
STUDY MONITOR	Joanne R. Jackson	B.S.
RODENT TOXICOLOGY SECTION		
SUPERVISOR	Joseph M. Fasanella	A.A., AALAS L.A.T.
TECHNICIAN-IN-CHARGE	Thomas E. Jones	B.S., AALAS L.A.T.
DIET PREPARATION		
MANAGER	Jeffrey P. Lefrancois	B.S.
VETERINARIAN	Henry F. Bolte	D.V.M., Ph.D.
SUPERVISOR, CLINICAL LAB	Andrew Lewandowski	B.S.
QUALITY ASSURANCE & SCIENCE INFORMATION		
MANAGER	Craig M. Lamb	B.A.

Appendix F
A Seven Day Dietary Study
with UC54229 in Rats

Quality Assurance Statement

Listed below are dates that this study was inspected by the Quality Assurance Unit of Bio/dynamics, Inc. and the dates findings were reported to the Study Director and Management.

Date(s) of Inspection	Reported to Study Director	Reported to Management
6/8/83	6/9/83	6/9 & 6/10/83

Craig M. Lamb
Manager of Quality Assurance
and Science Information

6/10/83
Date

Item 440

HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180, U S A

FOUR-WEEK DIETARY STUDY IN RATS

UC-54229

FINAL REPORT

Submitted to

Union Carbide Agricultural Products Company, Inc.
Research Triangle Park, N.C.

October 25, 1984

SUMMARY

(6)

HAZLETON
LABORATORIES AMERICA, INC.

SPONSOR: Union Carbide Agricultural Product Company, Inc. DATE: October 25, 1984

MATERIAL: UC-54229

SUBJECT: FINAL REPORT
Four-Week Dietary Study in Rats
Project No. 400-659

SUMMARY

The test material, UC-54229, was fed to Sprague-Dawley rats for four weeks at dietary levels of 133, 237, 422, 750, or 1,330 ppm. The purpose of the study was to establish dose levels for a subsequent subchronic toxicity study.

Treatment of rats with UC-54229 produced dose-related effects on the incidence of clinical signs, behavior, polypnea, depressed weight gain, and increased food consumption. Plasma and brain acetylcholinesterase was significantly inhibited (inhibition greater than 25% of control value) in all treated male groups after four weeks. Plasma acetylcholinesterase in females appeared to be less sensitive than that of males, but female brain acetylcholinesterase was significantly inhibited at all treatment levels.

Body weights in both sexes were lower at termination in the higher dose levels. Absolute heart and liver weights were lower in the higher dose groups. The organ to body weight ratios were increased for brain, kidney, and testes in the higher dose groups for either or both sexes.

HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180, U S A

SUBJECT: Four-Week Dietary Study in Rats and
Project No. 400-659

We, the undersigned, hereby declare that the work was performed under our supervision, according to the procedures herein described.

Study Director:

WILLARD M. WEATHERHOLTZ, PH.D.
Life Sciences Division

Laboratory Supervision:

for GEORGE A. BURDOCK, PH.D.
Diplomate, American Board of Toxicology
Life Sciences Division

Clinical Pathology:

RICHARD D. ALSAKER, D.V.M., M.S.
Diplomate, American College of Veterinary Pathologists
Life Sciences Division

Report Preparation:

BARBARA L. LEARD, B.S.
Life Sciences Division

jc

HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180, U S A

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HAZLETON
LABORATORIES AMERICA, INC.

SPONSOR: Union Carbide Agricultural Product Company, Inc. DATE: October 25, 1984

MATERIAL: UC-54229

SUBJECT: FINAL REPORT
Four-Week Dietary Study in Rats
Project No. 400-659

SUMMARY

The test material, UC-54229, was fed to Sprague-Dawley rats for four weeks at dietary levels of 133, 237, 422, 750, or 1,330 ppm. The purpose of the study was to establish dose levels for a subsequent subchronic toxicity study.

Treatment of rats with UC-54229 produced dose-related effects on the incidence of clinical signs, behavior, polypnea, depressed weight gain, and increased food consumption. Plasma and brain acetylcholinesterase was significantly inhibited (inhibition greater than 25% of control value) in all treated male groups after four weeks. Plasma acetylcholinesterase in females appeared to be less sensitive than that of males, but female brain acetylcholinesterase was significantly inhibited at all treatment levels.

Body weights in both sexes were lower at termination in the higher dose levels. Absolute heart and liver weights were lower in the higher dose groups. The organ to body weight ratios were increased for brain, kidney, and testes in the higher dose groups for either or both sexes.

INTRODUCTION

The purpose of this study was to estimate the toxicity of an agricultural chemical, UC-54229, when fed daily to rats for four weeks and to develop dose levels for a subchronic study. Initiation was on January 20, 1983, and terminal necropsies were performed on February 21 and 22, 1983.

VEHICLES AND TEST MATERIAL

Purina Rodent Laboratory Chow® #5001 was the basal diet. The vehicles were corn oil and acetone.

The test material, UC-54229, a creamy white powder with lumps, was received from the sponsor and stored in the freezer. The material was 95.1% active, which was adjusted to 100% for purposes of diet preparation calculations. The test material was taken from the freezer when needed and placed in a desiccator to equilibrate to room temperature before opening and use.

The receipt dates and lot numbers for these materials are as follows:

Material	Lot Number	Receipt Date	Weeks used on Study
Acetone	KPLS	1-3-83	1-5[a]
Corn oil	80235	7-13-82	1-5
UC-54229	22-WYF-74 #1	9-22-82	1-5

[a]February 17, 1983 was the last day of Week 4, and terminal necropsies were performed on February 21 and 22, 1983. These last 5 days therefore are considered to be Week 5.

Information on the diet analysis was obtained from the sponsor and is presented as follows:

Lot Number	Sample Weight (kg)	Assay (% weight)	Standard Deviation	Water (% weight)
22-WYF-74-1	1.5	95.1	0.53	4.9

TEST ANIMALS

Sprague-Dawley rats (CD-Crl:CD(SD)BR) were chosen to be the test animals for this study because historically rats have been used in safety evaluation studies and are required by appropriate regulatory agencies. A total of 84 males and 83 females were received. All animals were received from Charles River Breeding Laboratories, Kingston, New York. The animals were acclimated to laboratory conditions for approximately four weeks prior to study initiation. During this time, the animals were examined for health status by a staff veterinarian. The initial body weight ranged from 264.6 to 358.6 g for the males and from 151.8 to 236.0 g for the females.

The animals were individually identified by a numbered ear tag, and were individually housed in elevated wire-mesh cages marked with the corresponding animal number. Food and tap water were available ad libitum. Food was withheld overnight prior to blood collection except when acetylcholinesterase inhibition was to be evaluated. Blood was taken for acetylcholinesterase activity measurement from animals maintained constantly on test diets. Results of routine food and water analyses are on file with the Department of Veterinary Medicine at

Hazleton Laboratories America, Inc. A 12-hour light/dark cycle was maintained daily. The room temperature and humidity were monitored daily.

METHODS

Groups and Dosage Levels

Prior to study initiation, 60 clinically acceptable rats of each sex were randomized via a computerized HLA randomization program and were assigned to the following groups:

Group	No. of Animals Males	No. of Animals Females	Dosage Levels (ppm)
1 (Control)	10	10	0
2	10	10	133
3	10	10	237
4	10	10	422
5	10	10	750
6	10	10	1,330

The unused animals were asphyxiated with CO_2.

Compound Preparation and Administration

Mixtures of the test material with commercial feed were made in the following manner. The test material was taken from the freezer and placed in a desiccator to thaw at room temperature. When thawed, the material was ground with a mortar and pestle, and an appropriate amount of the test material was dissolved in 100 mL of acetone by stirring in an automatic stirrer for approximately two minutes. When the test material had dissolved, 20 g of corn oil (or 1% of feed volume) were added to the mixture and stirred for one to two minutes.

The indicated amount of Purina Rodent Laboratory Chow® #5001 was mixed for one hour in a Hobart mixer with the test material/acetone/corn oil mixture. From this concentrated premix of 10,000 ppm, the appropriate dietary levels were mixed in the Hobart.

Test mixtures at the use concentrations were prepared fresh weekly. Samples of each concentration were taken once weekly and stored at Hazleton Laboratories America, Inc.

Observations and Records

All animals were observed for mortality and moribundity twice each day. Clinical signs (gross signs of toxic and/or pharmacologic effects) and body weights were recorded at initiation, weekly thereafter, and at termination. Food consumption was recorded weekly.

Clinical Pathology

Clinical pathology determinations were made as follows:

Interval	No. of Animals Males	No. of Animals Females	Groups	Parameters
Initial	10	10	-	Hematology, Serum Chemistry
	10	10	-	Acetylcholinesterase (Plasma, RBC, Brain)
Week 4	5	5	1,4,6	Hematology, Serum Chemistry
	5[a]	5[a]	All	Acetylcholinesterase (Plasma, RBC, Brain)

[a] The remaining 5 rats/sex in groups 2, 3 and 6, were necropsied only, and did not have actylcholinesterase activity evaluated.

The following parameters were evaluated:

Hematology

Total Leukocyte Count (WBC)
Erythrocyte Count (RBC)
Hematocrit (HCT)
Hemoglobin (HGB)
Platelet Count (PLATELET)
Leukocyte Differential Counts
Erythrocyte and Leukocyte Morphology

Clinical Chemistry

Urea Nitrogen (BUN)
Aspartate Aminotransferase (AST)
Glucose (GLUCOSE)
Total Protein (T PROT)

Cholinesterase

Plasma (PCHE-COL)
Erythrocyte (RCHE-COL)
Brain (BCHE-COL)

The animals were fasted overnight before the hematology and clinical chemistry samples were collected; however, all acetylcholinesterase determinations were made on non-fasted animals. All blood samples were collected via orbital sinus puncture. The brain samples for the brain acetylcholinesterase determinations were collected immediately after each animal had been sacrificed. References for the clinical pathology methods are presented in Appendix 5.

Sacrifice and Necropsy

All surviving animals were sacrificed after four weeks of treatment. Sacrifice was by exsanguination under sodium pentobarbital anesthesia. The rats were necropsied by appropriately trained personnel under procedures supervised by board-certified pathologists. Observations were recorded. Necropsies were also performed on all animals that died during the course of the study.

Organ Weights

After careful dissection and trimming of fat and other contiguous tissue in a uniform manner, the following organs from each animal sacrificed at termination were weighed, and organ/body weight ratios were determined:

Before Fixation	After Fixation
Brain	Ovaries
Heart	
Liver	
Kidneys	
Testes with epididymides	

Tissue Preservation

The following tissues from each animal were preserved in 10% neutral buffered formalin:

Brain	Kidneys
Pituitary	Adrenals
Spinal cord (thoracic, lumbar)	Stomach
Eyes	Pancreas
Salivary gland (mandibular)	Cecum, colon
Thyroid	Duodenum, jejunum, ileum
Parathyroids	Mesenteric lymph nodes
Thymus	Urinary bladder
Trachea	Testes with epididymides
Esophagus	Prostate
Lungs	Ovaries
Heart	Uterus
Liver	Bone (femur)
Spleen	Bone marrow (sternum)
	Nerve muscle (skeletal)
	Lesions (if present)

Statistical Analyses

Absolute body weights, total food consumption, clinical pathology data (except leukocyte differentials, erythrocyte morphology, and urinalysis), and organ weight data of the control group were compared

statistically against the data of the compound-treated groups of the same sex. Absolute body weights were evaluated at initiation and at Week 4; and total food consumption was evaluated from initiation through Week 4.

Analyses of the above data were performed in the following order. Levene's test for homogeneity of variances (Levene, 1960; Draper and Hunter, 1969) was performed and if the variances proved to be homogeneous, the data were analyzed by one-way classification analysis of variance (ANOVA) (Winer, 1971). If the variances proved to be heterogeneous, a series of transformations was performed until variance homogeneity was achieved. These transformations were: $\log_{10}$, square (X^2), square root ($X^{1/2}$), reciprocal (1/X), angular (arcsine $X^{1/2}$), and rank, in that order. If rank transformation was ineffective in removing variance heterogeneity, ANOVA of ranked data was completed. If ANOVA of untransformed or transformed data was significant, Dunnett's t-test (Dunnett, 1955 and 1964) was used for control vs. compound-treated group mean comparisons. If ANOVA was not significant, the analysis was complete.

Data transformations are designated throughout this report as follows:

A = Data analyzed following $\log_{10}$ transformation.

B = Data analyzed following square (X^2) transformation.

C = Data analyzed following square root ($X^{1/2}$) transformation.

D = Data analyzed following reciprocal (1/X) transformation.

E = Data analyzed following angular (arcsine $X^{1/2}$) transformation.

F = Data analyzed following rank transformation.

For mean tables, the above indications followed by the letters M, F, or B indicate the transformation occurred for either the Male, Female, or Both male and female groups.

Tests for homogeneity of variances and ANOVA were evaluated at the 5.0% one-tailed probability level. Control vs. compound-treated group mean comparisons of the above data were evaluated at the 5.0% two-tailed probability level. In addition to the above data, cumulative survival values were analyzed using the National Cancer Institute Package (Thomas, Breslow, and Gart, 1977). Trend analysis of survival was evaluated at the 5.0% one-tailed probability level while control vs. compound-treated group comparisons of survival were evaluated at the 5.0% two-tailed level.

Statistical references are appended to this report, and statistically significant differences, as indicated by the aforementioned tests, are designated throughout this report by the term "significant" and/or as follows:

S+ = Significantly higher than the control value.

S- = Significantly lower than the control value.

Specimen, Raw Data, and Final Report Storage

All specimens, raw data, and the final report are stored in the archives of Hazleton Laboratories America, Inc.

RESULTS

Mortality and Clinical Signs

Cumulative survival data are presented in Table 1. The only unscheduled deaths occurred during Week 4, when five animals were found dead (one female from the control group, one female from Group 4, one male and one female from Group 5, and one male from Group 6).

No significant differences were detected in the cumulative survival analysis.

Treatment-related clinical signs noted during this study included a hunched position, a rough haircoat, and hyperactivity during Weeks 2-4, primarily in the two highest dose groups of both sexes. The high-level dose group of both sexes also had an increased incidence of polypnea during Week 3.

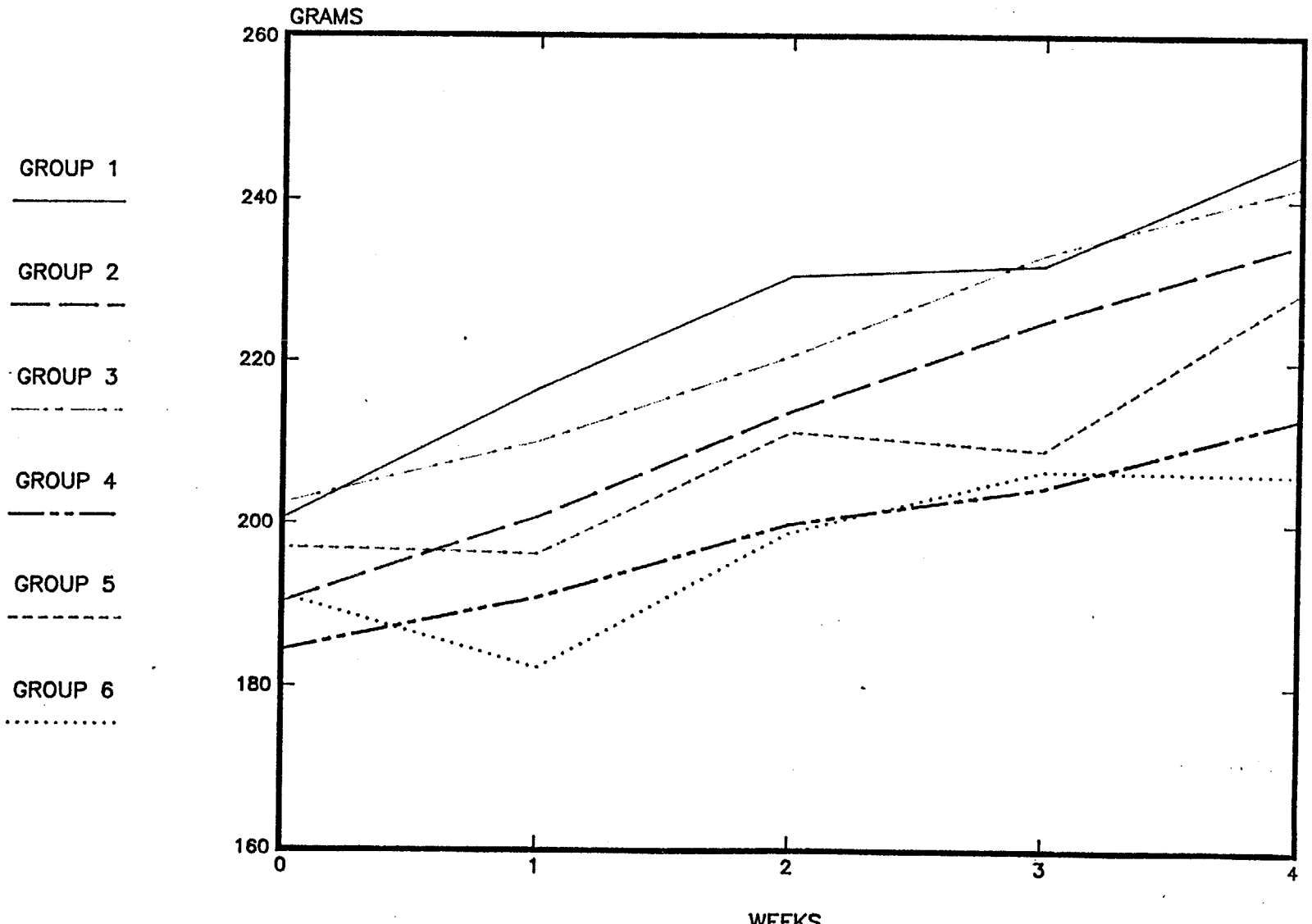
Body Weights and Food Consumption

Weekly mean body weights and food consumption values are presented in Tables 1 and 2, respectively. Individual body weights and food consumption values are presented in Appendices 1 and 2, respectively. Weekly mean compound consumption is presented in Table 3.

The mean body weight of Group 6 males and females was lower at Week 1 than at initiation. Statistical analysis revealed a significantly depressed group mean body weight at Week 4 for males in Groups 4, 5, and 6, and females in Groups 4 and 6 when compared to the control animals.

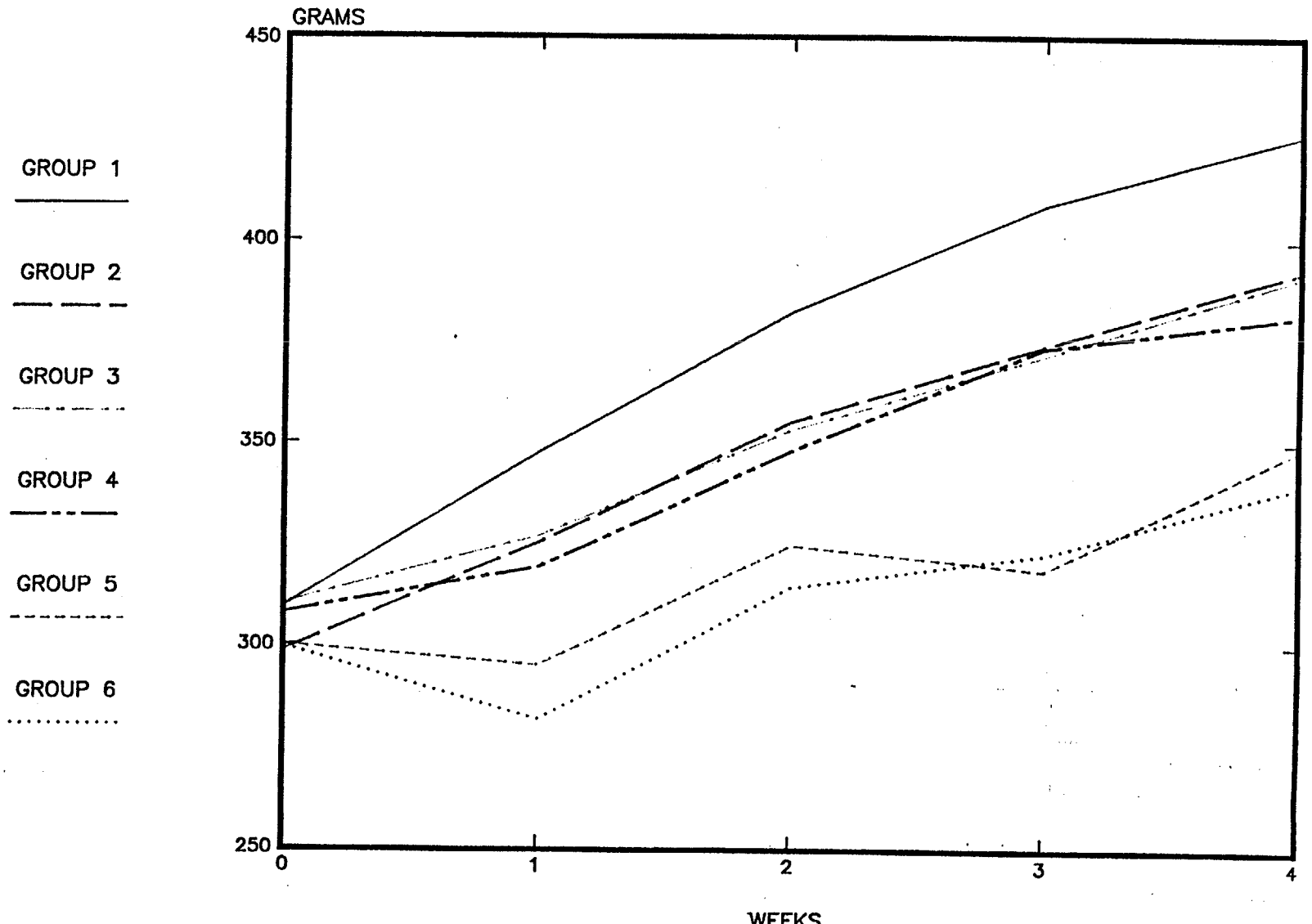
MEAN BODY WEIGHTS

FEMALES 400–659



MEAN BODY WEIGHTS

MALES 400–659



Statistical analysis of the total food consumption through Week 4 revealed a significantly higher value for the females in Groups 3, 4, 5, and 6.

Mean compound consumption generally decreased from week to week for all groups.

Clinical Pathology

Mean hematology and clinical chemistry data are presented in Tables 4 and 5, respectively. These data are presented individually in Appendices 3 and 4, respectively. The percent inhibition of acetylcholinesterase values is summarized in Text table 1.

There were no significant differences detected in the hematology data for male or female treatment groups when compared to their respective control group.

Among the clinical chemistry parameters evaluated at Week 4, blood urea nitrogen and aspartate aminotransferase values were significantly higher for the females in Group 4 when compared to the females in the control group. No significant differences were found when values for males in the treated group were compared to the values from the control group.

Plasma and brain acetylcholinesterase values for males in all treated groups at Week 4 were significantly lower than the values of males in the control group. In addition, brain acetylcholinesterase

values for the females in Groups 3, 4, and 6 were also significantly lower than the control values. The biologically significant values for the acetylcholinesterase data are those that are more than 25% inhibited when compared to the control. Using this criterion, plasma and brain acetylcholinesterase for the males in the treated groups and brain acetylcholinesterase values for the females in the treated groups were biologically as well as statistically significant. These values are presented in the following text table.

Gross Pathology

Summaries of gross pathology findings are presented in Tables 6A (animals sacrificed at Week 4) and 6B (animals with unscheduled deaths).

The incidence of gross necropsy finding from animals sacrificed at termination and from the five animals that were found dead were incidental and did not appear to be related to treatment.

Organ Weights

Mean organ weight and organ to terminal body weight ratio data are presented in Table 7. Mean terminal body weights for males in Groups 5 and 6 and females in Groups 4, 5, and 6 were significantly lower than those of the control.

Among the terminally sacrificed animals, mean absolute liver weights for the males in Groups 5 and 6 and the females in Group 6, and the mean absolute heart weight for males in Group 6, were significantly lower than those of the control group.

The following organ to terminal body weight ratios were significantly higher than those of the control group.

Organ	Group	Sex
Brain	2, 4, 5, 6	Female
	5, 6	Male
Kidney	5, 6	Female
Heart	4, 5	Female
Testes	5, 6	Male

CONCLUSION

Feeding UC-54229 to Sprague-Dawley rats for four weeks provided preliminary data useful in setting dose levels for a subchronic toxicity study. The most sensitive parameter measured was brain acetylcholinesterase, as all treated groups showed significant (greater than 25%) depression. Other parameters, including mortality, body weight, organ weights, and organ-to-body weight ratios, were also affected.

Text Table 1

Percent Inhibition of Cholinesterase Values

Four-Week Dietary Study of UC-54229 in Rats

Group and Dose Level	% Inhibition Relative to Control Values		
	PCHE-COL	RCHE-COL	BCHE-COL
	Males		
2 133 ppm	33	10	43
3 237 ppm	29	2	51
4 422 ppm	48	6	51
5 750 ppm	43	8	56
6 1330 ppm	48	10	60
	Females		
2 133 ppm	13	0	28
3 237 ppm	34	0	34
4 422 ppm	11	0	38
5 750 ppm	26	0	32
6 1330 ppm	17	0	54

NOTE: All samples were obtained after four weeks of compound administration. All values at or below are presented as zero.

Key to Table 1

S- = Value is significantly lower than control when evaluated at the week indicated.

A = Data analyzed following Log_{10} transformation.

F = Data analyzed following rank transformation.

f = Growth rate analyzed following rank transformation.

Table 1
Mean Body Weights and Standard Deviations
Four-Week Dietary Study of UC-54229 in Rats

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** MALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	133.000	237.000	422.000	750.000
WEEKS ON STUDY						
START	MEAN (GRAMS)	309.6	298.7	310.2	307.9	300.0
	S.D.	21.08	25.29	19.10	19.77	18.97
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
1	MEAN (GRAMS)	347.5	325.1	326.8	319.0	294.9
	S.D.	23.62	30.28	20.26	20.65	24.17
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
2	MEAN (GRAMS)	382.3	355.1	353.1	347.9	324.5
	S.D.	27.40	34.76	26.35	23.73	18.60
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
3	MEAN (GRAMS)	408.9	374.0	371.6	373.5	318.3
	S.D.	32.31	41.13	26.55	29.92	59.38
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
4	MEAN (GRAMS)	426.3	392.5	391.2	381.7 S-	348.3 S-
	S.D.	32.80	36.49	31.81	33.20	40.63
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	9/ 10

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** MALES *****

GROUP		6
LEVEL (PPM)		1330.000
WEEKS ON STUDY		
START	MEAN (GRAMS)	299.5
	S.D.	18.22
	ADJUSTED SURVIVAL	10/ 10
1	MEAN (GRAMS)	281.6
	S.D.	10.99
	ADJUSTED SURVIVAL	10/ 10
2	MEAN (GRAMS)	314.1
	S.D.	17.09
	ADJUSTED SURVIVAL	10/ 10
3	MEAN (GRAMS)	322.3
	S.D.	43.67
	ADJUSTED SURVIVAL	10/ 10
4	MEAN (GRAMS)	339.5 S-
	S.D.	17.26
	ADJUSTED SURVIVAL	9/ 10

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	133.000	237.000	422.000	750.000
WEEKS ON STUDY						
	MEAN (GRAMS)	200.6	190.2	202.5	184.4	196.9
START	S.D.	12.94	25.33	10.78	12.44	10.61
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)[F]	216.5	200.7	210.1	190.7	196.1
1	S.D.	13.80	28.06	13.57	13.28	15.07
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	230.5	213.8	220.6	199.9	211.3
2	S.D.	14.13	29.35	18.12	17.92	15.35
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	231.9	224.9	233.2	204.5	209.1
3	S.D.	29.64	30.11	19.76	24.32	29.63
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)[A,f]	245.7	234.6	241.8	213.1[S-]	228.5
4	S.D.	17.87	32.83	23.16	19.05	17.57
	ADJUSTED SURVIVAL	9/ 10	10/ 10	10/ 10	9/ 10	9/ 10

STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		6
LEVEL (PPM)		1330.000
WEEKS ON STUDY		
START	MEAN (GRAMS)	190.9
	S.D.	12.43
	ADJUSTED SURVIVAL	10/ 10
1	MEAN (GRAMS)	182.1
	S.D.	13.16
	ADJUSTED SURVIVAL	10/ 10
2	MEAN (GRAMS)	198.8
	S.D.	15.30
	ADJUSTED SURVIVAL	10/ 10
3	MEAN (GRAMS)	206.6
	S.D.	11.28
	ADJUSTED SURVIVAL	10/ 10
4	MEAN (GRAMS)[A,f]	206.2[S-]
	S.D.	12.83
	ADJUSTED SURVIVAL	10/ 10

Table 2
Mean Food Consumption and Standard Deviations
Four-Week Dietary Study of UC-54229 in Rats

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** MALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	133.000	237.000	422.000	750.000
WEEKS ON STUDY						
	MEAN (GM/WEEK)	.0	.0	.0	.0	.0
START	S.D.	.00	.00	.00	.00	.00
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	204.8	193.3	208.6	233.8	220.2
1	S.D.	12.66	34.67	20.73	29.01	34.87
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	195.7	192.7	219.5	214.3	205.0
2	S.D.	18.83	23.12	29.52	16.71	28.87
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	207.6	190.1	203.1	213.8	198.8
3	S.D.	17.63	22.54	25.13	17.08	65.52
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	193.3	193.4	215.7	207.0	199.6
4	S.D.	20.63	20.63	28.69	28.71	20.13
	SAMPLE SIZE	10	10	10	10	9

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** MALES *****

GROUP		6
LEVEL (PPM)		1330.000
WEEKS ON STUDY		
START	MEAN (GM/WEEK)	.0
	S.D.	.00
	SAMPLE SIZE	10
1	MEAN (GM/WEEK)	206.1
	S.D.	47.73
	SAMPLE SIZE	10
2	MEAN (GM/WEEK)	189.5
	S.D.	12.91
	SAMPLE SIZE	10
3	MEAN (GM/WEEK)	197.7
	S.D.	28.38
	SAMPLE SIZE	10
4	MEAN (GM/WEEK)	166.3
	S.D.	19.82
	SAMPLE SIZE	9

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	133.000	237.000	422.000	750.000
WEEKS ON STUDY						
	MEAN (GM/WEEK)	.0	.0	.0	.0	.0
START	S.D.	.00	.00	.00	.00	.00
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	149.3	174.4	188.5	199.6	222.1
1	S.D.	16.52	39.97	44.64	42.03	41.09
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	164.6	175.9	201.2	218.8	194.2
2	S.D.	41.06	40.62	44.68	50.68	40.46
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	159.6	173.7	213.3	199.8	204.3
3	S.D.	41.41	42.94	38.13	70.00	46.52
	SAMPLE SIZE	10	10	10	10	10
	MEAN (GM/WEEK)	136.6	152.2	193.8 S+	180.3 S+	210.6 S+
4	S.D.	18.84	36.62	45.59	63.70	46.89
	SAMPLE SIZE	9	10	10	9	9

STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		6
LEVEL (PPM)		1330.000
WEEKS ON STUDY		
START	MEAN (GM/WEEK)	.0
	S.D.	.00
	SAMPLE SIZE	10
1	MEAN (GM/WEEK)	243.8
	S.D.	9.05
	SAMPLE SIZE	10
2	MEAN (GM/WEEK)	177.4
	S.D.	36.70
	SAMPLE SIZE	10
3	MEAN (GM/WEEK)	202.7
	S.D.	46.48
	SAMPLE SIZE	10
4	MEAN (GM/WEEK)	178.1 St
	S.D.	46.80
	SAMPLE SIZE	10

Table 3
Mean Compound Consumption and Standard Deviations
Four-Week Dietary Study of UC-54229 in Rats

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** MALES *****

GROUP	1	2	3	4	5
LEVEL (PPM)	.000	133.000	237.000	422.000	750.000
WEEKS ON STUDY					
START MEAN (MG/DAY/KG)	.00	.00	.00	.00	.00
1 MEAN (MG/DAY/KG)	.00	11.30	21.61	44.19	80.01
2 MEAN (MG/DAY/KG)	.00	10.31	21.05	37.15	67.69
3 MEAN (MG/DAY/KG)	.00	9.66	18.51	34.50	66.90
4 MEAN (MG/DAY/KG)	.00	9.36	18.67	32.69	61.41

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** FEMALES *****

GROUP	1	2	3	4	5
LEVEL (PPM)	.000	133.000	237.000	422.000	750.00
WEEKS ON STUDY					
START MEAN (MG/DAY/KG)	.00	.00	.00	.00	.00
1 MEAN (MG/DAY/KG)	.00	16.51	30.38	63.11	121.34
2 MEAN (MG/DAY/KG)	.00	15.63	30.88	65.98	98.49
3 MEAN (MG/DAY/KG)	.00	14.67	30.97	58.90	104.71
4 MEAN (MG/DAY/KG)	.00	12.33	27.14	51.01	98.77

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** MALES *****

GROUP	6
LEVEL (PPM)	1330.000

WEEKS ON STUDY		
START	MEAN (MG/DAY/KG)	.00
1	MEAN (MG/DAY/KG)	139.06
2	MEAN (MG/DAY/KG)	114.64
3	MEAN (MG/DAY/KG)	116.53
4	MEAN (MG/DAY/KG)	93.07

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STUDY TITLE FOUR-WEK DIETARY STUDY IN RATS
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** FEMALES *****

GROUP	6
LEVEL (PPM)	1330.000

WEEKS ON STUDY		
START	MEAN (MG/DAY/KG)	.00
1	MEAN (MG/DAY/KG)	254.34
2	MEAN (MG/DAY/KG)	169.50
3	MEAN (MG/DAY/KG)	186.42
4	MEAN (MG/DAY/KG)	164.14

Explanation of Footnotes for Tables 4 and 5

BF = Female data analyzed following square (X^2) transformation.

BM = Male data analyzed following square (X^2) transformation.

FF = Female data analyzed following rank transformation.

FM = Male data analyzed following rank transformation.

Table 4
Mean Clinical Hematology Values with Standard Deviations
Four-Week Dietary Study of UC-54229 in Rats

Interval	Group and Dose Level		WBC[BM] (th/μL)	RBC (mi/μL)	HGB[FF] (gm/dl)	HCT (%)	PLATELET (th/μL)
				Males			
Initial	Untreated	Mean	12.1	8.03	17.1	51.3	1049
		S.D.	2.03	0.403	0.57	1.45	89.8
		N	10	10	10	10	10
Week 4	1 Control	Mean	14.4	8.45	17.0	49.0	1137
		S.D.	1.910	0.210	.43	1.91	138.5
		N	5	5	5	5	5
	4 422 ppm	Mean	12.3	8.65	17.1	50.9	1016
		S.D.	4.18	0.367	0.79	1.79	101.9
		N	5	5	5	5	5
	6 1330 ppm	Mean	13.3	8.44	16.6	49.5	937
		S.D.	2.28	0.395	0.44	1.14	141.8
		N	5	5	5	5	5
				Females			
Initial	Untreated	Mean	10.8	7.87	18.0	46.7	1084
		S.D.	2.85	0.801	0.98	5.14	98.5
		N	9	9	9	9	9
Week 4	1 Control	Mean	11.6	8.62	17.1	49.2	1117
		S.D.	0.59	0.407	0.67	3.69	121.5
		N	5	5	5	5	5
	4 422 ppm	Mean	10.2	8.86	15.2	51.3	1158
		S.D.	1.08	0.327	5.28	1.55	127.3
		N	4	4	4	4	4
	6 1330 ppm	Mean	9.2	8.65	17.2	49.6	1179
		S.D.	2.86	0.475	0.54	1.18	193.9
		N	5	5	5	5	5

Table 5A
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Rats
Males

Interval	Group and Dose Level		PCHE-COL (mcm/ml)	RCHE-COL (mcm/ml)	BCHE-COL (mcm/ml)
Initial	Untreated	Mean	2.4	4.8	52.7
		S.D.	0.36	0.41	2.63
		N	10	10	10
Week 4	1 Control	Mean	2.1	5.0	51.2
		S.D.	0.16	0.39	1.33
		N	5	5	5
	2 133 ppm	Mean	1.4S-	4.5	29.0S-
		S.D.	0.24	0.34	4.53
		N	5	5	5
	3 237 ppm	Mean	1.5S-	4.9	25.2S-
		S.D.	0.19	0.69	4.76
		N	5	5	5
	4 422 ppm	Mean	1.1S-	4.7	25.2S-
		S.D.	0.09	0.29	5.89
		N	5	5	5
	5 750 ppm	Mean	1.2S-	4.6	22.6S-
		S.D.	0.28	0.42	3.30
		N	5	5	5
	6 1330 ppm	Mean	1.1S-	4.5	20.4S-
		S.D.	0.16	0.38	5.98
		N	5	5	5

Table 5A - Continued
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Rats
Females

	Group and Dose Level		PCHE-COL (mcm/ml)	RCHE-COL (mcm/ml)	BCHE-COL[F] (mcm/ml)
Initial	Untreated	Mean	6.8	4.6	53.2
		S.D.	1.60	0.53	2.11
		N	8	8	8
Week 4	1 Control	Mean	8.2	4.7	50.0
		S.D.	2.40	0.66	2.05
		N	5	5	5
	2 133 ppm	Mean	7.1	5.1	35.8
		S.D.	1.78	0.51	4.40
		N	5	5	5
	3 237 ppm	Mean	5.4	4.8	33.2[S-]
		S.D.	0.74	0.23	2.90
		N	5	5	5
	4 422 ppm	Mean	7.3	4.9	31.2[S-]
		S.D.	2.32	0.47	4.20
		N	5	5	5
	5 750 ppm	Mean	6.1	4.7	34.2
		S.D.	1.40	0.53	10.03
		N	5	5	5
	6 1330 ppm	Mean	6.8	4.7	23.0[S-]
		S.D.	2.44	0.46	5.83
		N	5	5	5

[F] Analyzed following rank transformation.

Table 5A - Continued
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Rats
Males

Interval	Group and Dose Level		T PROT (gm/dl)	BUN (mg/dl)	GLUCOSE (mg/dl)	AST (IU/l)
Initial	Untreated	Mean	5.8	13.8	90	77
		S.D.	0.13	3.26	6.0	8.0
		N	10	10	10	10
Week 4	1 Control	Mean	6.0	14.8	89	100
		S.D.	0.19	2.05	10.6	13.8
		N	5	5	5	5
	4 422 ppm	Mean	6.1	17.4	78	107
		S.D.	0.27	2.30	6.2	19.2
		N	5	5	5	5
	6 1330 ppm	Mean	6.0	16.6	80	85
		S.D.	0.20	2.88	4.0	4.6
		N	5	5	5	5
			Females			
Initial	Untreated	Mean	6.0	14.2	91	73
		S.D.	0.35	2.33	7.6	9.6
		N	9	9	9	9
Week 4	1 Control	Mean	6.2	15.3	79	71
		S.D.	0.25	1.71	6.8	5.9
		N	4	4	4	4
	4 422 ppm	Mean	6.1	20.5 S+	82	98 S+
		S.D.	0.24	3.00	5.7	3.1
		N	4	4	4	4
	6 1330 ppm	Mean	6.6	18.2	91	74
		S.D.	0.26	2.28	7.2	11.5
		N	5	5	5	5

Table 6A
Gross Pathology Observations Incidence Summary
Animals Sacrificed at Termination
Four-Week Dietary Study of UC-54229 in Rats

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN RATS

GROSS PATHOLOGY INCIDENCE SUMMARY

PRINTED: 12-MAR-84
PAGE: 1

STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T,1;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE	--- NUMBER-OF-ANIMALS-AFFECTED ---											
SEX:	MALE						FEMALE					
GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
NUMBER:	10	10	10	10	9	9	9	10	10	9	9	10
** TOP OF LIST **												
LIVER (LI) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
DARK	0	0	0	0	0	0	0	0	0	0	0	0
SPLEEN (SP) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
SMALL	0	0	0	0	0	0	0	0	0	0	0	0
RAISED AREA(S)	0	0	0	0	0	1	0	0	0	0	0	0
STOMACH (ST) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
MUCOSA,DARK	0	0	0	0	0	0	0	0	0	0	0	0
MUCOSA,DARK FILMY MATERIAL	0	0	0	0	0	0	0	0	0	0	0	0
ADRENALS (AD) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
DARK	0	0	0	0	0	0	0	0	0	0	0	0
BRAIN (BR) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
PROMINENT VESSELS	0	0	0	0	0	0	0	0	0	0	0	0
MENINGES,PROMINENT VESSELS	0	0	0	0	0	0	0	0	0	0	0	0
PERITONEAL CAVIT (PC) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
ADIPOSE TISS.,SMALL MASS(ES)	0	0	0	0	0	0	0	0	1	0	0	0
LUNG (LU) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
DARK FOCUS(I)/AREA(S)	0	1	0	0	1	0	0	0	0	0	0	0
INDENTATION(S)/DEPRESSION(S)	0	0	0	0	0	1	0	0	0	0	0	0
KIDNEYS (KD) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
DARK	0	0	0	0	0	0	0	0	0	0	0	0
DILATED PELVIS(ES)	0	0	0	1	0	0	1	0	0	0	1	0
FLUID FILLED	0	0	0	0	0	0	1	0	0	0	0	0
UTERUS (UT) NUMBER EXAMINED:	0	0	0	0	0	0	9	10	10	9	9	10
DISTENDED	0	0	0	0	0	0	1	1	2	0	4	1
INTRALUMINAL CLEAR FLUID	0	0	0	0	0	0	1	1	2	0	4	1
CRANIAL CAVITY (CC) NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN RATS

GROSS PATHOLOGY INCIDENCE SUMMARY

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STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH:T,1;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER-OF-ANIMALS-AFFECTED ---											
	SEX:	MALE						FEMALE					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	10	10	10	10	9	9	9	10	10	9	9	10
OVARIES (OV)	NUMBER EXAMINED:	0	0	0	0	0	0	9	10	10	9	9	10
CYST(S)		0	0	0	0	0	0	0	0	0	1	1	0
TESTES W/EPIDID (TP)	NUMBER EXAMINED:	10	10	10	10	9	9	0	0	0	0	0	0
UNEQUAL SIZE		0	1	0	0	0	0	0	0	0	0	0	0
SOFT (FLACCID)		0	1	0	0	0	0	0	0	0	0	0	0
DARK/PALE MATERIAL		0	1	0	0	0	0	0	0	0	0	0	0
CECUM (CE)	NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
WALLS REDDENED		0	0	0	1	0	0	0	0	0	0	0	0
EYE(S) (EY)	NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
DARK INTRAOCULAR MATERIAL		0	0	0	1	0	0	0	0	0	0	0	0
CLOUDY		0	0	0	1	0	0	0	0	0	0	0	0
MESENTERIC L.N. (MS)	NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
ENLARGED		0	0	0	1	0	0	0	0	0	0	0	0
DARK		0	0	0	1	0	0	0	0	0	0	0	0
SALIVARY GLD.(S) (SG)	NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
SKIN (SK)	NUMBER EXAMINED:	10	10	10	10	9	9	9	10	10	9	9	10
SORE(S)		0	0	0	1	0	2	0	0	0	0	0	0

** END OF LIST **

Table 6B
Gross Pathology Observations Incidence Summary
Animals with Unscheduled Deaths
Four-Week Dietary Study of UC-54229 in Rats

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR WEEK DIETARY STUDY IN RATS

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GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=D,M,A;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER OF ANIMALS AFFECTED ---											
	SEX:	MALE						FEMALE					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	0	0	0	0	1	1	1	0	0	1	1	0
** TOP OF LIST **													
LIVER (LI)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
DARK		0	0	0	0	0	1	0	0	0	0	0	0
SPLEEN (SP)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
SMALL		0	0	0	0	0	0	1	0	0	0	0	0
RAISED AREA(S)		0	0	0	0	0	0	0	0	0	0	0	0
STOMACH (ST)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
MUCOSA,DARK		0	0	0	0	0	1	1	0	0	0	0	0
MUCOSA,DARK FILMY MATERIAL		0	0	0	0	0	1	0	0	0	0	0	0
ADRENALS (AD)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
DARK		0	0	0	0	0	0	1	0	0	0	0	0
BRAIN (BR)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
PROMINENT VESSELS		0	0	0	0	1	1	0	0	0	1	0	0
MENINGES,PROMINENT VESSELS		0	0	0	0	0	1	0	0	0	1	0	0
PERITONEAL CAVIT (PC)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
ADIPOSE TISS.,SMALL MASS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
LUNG (LU)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
DARK FOCUS(I)/AREA(S)		0	0	0	0	1	1	0	0	0	0	1	0
INDENTATION(S)/DEPRESSION(S)		0	0	0	0	0	0	0	0	0	0	0	0
KIDNEYS (KD)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
DARK		0	0	0	0	0	1	0	0	0	0	0	0
DILATED PELVIS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
FLUID FILLED		0	0	0	0	0	0	0	0	0	0	0	0
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0	0	0	1	0	0	1	1	0
DISTENDED		0	0	0	0	0	0	0	0	0	0	0	0
INTRALUMINAL CLEAR FLUID		0	0	0	0	0	0	0	0	0	0	0	0
CRANIAL CAVITY (CC)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN RATS

GROSS PATHOLOGY INCIDENCE SUMMARY

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STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=D,M,A;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER-OF-ANIMALS-AFFECTED ---											
	SEX:	MALE						FEMALE					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	0	0	0	0	1	1	1	0	0	1	1	0
OVARIES (OV)	NUMBER EXAMINED:	0	0	0	0	0	0	1	0	0	1	1	0
CYST(S)		0	0	0	0	0	0	0	0	0	0	0	0
TESTES W/EPIDID (TP)	NUMBER EXAMINED:	0	0	0	0	1	1	0	0	0	0	0	0
UNEQUAL SIZE		0	0	0	0	0	0	0	0	0	0	0	0
SOFT (FLACCID)		0	0	0	0	0	0	0	0	0	0	0	0
DARK/PALE MATERIAL		0	0	0	0	0	0	0	0	0	0	0	0
CECUM (CE)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
WALLS REDDENED		0	0	0	0	0	0	0	0	0	0	0	0
EYE(S) (EY)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
DARK INTRAOCULAR MATERIAL		0	0	0	0	0	0	0	0	0	0	0	0
CLOUDY		0	0	0	0	0	0	0	0	0	0	0	0
MESENTERIC L.N. (MS)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	0
DARK		0	0	0	0	0	0	0	0	0	0	0	0
SALIVARY GLD.(S) (SG)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
SKIN (SK)	NUMBER EXAMINED:	0	0	0	0	1	1	1	0	0	1	1	0
SORE(S)		0	0	0	0	0	0	0	0	0	0	0	0

** END OF LIST **

Explanation of Footnotes for Table 7

BF = Female data analyzed following square (X^2) transformation.

FF = Female data analyzed following rank transformation.

FM = Male data analyzed following rank transformation.

Table 7
Absolute Organ Weight Means and
Organ to Terminal Body Weight Ratio Means
Four-Week Dietary Study of UC-54229 in Rats
Fasted and Non-fasted Animals

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN RATS

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MEAN ABSOLUTE ORGAN WEIGHTS (g)

STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	10	10	10	10	9	9	9	10	10	9	9	10
>>> BR - BRAIN <<<												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	1.982	1.999	2.007	2.073	2.070	2.008	1.891	1.915	1.889	1.863	1.914	1.885
STAND DEV:	.084	.065	.077	.189	.110	.115	.062	.135	.062	.068	.075	.065
>>> TP - TESTES W/EPIDID <<<												
# IN GRP.:	10	10	10	10	9	9	0	0	0	0	0	0
MEAN:	4.441	4.660	4.454	4.598	4.571	4.319						
STAND DEV:	.336	.379	.188	.408	.279	.438						
FM >>> KD - KIDNEYS <<< BF												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	3.256	3.239	3.262	3.315	2.945	2.969	1.891	1.907	2.055	1.759	1.977	1.905
STAND DEV:	.350	.596	.417	.281	.220	.289	.194	.298	.136	.287	.258	.137
>>> HT - HEART <<< FF												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	1.278	1.312	1.250	1.226	1.230	1.085 S-	.793	.795	.805	.814	.832	.757
STAND DEV:	.096	.213	.142	.140	.140	.131	.055	.084	.079	.173	.175	.068
>>> LI - LIVER <<<												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	16.43	15.62	15.13	14.45	12.84 S-	12.21 S-	9.57	9.06	9.39	8.05	8.21	7.98 S-
STAND DEV:	2.08	1.88	1.79	1.98	1.73	.88	.85	1.58	1.42	.90	1.88	.85
>>> OV - OVARIES <<<												
# IN GRP.:	0	0	0	0	0	0	9	10	10	9	9	10
MEAN:							.1174	.1127	.1193	.1110	.1118	.1066
STAND DEV:							.0114	.0204	.0234	.0170	.0134	.0196
TERMINAL BODY WEIGHT												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	441.1	410.6	411.4	405.6	356.8 S-	350.8 S-	258.1	241.0	251.3	226.4 S-	227.1 S-	220.2 S-
STAND DEV:	26.92	44.70	32.21	36.04	55.51	36.57	16.82	27.29	24.68	17.23	31.33	13.57

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN RATS

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MEAN ORGAN/TERMINAL BODY WEIGHT RATIOS (%)

STUDY NUMBER: 400659

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	10	10	10	10	9	9	9	10	10	9	9	10
))) BR - BRAIN (((FF												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	.4505	.4906	.4905	.5129	.5922 S+	.5787 S+	.7348	.8003 S+	.7579	.8266 S+	.8590 S+	.8580 S+
STAND DEV:	.0268	.0408	.0414	.0435	.0960	.0773	.0395	.0679	.0761	.0581	.1415	.0457
))) TP - TESTES W/EPIDID (((												
# IN GRP.:	10	10	10	10	9	9	0	0	0	0	0	0
MEAN:	1.0074	1.1413	1.0888	1.1390	1.3085 S+	1.2395 S+						
STAND DEV:	.0614	.1042	.0997	.1136	.2213	.1495						
))) KD - KIDNEYS (((												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	.7397	.7851	.7927	.8184	.8450	.8573	.7337	.7934	.8222	.7757	.8722 S+	.8658 S+
STAND DEV:	.0841	.0829	.0791	.0346	.1624	.1511	.0686	.1021	.0699	.1005	.0329	.0453
FM))) HT - HEART (((												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	.2899	.3203	.3041	.3037	.3555	.3109	.3076	.3331	.3211	.3577 S+	.3655 S+	.3445
STAND DEV:	.0167	.0466	.0276	.0388	.0940	.0358	.0175	.0468	.0234	.0554	.0509	.0338
))) LI - LIVER (((FF												
# IN GRP.:	10	10	10	10	9	9	9	10	10	9	9	10
MEAN:	3.721	3.807	3.668	3.563	3.644	3.508	3.705	3.758	3.722	3.550	3.579	3.619
STAND DEV:	.387	.201	.193	.342	.512	.398	.161	.482	.253	.170	.481	.265
))) OV - OVARIES (((												
# IN GRP.:	0	0	0	0	0	0	9	10	10	9	9	10
MEAN:							.0456	.0469	.0475	.0489	.0500	.0483
STAND DEV:							.0047	.0080	.0076	.0044	.0085	.0094

Appendix 1
Individual Body Weights (grams)
Four-Week Dietary Study of UC-54229 in Rats

APPENDIX - 1

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400659

KEY TO SYMBOLS: * DEAD ANIMAL

GROUP 1 - CONTROL

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20516	299.4	335.6	380.4	403.7	436.2	
20517	296.7	346.6	371.8	398.5	419.6	
20518	316.3	340.9	370.0	382.6	407.3	
20519	341.9	385.8	428.9	465.2	492.2	
20520	297.2	331.5	361.7	378.9	403.6	
20521	299.7	339.7	375.2	401.9	411.5	
20522	294.1	325.3	358.4	380.1	388.6	
20523	351.5	395.5	436.6	468.8	475.2	
20524	289.8	332.4	374.3	404.3	414.5	
20525	309.6	342.2	366.1	405.3	414.0	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 1 - CONTROL
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20526	213.6	241.5	254.3	248.8	266.2	
20527	207.8	223.9	236.9	251.9	253.4	
20528	187.7	202.4	218.7	229.0	238.1	
20529	205.2	214.4	229.2	244.0	255.5	
20530	218.5	232.9	246.8	264.3	267.9	
20531	188.9	205.0	219.7	228.1	225.2	
20532	191.0	207.5	221.8	228.2	230.3	
20533	201.8	214.5	224.7	157.6	*	
20534	211.7	223.9	242.4	248.6	255.2	
20535	180.0	199.5	210.1	218.2	219.6	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 2 - 133.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20536	314.6	348.0	378.7	403.0	427.0	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20537	276.2	298.3	330.6	350.1	375.2	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20538	312.2	339.8	360.9	389.8	406.6	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20539	301.9	323.3	371.6	385.2	405.6	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20540	287.2	316.1	342.2	354.4	371.2	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20541	275.6	296.6	308.5	321.3	340.2	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20542	284.9	310.8	347.0	365.3	381.6	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20543	279.9	297.2	326.9	334.6	358.0	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20544	295.9	325.9	350.8	369.7	392.5	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20545	358.6	395.2	433.8	466.9	467.5	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400659

GROUP 2 - 133.0000 (PPM)

FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20546	201.0	209.4	223.9	239.1	247.1	
20547	174.6	178.2	190.4	202.6	209.5	
20548	184.8	190.2	206.3	218.3	231.4	
20549	187.4	199.2	215.3	223.7	230.7	
20550	236.0	249.3	261.5	273.4	282.4	
20551	212.7	232.2	248.5	259.6	273.9	
20552	212.8	226.4	239.5	251.1	270.6	
20553	168.3	178.7	191.6	199.3	206.6	
20554	151.8	161.3	170.2	180.1	189.5	
20555	172.6	182.2	191.2	202.3	203.9	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 3 - 237.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20556	304.9	320.5	345.0	359.3	376.7	
20557	305.1	330.2	372.7	392.4	414.8	
20558	326.3	346.4	377.3	393.7	409.6	
20559	315.2	340.1	365.7	373.6	416.6	
20560	323.5	327.7	352.3	372.0	387.1	
20561	273.3	291.0	302.6	331.7	337.5	
20562	290.4	309.6	331.0	348.4	363.6	
20563	315.4	320.2	349.7	370.9	391.9	
20564	341.4	364.1	395.6	423.5	447.0	
20565	306.4	318.5	339.0	350.6	367.1	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 3 - 237.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20566	202.8	208.0	228.9	243.8	245.6	
20567	202.7	210.4	222.4	223.6	253.6	
20568	195.8	208.9	218.7	226.3	233.3	
20569	198.2	206.8	226.6	232.9	239.4	
20570	187.5	190.9	198.8	204.3	210.5	
20571	214.6	234.9	248.1	271.7	283.5	
20572	193.5	206.8	205.3	225.4	220.3	
20573	222.7	231.7	245.4	258.6	274.3	
20574	195.9	204.5	219.2	225.8	231.0	
20575	211.3	197.9	193.0	219.7	226.3	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 4 - 422.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20576	313.2	322.1	347.4	367.8	381.9	
20577	339.1	342.9	384.6	409.5	423.4	
20578	311.5	311.9	337.0	361.1	385.7	
20579	290.8	313.5	344.4	368.3	388.9	
20580	296.4	312.0	334.9	355.3	370.5	
20581	310.5	323.0	352.3	363.7	363.1	
20582	305.1	310.2	337.3	398.0	398.8	
20583	331.3	351.7	375.9	412.5	423.9	
20584	269.2	275.5	300.6	311.7	307.6	
20585	312.3	327.5	364.2	387.0	372.9	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 4 - 422.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20586	178.3	181.8	192.8	201.6	214.1	
20587	169.3	174.5	187.6	201.7	200.4	
20588	191.7	193.7	207.7	216.7	217.6	
20589	182.3	192.0	200.4	218.3	228.9	
20590	195.3	207.4	220.9	235.0	244.3	
20591	200.1	205.0	217.4	226.0	222.5	
20592	164.3	168.8	166.1	184.4	178.6	
20593	174.8	182.5	180.3	200.4	198.3	
20594	190.3	202.1	215.3	148.9	*	
20595	197.6	199.3	210.7	212.3	213.2	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 5 - 750.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20596	300.8	299.6	319.0	332.3	339.6	
20597	314.5	258.1	303.5	335.2	320.8	
20598	328.7	327.4	317.3	212.3	*	
20599	290.3	285.6	328.0	338.1	363.1	
20600	318.0	321.6	346.4	365.1	377.6	
20601	264.6	278.3	308.1	322.4	337.1	
20602	287.5	296.9	324.9	341.1	362.2	
20603	312.7	327.9	363.5	391.7	417.9	
20604	297.1	277.9	326.8	332.9	346.6	
20605	285.6	275.7	307.1	212.0	270.0	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 5 - 750.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20606	219.8	229.9	235.5	248.8	253.3	
20607	193.6	201.5	218.0	232.3	242.4	
20608	195.7	188.3	204.9	208.7	206.7	
20609	188.5	190.9	182.7	163.3	206.4	
20610	195.5	199.7	211.7	224.9	232.8	
20611	199.3	171.2	212.5	223.7	238.9	
20612	182.7	185.9	193.9	199.6	206.5	
20613	189.2	194.5	207.9	220.4	232.6	
20614	196.2	202.7	217.8	214.4	236.8	
20615	208.6	196.6	227.8	154.5	*	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 6 - 1330.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20616	298.6	288.8	316.8	338.9	353.7	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20617	287.0	276.5	306.1	214.5	*	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20618	300.2	278.0	297.1	316.8	332.3	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20619	293.9	262.4	301.8	311.7	324.9	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20620	294.7	286.4	316.5	320.6	341.1	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20621	330.1	299.6	340.8	372.5	359.1	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20622	299.2	295.1	326.4	339.2	336.2	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20623	278.4	272.9	296.5	317.0	319.6	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20624	331.8	278.0	340.4	370.1	367.4	
ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20625	280.8	278.5	298.4	322.2	320.9	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400659

GROUP 6 - 1330.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20626	213.2	198.6	217.3	210.5	231.1	
20627	189.0	181.7	199.7	206.5	210.7	
20628	179.4	175.6	189.3	192.6	201.6	
20629	186.2	176.3	181.4	200.9	189.0	
20630	170.3	161.7	180.5	189.8	196.6	
20631	203.0	194.4	223.3	222.7	217.4	
20632	182.1	170.4	184.1	203.2	194.3	
20633	191.5	176.5	199.0	205.3	205.0	
20634	198.6	203.9	213.5	225.0	216.8	
20635	196.2	182.4	200.4	209.3	199.1	

Appendix 2
Individual Food Consumption (grams)
Four-Week Dietary Study of UC-54229 in Rats

APPENDIX - 2

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400659

KEY TO SYMBOLS: * DEAD ANIMAL, ** INVALID FOOD VALUE

GROUP 1 - CONTROL

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20516	.0	186.9	195.9	203.1	199.1	
20517	.0	211.5	196.8	207.0	202.0	
20518	.0	193.7	187.1	184.7	185.4	
20519	.0	228.1	229.5	247.2	239.6	
20520	.0	206.3	196.5	203.5	200.6	
20521	.0	200.3	190.3	198.0	170.9	
20522	.0	194.2	187.8	188.9	164.1	
20523	.0	214.4	217.4	221.0	189.4	
20524	.0	196.6	197.7	208.7	196.9	
20525	.0	215.6	158.2	214.4	184.5	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 1 - CONTROL
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20526	.0	143.9	142.7	131.3	142.4	
20527	.0	182.2	235.7	155.2	151.7	
20528	.0	136.5	133.8	130.8	130.4	
20529	.0	141.9	137.4	138.8	141.6	
20530	.0	143.6	147.0	238.1	137.7	
20531	.0	136.6	137.3	151.7	118.7	
20532	.0	157.9	154.9	143.9	128.2	
20533	.0	136.5	135.9	127.4	*	
20534	.0	173.8	240.0	234.5	171.8	
20535	.0	139.6	181.6	144.4	106.9	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 2 - 133.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20536	.0	184.7	188.7	193.7	198.1	
20537	.0	159.3	178.1	178.5	182.9	
20538	.0	194.3	181.7	193.6	199.6	
20539	.0	258.0	210.5	209.4	222.0	
20540	.0	184.2	206.6	181.6	175.6	
20541	.0	163.3	161.4	155.3	163.6	
20542	.0	172.5	180.1	181.3	179.0	
20543	.0	168.5	185.6	171.8	180.9	
20544	.0	197.4	188.9	198.4	204.6	
20545	.0	251.2	245.1	237.8	227.3	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 2 - 133.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20546	.0	143.7	167.6	178.2	143.4	
20547	.0	260.8	225.5	240.0	244.8	
20548	.0	217.2	143.5	245.2	165.7	
20549	.0	166.5	159.9	139.3	139.5	
20550	.0	174.8	160.9	159.9	155.4	
20551	.0	165.9	162.3	155.2	155.8	
20552	.0	148.4	154.9	147.9	155.1	
20553	.0	186.5	236.2	173.8	125.6	
20554	.0	119.8	117.0	107.3	113.7	
20555	.0	160.2	231.2	190.2	123.0	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 3 - 237.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20556	.0	228.4	262.4	189.6	245.1	
20557	.0	184.3	208.4	207.6	202.7	
20558	.0	195.4	203.1	195.2	194.5	
20559	.0	210.7	201.1	234.4	237.7	
20560	.0	199.1	191.2	194.2	200.5	
20561	.0	237.1	268.3	234.9	247.1	
20562	.0	173.2	178.4	171.3	167.2	
20563	.0	226.9	235.7	181.8	239.9	
20564	.0	208.1	230.8	240.7	236.1	
20565	.0	223.3	216.0	181.4	186.2	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 3 - 237.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20566	.0	225.1	240.7	223.4	226.9	
20567	.0	136.5	159.0	231.8	173.6	
20568	.0	147.3	176.8	162.5	154.3	
20569	.0	148.2	182.3	238.8	137.3	
20570	.0	251.1	226.2	239.1	243.8	
20571	.0	165.8	206.1	251.1	241.2	
20572	.0	241.3	264.5	247.9	237.7	
20573	.0	164.0	142.9	146.7	145.2	
20574	.0	168.8	154.2	172.7	148.1	
20575	.0	237.1	259.6	219.2	230.2	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 4 - 422.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20576	.0	249.0	208.4	207.7	211.5	
20577	.0	172.0	221.2	219.1	212.4	
20578	.0	253.0	219.8	196.5	203.1	
20579	.0	224.7	204.0	214.1	208.4	
20580	.0	249.6	190.0	198.4	189.8	
20581	.0	191.8	219.2	214.4	179.0	
20582	.0	256.3	250.4	236.5	247.7	
20583	.0	247.3	195.5	238.4	242.0	
20584	.0	248.6	216.3	186.4	151.4	
20585	.0	246.1	218.6	226.1	224.3	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 4 - 422.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20586	.0	183.8	131.7	129.5	122.0	
20587	.0	232.4	246.7	242.6	250.8	
20588	.0	240.7	255.7	234.8	263.2	
20589	.0	244.4	259.1	244.4	227.1	
20590	.0	200.0	227.7	161.5	154.9	
20591	.0	118.4	235.7	256.8	111.2	
20592	.0	196.0	268.7	235.2	241.4	
20593	.0	233.0	250.3	191.1	124.6	
20594	.0	143.6	149.0	43.2	*	
20595	.0	204.2	163.6	259.3	127.6	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 5 - 750.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20596	.0	235.4	242.6	240.1	226.3	
20597	.0	248.2	252.4	201.6	200.3	
20598	.0	181.2	149.4	23.4	*	
20599	.0	248.1	210.8	229.0	197.7	
20600	.0	235.5	208.7	227.7	192.9	
20601	.0	153.6	182.1	234.9	166.3	
20602	.0	192.2	192.4	191.4	196.0	
20603	.0	248.4	206.4	241.5	230.7	
20604	.0	254.2	203.9	223.7	180.8	
20605	.0	205.3	201.2	174.2	205.7	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 5 - 750.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20606	.0	226.6	157.2	142.2	137.5	
20607	.0	222.4	167.1	138.4	134.8	
20608	.0	254.5	232.4	141.6	258.2	
20609	.0	254.1	246.1	224.8	232.1	
20610	.0	234.4	215.1	237.9	254.0	
20611	.0	236.3	224.0	245.6	241.8	
20612	.0	204.4	235.3	242.4	225.8	
20613	.0	113.2	163.4	191.6	187.9	
20614	.0	230.6	131.6	235.7	223.6	
20615	.0	244.5	169.8	242.9	*	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 5 - 1330.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20616	.0	198.4	187.6	180.0	173.2	
20617	.0	205.6	189.2	234.8	*	
20618	.0	252.1	185.1	185.5	172.1	
20619	.0	153.6	183.4	163.3	192.3	
20620	.0	255.9	189.4	225.7	185.1	
20621	.0	239.8	201.2	193.9	152.1	
20622	.0	142.4	183.2	160.9	131.5	
20623	.0	251.0	180.4	231.2	151.8	
20624	.0	229.3	220.6	222.5	183.2	
20625	.0	133.0	174.9	179.3	155.2	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400659

GROUP 6 - 1330.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
20626	.0	230.5	154.7	249.2	172.7	
20627	.0	248.4	161.7	249.4	138.4	
20628	.0	228.4	154.6	130.7	132.7	
20629	.0	251.5	243.6	233.5	257.0	
20630	.0	247.6	186.7	238.7	238.0	
20631	.0	239.4	156.0	232.7	191.7	
20632	.0	245.2	240.3	233.2	213.5	
20633	.0	256.7	154.5	144.7	178.5	
20634	.0	249.5	182.1	163.9	126.0	
20635	.0	241.1	139.8	150.9	132.5	

400-659

Standard Key to Hematology

Leukocyte Differentials

BLAST = Blast Cells
BAND = Band Neutrophils
LYMPH = Lymphocytes
EOSIN = Eosinophils
META = Metamyelocytes
SEG = Segmented Neutrophils
MONO = Monocytes
BASO = Basophils

Erythrocyte and Leukocyte Morphology

ANISO = Anisocytes
ECHINO = Echinocytes
TARGET = Target Cells
HYPO = Hypochromic Cells
MICRO = Microcytes
BURR = Burr Cells
POIK = Poikilocytes
ACANTH = Acanthocytes
BASOSTIP = Basophilic Stippled Cells
POLY = Polychromatophilic Cells
MACRO = Macrocytes
CRENATED = Crenated Cells

Presence of the above cell types are indicated as:

- = No finding noted
T = Trace numbers present
1 = Slight numbers present
2 = Moderate numbers present
3 = Marked numbers present
4 = Severe numbers present

HJBODY = Howell-Jolly Bodies
TOXIC = Toxic Granulation
SMUDGE = Smudge Cells
PLTCLUMP = Platelet Clumps
RECTRBC = Rectangular RBC's
FILARIA = Microfilaria
DOHLE = Dohle Bodies

Presence of the above cell types are indicated as:

- = No cells present
F = Few cells present
M = Many cells present

or

- = No cells present
P = Cells present (not quantitated)

NRBC = Nucleated RBC's
IM LYMPH = Immature Lymphocytes
REACTLYM = Reactive Lymphocytes
PLASMA = Plasma Cells

Presence of the above cell types are indicated as a percentage of 100 white blood cells counted.

400-659

Standard Key to Hemolysis

HT = Trace Hemolysis

H1 = Slight Hemolysis

H2 = Moderate Hemolysis

H3 = Marked Hemolysis

H4 = Severe Hemolysis

Appendix 3
Individual and Mean Clinical Hematology Values
Four-Week Dietary Study of UC-54229 in Rats

PROJECT: S400659 SPECIES: RAT SEX: MALES WEEK: 0 PAGE: 1

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:		
B001-2	15.1	7.93	17.1	52.1	877
B009-2	11.8	7.88	16.6	50.0	1033
B020-2	15.2	8.12	17.5	51.5	1094
B021-2	8.6	7.30	15.9	48.4	994
B025-2	10.8	8.49	17.5	52.7	1039
B026-2	11.5	8.30	17.2	52.3	1041
B029-2	12.4	8.49	17.3	51.6	1017
B035-1	12.9	7.75	17.9	51.6	1069
B039-2	10.4	8.42	17.4	52.9	1233
B040-1	12.8	7.63	16.8	49.7	1097
MEAN	12.1	8.03	17.1	51.3	1049
S.D.	2.03	.403	.57	1.45	89.8

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:		
B002-1	12.9	7.85	18.1	48.8	1162
B006-1	11.9	8.48	19.1	50.9	1029
B009-1	6.4	7.34	16.8	41.0	1131
B011-2	12.0	8.79	19.0	52.2	1179
B021-1	14.9	6.33	16.1	37.0	985
B025-2	12.7	8.06	18.2	48.3	1094
B030-2	6.8	8.75	18.5	50.4	948
B032-1	9.4	7.21	18.1	43.1	1231
B036-2	10.6	8.00	18.3	48.5	999
MEAN	10.8	7.87	18.0	46.7	1084
S.D.	2.85	.801	.98	5.14	98.5

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	WBC[B] TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:		
B20521	12.2	8.38	16.4	49.3	1081
B20522	14.8	8.12	17.2	45.8	1282
B20523	12.8	8.48	17.5	51.0	1026
B20524	15.7	8.64	16.8	49.3	1289
B20525	16.7	8.61	17.2	49.5	1006
MEAN	14.4	8.45	17.0	49.0	1137
S.D.	1.91	.210	.43	1.91	138.5
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM		
B20581	17.8	8.54	16.9	50.4	1026
B20582	9.3	8.20	16.4	48.4	1167
B20583	8.4	8.73	17.1	50.5	936
B20584	15.6	8.58	16.6	51.8	909
B20585	10.2	9.21	18.4	53.2	1044
MEAN	12.3	8.65	17.1	50.9	1016
S.D.	4.18	.367	.79	1.79	101.9
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM		
B20621	10.9	8.25	16.4	49.2	890
B20622	16.9	8.87	16.9	50.0	1187
B20623	12.9	8.10	15.9	47.8	871
B20624	12.0	8.12	16.6	49.4	837
B20625	13.8	8.87	17.0	50.9	900
MEAN	13.3	8.44	16.6	49.5	937
S.D.	2.28	.395	.44	1.14	141.8

[B] Analyzed following X^2 transformation.

PROJECT: S400659 SPECIES: RAT SEX: FEMALES WEEK : 4 PAGE: 1

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB[F] GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:		
B20531	10.7	8.32	16.7	46.3	1293
B20532	11.8	8.67	17.0	48.2	1035
B20534	12.0	8.32	16.7	47.7	1037
B20535	11.8	9.18	18.1	54.6	1103
MEAN	11.6	8.62	17.1	49.2	1117
S.D.	.59	.407	.67	3.69	121.5
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM		
B20590	NO TEST	NO TEST	NO TEST	NO TEST	NO TEST
B20591	11.4	8.75	18.1	51.1	1333
B20592	8.8	8.55	17.4	50.5	1098
B20593	10.1	8.83	7.3	50.2	1038
B20595	10.5	9.32	18.0	53.6	1163
MEAN	10.2	8.86	15.2	51.3	1158
S.D.	1.08	.327	5.28	1.55	127.3
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM		
B20631	5.5	8.03	16.4	48.4	933
B20632	10.9	8.48	17.8	49.4	1083
B20633	7.6	8.80	17.2	51.6	1223
B20634	12.9	9.33	17.5	49.4	1195
B20635	9.3	8.59	16.9	49.4	1459
MEAN	9.2	8.65	17.2	49.6	1179
S.D.	2.86	.475	.54	1.18	193.9

[F] Analyzed following rank transformation.

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APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

MALES WEEK : 0

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B001-2	0	0	0	7	90	3	0	0
B009-2	0	0	0	12	82	1	5	0
B020-2	0	0	0	14	85	0	1	0
B021-2	0	0	0	9	89	1	1	0
B025-2	0	0	0	9	88	2	1	0
B026-2	0	0	0	9	89	2	0	0
B029-2	0	0	0	15	82	2	1	0
B035-1	0	0	0	8	87	3	2	0
B039-2	0	0	0	19	80	0	1	0
B040-1	0	0	0	18	81	1	0	0

PROJECT: S400659 SPECIES: RAT SEX: FEMALES WEEK : 0 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54299 IN RATS

FEMALES WEEK : 0

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B002-1	0	0	0	5	91	3	1	0
B006-1	0	0	0	5	91	4	0	0
B009-1	0	0	0	5	88	5	2	0
B011-2	0	0	0	6	91	3	0	0
B021-1	0	0	0	7	90	3	0	0
B025-2	0	0	0	6	91	1	2	0
B030-2	0	0	0	16	83	1	0	0
B032-1	0	0	0	7	88	4	1	0
B036-2	0	0	0	4	93	2	1	0

PROJECT: S400659 SPECIES: RAT SEX: MALES WEEK : 0 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

MALES WEEK : 0

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY
B001-2	-	T	-	1	1
B009-2	T	T	-	1	1
B020-2	T	3	T	1	1
B021-2	T	4	-	1	1
B025-2	T	3	-	1	1
B026-2	-	T	-	1	1
B029-2	T	4	-	T	1
B035-1	T	T	-	1	1
B039-2	T	2	-	T	1
B040-1	T	3	-	1	1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

FEMALES WEEK : 0

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY
B002-1	T	3	-	1	1
B006-1	-	4	-	T	T
B009-1	T	4	T	1	1
B011-2	-	4	-	T	T
B021-1	-	4	-	T	T
B025-2	T	4	-	T	T
B030-2	-	4	-	T	T
B032-1	T	4	-	T	T
B036-2	-	4	-	T	T

PROJECT: S400659 SPECIES: RAT SEX: MALES WEEK : 4 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

MALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20521	0	0	0	4	95	0	1	0
B20522	0	0	0	15	81	3	1	0
B20523	0	0	0	4	94	1	1	0
B20524	0	0	0	21	79	0	0	0
B20525	0	0	0	16	82	1	1	0

GROUP: 4 DOSE LEVEL: 422 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20581	0	0	0	3	93	3	1	0
B20582	0	0	0	17	78	5	0	0
B20583	0	0	0	10	85	4	0	1
B20584	0	0	0	28	69	3	0	0
B20585	0	0	0	16	78	2	4	0

GROUP: 6 DOSE LEVEL: 1330 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20621	0	0	0	20	77	3	0	0
B20622	0	0	0	13	85	2	0	0
B20623	0	0	0	6	92	2	0	0
B20624	0	0	0	9	87	2	2	0
B20625	0	0	0	18	74	5	3	0

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

FEMALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20531	0	0	0	5	93	2	0	0
B20532	0	0	0	4	93	1	2	0
B20534	0	0	0	13	83	4	0	0
B20535	0	0	0	10	86	3	1	0

GROUP: 4 DOSE LEVEL: 422 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20591	0	0	0	14	79	2	5	0
B20592	0	0	0	14	81	2	3	0
B20593	0	0	0	8	89	1	2	0
B20595	0	0	0	10	88	1	1	0

GROUP: 6 DOSE LEVEL: 1330 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
B20631	0	0	0	29	68	1	2	0
B20632	0	0	0	6	91	1	1	1
B20633	0	0	0	11	85	2	2	0
B20634	0	0	0	12	86	2	0	0
B20635	0	0	0	21	76	3	0	0

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

MALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20521	-	T	-	T	T	1
G20522	-	3	T	T	T	-
G20523	T	2	-	1	T	-
G20524	T	1	-	1	T	-
G20525	T	1	-	T	T	-

GROUP: 4 DOSE LEVEL: 422 DOSAGE UNIT: PPM

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20581	-	3	T	T	T	-
G20582	T	3	-	T	T	-
G20583	T	1	-	T	1	-
G20584	-	T	-	1	T	-
G20585	-	2	-	T	T	-

GROUP: 6 DOSE LEVEL: 1330 DOSAGE UNIT: PPM

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20621	T	T	-	T	T	-
G20622	T	1	T	T	T	-
G20623	-	1	-	T	T	-
G20624	-	3	T	1	T	-
G20625	-	1	T	T	T	-

PROJECT: S400659 SPECIES: RAT SEX: FEMALES WEEK : 4 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

FEMALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20531	-	4	-	T	T	-
G20532	-	3	-	T	T	1
G20534	-	2	-	T	T	-
G20535	-	T	-	T	T	-

GROUP: 4 DOSE LEVEL: 422 DOSAGE UNIT: PPM

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20591	-	4	-	T	T	-
G20592	-	2	-	T	T	-
G20593	-	3	-	T	T	-
G20595	-	T	-	T	T	-

GROUP: 6 DOSE LEVEL: 1330 DOSAGE UNIT: PPM

ANIMAL	POIK	ECHINO	ACANTH	TARGET	POLY	REACTLYM
G20631	-	T	-	T	1	-
G20632	-	4	-	T	1	-
G20633	-	T	-	T	T	-
G20634	T	2	T	T	T	-
G20635	-	T	-	T	1	1

Standard Key to Serum Hemolysis

HT = Trace Hemolysis

H1 = Slight Hemolysis

H2 = Moderate Hemolysis

H3 = Marked Hemolysis

H4 = Severe Hemolysis

Footnotes to Appendix 4

F = Data analyzed following rank transformation.

NOTE: All acetylcholinesterase values are based samples from nonfasted animals.

Appendix 4
Individual and Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Rats

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
B001-2	5.6	12.0	99	84
B009-2HT	5.6	19.0	95	88
B020-2	5.8	13.0	84	71
B021-2	5.6	10.0	78	77
B025-2HT	5.8	11.0	87	74
B026-2	6.0	12.0	88	85
B029-2	5.7	14.0	95	70
B035-1HT	5.9	13.0	92	80
B039-2	5.8	20.0	89	62
B040-1H1	5.8	14.0	90	81
MEAN	5.8	13.8	90	77
S.D.	.13	3.26	6.0	8.0

PROJECT: S400659 SPECIES: RAT SEX: FEMALES WEEK : 0 PAGE: 1

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
B002-1	5.8	18.0	84	77
B006-1HT	6.4	13.0	94	90
B009-1HT	5.7	13.0	87	70
B011-2HT	6.5	12.0	77	78
B021-1	5.9	13.0	96	66
B025-2	6.4	18.0	103	59
B030-2H1	6.2	14.0	89	76
B032-1HT	5.6	12.0	96	62
B036-2HT	5.7	15.0	91	78
MEAN	6.0	14.2	91	73
S.D.	.35	2.33	7.6	9.6

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	RCHE-COL MCM/ML	PCHE-COL MCM/ML	BCHE-COL MCM/ML
B005-1	4.4	3.3	48.8
B012-2	4.9	2.2	52.2
B016-2	5.5	2.2	50.0
B017-1	4.8	2.6	53.3
B017-2	4.2	2.2	57.8
B018-1	4.8	2.3	54.4
B024-1	5.1	2.1	54.4
B035-2	4.9	2.3	51.6
B038-2	4.2	2.3	50.5
B042-2HT[a]	4.9	2.7	53.8
MEAN	4.8	2.4	52.7
S.D.	.41	.36	2.63

[a] Hemolysis refers to RBC only.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	RCHE-COL MCM/ML	PCHE-COL MCM/ML	BCHE-COL MCM/ML
B001-1	4.9	7.8	54.6
B008-2	5.2	5.3	50.8
B012-2	5.1	6.6	53.0
B014-2	4.0	6.3	53.0
B023-1	4.2	6.6	53.3
B027-2	5.2	5.6	54.4
B029-1	4.0	10.2	56.6
B035-2	4.5	5.6	50.0
MEAN	4.6	6.8	53.2
S.D.	.53	1.60	2.11

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	PCHE-COL MCM/ML	RCHE-COL MCM/ML	BCHE-COL MCM/ML
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:
B20516	2.4	5.0	52.6
B20517	2.0	5.4	50.9
B20518	2.1	4.9	52.6
B20519H1[a]	2.0	5.3	50.3
B20520	2.1	4.4	49.7
MEAN	2.1	5.0	51.2
S.D.	.16	.39	1.33
GROUP: 02	DOSE LEVEL: 133		DOSAGE UNIT: PPM
B20536	1.2	4.6	29.8
B20537H1	1.4	4.8	23.7
B20538	1.2	4.4	26.9
B20539	1.8	3.9	28.7
B20540HT	1.4	4.6	36.0
MEAN	1.4 S-	4.5	29.0 S-
S.D.	.24	.34	4.53
GROUP: 03	DOSE LEVEL: 237		DOSAGE UNIT: PPM
B20556	1.4	4.2	26.6
B20557	1.4	5.4	20.5
B20558	1.4	4.3	23.4
B20559HT	1.8	4.9	32.8
B20560	1.3	5.8	22.8
MEAN	1.5 S-	4.9	25.2 S-
S.D.	.19	.69	4.76
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM
B20576	1.2	4.4	21.0
B20577H1	1.0	4.9	21.6
B20578H1	1.2	4.3	21.6
B20579	1.2	4.8	34.8
B20580	1.1	4.9	26.9
MEAN	1.1 S-	4.7	25.2 S-
S.D.	.09	.29	5.89

[a] Hemolysis refers to RBC only.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	PCHE-COL MCM/ML	RCHE-COL MCM/ML	BCHE-COL MCM/ML
GROUP: 05	DOSE LEVEL: 750		DOSAGE UNIT: PPM
B20596	.9	4.9	18.7
B20597	1.3	4.3	20.5
B20599	1.6	4.1	26.9
B20600	1.0	4.8	22.2
B20601HT	1.1	5.1	24.9
MEAN	1.2 S-	4.6	22.6 S-
S.D.	.28	.42	3.30
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM
B20616	1.0	5.1	30.1
B20618	1.2	4.5	17.0
B20619	1.3	4.2	20.5
B20620	1.1	4.3	19.9
B20621	.9	4.2	14.3
MEAN	1.1 S-	4.5	20.4 S-
S.D.	.16	.38	5.98

[a] Hemolysis refers to RBC only.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	PCHE-COL MCM/ML	RCHE-COL MCM/ML	BCHE-COL[F] MCM/ML
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:
B20526HT	6.5	5.1	50.9
B20527	8.9	4.8	51.8
B20528HT	6.7	4.4	46.5
B20529H1	12.1	3.7	50.3
B20530HT	6.7	5.4	50.6
MEAN	8.2	4.7	50.0
S.D.	2.40	.66	2.05
GROUP: 02	DOSE LEVEL: 133		DOSAGE UNIT: PPM
B20546HT	9.9	5.8	41.8
B20547	6.5	5.0	31.6
B20548HT	7.4	5.3	35.7
B20549	5.1	5.0	38.3
B20550HT	6.5	4.4	31.6
MEAN	7.1	5.1	35.8 S-
S.D.	1.78	.51	4.40
GROUP: 03	DOSE LEVEL: 237		DOSAGE UNIT: PPM
B20566	5.0	4.6	30.4
B20567HT	6.4	4.6	38.0
B20568H1	5.8	5.1	32.8
B20569	4.5	4.9	31.6
B20570	5.1	5.0	33.0
MEAN	5.4	4.8	33.2 S-
S.D.	.74	.23	2.90
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM
B20586HT	9.0	4.6	25.2
B20587H1	5.3	4.4	30.4
B20588HT	6.3	4.9	33.9
B20589H2	5.3	5.6	30.4
B20590	10.4	5.1	36.3
MEAN	7.3	4.9	31.2 S-
S.D.	2.32	.47	4.20

F = Data analyzed following rank transformation.
[a] Hemolysis refers to RBC only.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	PCHE-COL MCM/ML	RCHE-COL MCM/ML	BCHE-COL[F] MCM/ML
GROUP: 05	DOSE LEVEL: 750		DOSAGE UNIT: PPM
B20606	5.1	4.5	26.9
B20607H2	8.1	5.6	47.1
B20608	4.9	4.3	31.0
B20609H2	7.0	4.4	42.1
B50610	5.3	4.6	23.7
MEAN	6.1	4.7	34.2
S.D.	1.40	.53	10.03
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM
B20626	3.7	4.4	15.5
B20627	10.0	5.1	25.2
B20628	6.7	5.3	26.9
B20629	5.3	4.3	18.4
B20630	8.1	4.4	29.2
MEAN	6.8	4.7	23.0[S-]
S.D.	2.44	.46	5.83

[a] Hemolysis refers to RBC only.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:	
B20521	6.0	13.0	79	93
B20522HT	5.9	14.0	79	80
B20523HT	6.0	13.0	94	114
B20524HT	5.8	17.0	90	110
B20525	6.3	17.0	104	104
MEAN	6.0	14.8	89	100
S.D.	.19	2.05	10.6	13.8
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM	
B20581HT	5.8	15.0	76	92
B20582HT	5.8	18.0	88	108
B20583HT	6.3	15.0	78	90
B20584HT	6.3	20.0	71	138
B20585HT	6.3	19.0	78	106
MEAN	6.1	17.4	78	107
S.D.	.27	2.30	6.2	19.2
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM	
B20621HT	5.8	15.0	74	85
B20622HT	5.8	13.0	78	85
B20623HT	6.2	16.0	81	84
B20624HT	6.0	19.0	80	91
B20625HT	6.2	20.0	85	78
MEAN	6.0	16.6	80	85
S.D.	.20	2.88	4.0	4.6

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN RATS

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT:	
B20531	6.1	16.0	79	77
B20532HT	6.5	13.0	75	73
B20534HT	5.9	17.0	74	70
B20535H1	6.2	15.0	89	63
MEAN	6.2	15.3	79	71
S.D.	.25	1.71	6.8	5.9
GROUP: 04	DOSE LEVEL: 422		DOSAGE UNIT: PPM	
B20591HT	5.9	17.0	82	94
B20592HT	5.9	23.0	90	100
B20593HT	6.1	23.0	78	98
B20595HT	6.4	19.0	78	101
MEAN	6.1	20.5	82	98
S.D.	.24	3.00	5.7	3.1
GROUP: 06	DOSE LEVEL: 1330		DOSAGE UNIT: PPM	
B20631HT	6.2	17.0	96	70
B20632HT	6.7	16.0	89	75
B20633HT	6.5	22.0	79	86
B20634HT	6.7	18.0	96	57
B20635HT	6.9	18.0	94	83
MEAN	6.6	18.2	91	74
S.D.	.26	2.28	7.2	11.5

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Appendix 5
References
Four-Week Dietary Study of UC-54229 in Rats

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Appendix 5 - Continued
References
Four-Week Dietary Study of UC-54229 in Rats

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Item 439

HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE VIENNA VIRGINIA 22180 U S A

FOUR-WEEK DIETARY STUDY IN MICE

UC-54229

FINAL REPORT

Submitted to

Union Carbide Agricultural Products Company, Inc.
Research Triangle Park, N.C.

October 19, 1984

5

HAZLETON
LABORATORIES AMERICA, INC.

SPONSOR: Union Carbide Agricultural Product Company, Inc. DATE: October 19,1984

MATERIAL: UC-54229

SUBJECT: FINAL REPORT
Four-Week Dietary Study in Mice
Project No. 400-658

SUMMARY

The test material, UC-54229, was fed to CD-1® mice for four weeks at dietary levels of 0, 375, 750, 1500, 3000, or 6000 ppm for the purpose of setting dose levels for a subsequent subchronic toxicity study.

Significant effects related to treatment with UC-54229 were noted in several areas. Mortality occurred in both sexes exposed to UC-54229 at 6000 ppm (20% in males; 60% in females) after one week. Body weights were depressed in both sexes fed UC-54229 at levels higher than 750 ppm. Brain acetylcholinesterase values were depressed more than 25% in all treated animals when compared to controls. The absolute organ weights and organ-to-body weight ratios of treated animals were affected in animals that were fasted or nonfasted prior to termination. The liver and heart absolute weights, and brain weight ratios were most notably affected.

HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180 U.S.A.

SUBJECT: Four-Week Dietary Study in Mice
Project No. 400-658

We, the undersigned, hereby declare that the work was performed under our supervision, according to the procedures herein described.

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INTRODUCTION

The purpose of this study was to estimate the toxicity of an agricultural chemical, UC-54229, when fed daily to mice for four weeks. Initiation was on December 29, 1982, and terminal necropsies were performed on January 27 and 28, 1983.[a]

VEHICLES AND TEST MATERIAL

Purina Rodent Laboratory Chow® #5001 was the basal diet. The dispersion vehicles were corn oil and acetone.

The test material, UC-54229, a creamy white powder with lumps, was received from the sponsor and stored in the freezer. The material was 95.1% active, which was adjusted to 100% for purposes of diet preparation calculations. The test material was taken from the freezer when needed and placed in a desiccator to equilibrate to room temperature before opening and use.

The receipt dates and lot numbers for these materials are as follows:

Material	Lot Number	Receipt Date	Weeks used on Study
Acetone	KPHC	7-28-82	1-3
	KPLS	1-3-83	4-5[a]
Corn oil	80235	7-13-82	1-5
UC-54229	22-WYF-74 #1	9-22-82	1-5

[a] January 26, 1982 was the last day of Week 4, and terminal necropsies were performed on January 27, and 28, 1982. These last two days therefore are considered to be Week 5.

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Information on diet analysis was obtained from the sponsor and is presented as follows:

Lot Number	Sample Weight (kg)	Assay (% weight)	Standard Deviation	Water (% weight)
22-WYF-74-1	1.5	95.1	0.53	4.9

TEST ANIMALS

Cesarean derived mice (CD®-1) were chosen to be the test animals for this study. Mice were chosen because historically they have been used in safety evaluation studies and are required by appropriate regulatory agencies. A total of 84 males and 82 females were received from Charles River Breeding Laboratories, Kingston, New York. The animals were acclimated to laboratory conditions for approximately three weeks prior to initiation. During this time, the mice were examined for health status by a staff veterinarian. The initial body weights ranged from 27.2 to 35.6 grams for the males and from 19.7 to 28.6 grams for the females.

The mice were individually identified by a system of ear notches and toe clips, and were individually housed in elevated wire-mesh cages marked with the corresponding animal number. Food and tap water were available ad libitum. Food was withheld overnight prior to blood collection except when acetylcholinesterase inhibition was to be evaluated.

Blood was taken for acetylcholinesterase activity measurements from animals maintained constantly on test diets. Results of routine food and water analyses are on file with the Department of Veterinary Medicine at Hazleton Laboratories America, Inc. A 12-hour light/dark cycle was maintained daily. The room temperature mean was 74.4°F with a standard deviation of 0.53°, and the mean humidity was 30.2% with a standard deviation of 6.37%.

METHODS

Groups and Dosage Levels

Prior to initiation, 60 clinically acceptable mice of each sex were randomized via a computerized HLA randomization program and were assigned to the following groups:

Group	No. of Animals Males	No. of Animals Females	Dosage Levels (ppm)
1 (Control)	10	10	0
2	10	10	375
3	10	10	750
4	10	10	1500
5	10	10	3000
6	10	10	6000

The unused animals were asphyxiated with CO_2.

Compound Preparation and Administration

Mixtures of the test material with commercial feed were prepared in the following manner. The test material was taken from the freezer and placed in a desiccator to thaw at room temperature. When thawed, the material was ground in a mortar and pestle, and an appropriate amount of the test material was dissolved in 100 ml of acetone by stirring on an automatic stirrer for approximately two minutes. When the test material had dissolved, 20 g of corn oil (or 1% of feed volume) were added to the mixture and stirred for one to two minutes.

The indicated amount of Purina Rodent Laboratory Chow® #5001 was mixed for one hour in a Hobart mixer with the test material/acetone/corn oil mixture. From this concentrated premix of 10,000 ppm, the appropriate dietary levels were mixed in the Hobart.

Test mixtures at the use concentrations were prepared fresh weekly. Samples of each concentration were taken once weekly, and put into storage at Hazleton Laboratories America, Inc.

Observations and Records

All mice were observed for mortality and moribundity twice each day. Clinical signs (gross signs of toxic and/or pharmacologic effects) and body weights were recorded at initiation, weekly thereafter, and at termination. Food consumption was recorded weekly, and each mouse was examined and palpated for tissue masses and abdominal distention weekly.

Clinical Pathology

Clinical pathology determinations were made as follows:

Interval	No. of Animals Males	Females	Groups	Parameters
Initial	10	10	-	Hematology, Serum Chemistry
	10	10	-	Cholinesterase (Plasma, RBC, Brain)
Week 4	5	5	1,4,5	Hematology, Serum Chemistry
	5[a]	5[a]	All	Cholinesterase (Plasma, RBC, Brain)

The following parameters were evaluated:

Hematology

Total Leukocyte Count (WBC)
Erythrocyte Count (RBC)
Hematocrit (HCT)
Hemoglobin (HGB)
Platelet Count (PLATELET)
Leukocyte Differential Counts
Erythrocyte and Leukocyte Morphology

Clinical Chemistry

Urea Nitrogen (BUN)
Aspartate Aminotransferase (AST)
Glucose (GLUCOSE)
Total Protein (T PROT)

Cholinesterase

Plasma (PCHE-COL)
Erythrocyte (RCHE-COL)
Brain (BCHE-COL)

[a] The remaining 5 mice/sex for Groups 2, 3, and 6 were necropsied only, and did not have acetylcholinesterase activity evaluated.

The animals were fasted overnight before the hematology and clinical chemistry samples were collected; however, all acetylcholinesterase determinations were made on non-fasted animals. All blood samples were collected via orbital sinus puncture. References for the clinical pathology methods are presented in Appendix 5.

Sacrifice and Necropsy

All surviving mice were sacrificed after four weeks of treatment. Sacrifice was by exsanguination under sodium pentobarbital and the mice were necropsied by appropriately trained personnel using procedures supervised by board-certified pathologists. Observations were recorded. Necropsies were also performed on all animals that died during the course of the study.

Organ Weights

After careful dissection and trimming of fat and other contiguous tissue in a uniform manner, the following organs from each mouse sacrificed at termination were weighed, and organ/body weight ratios were determined:

Before Fixation	After Fixation
Brain	Ovaries
Heart	
Liver	
Kidneys	
Testes with epididymides	

Tissue Preservation

The following tissues from each mouse were preserved in 10% neutral buffered formalin:

Brain
Pituitary
Spinal cord (thoracic, lumbar)
Eyes
Salivary gland (mandibular)
Thyroid
Parathyroids
Thymus
Trachea
Esophagus
Lung
Heart
Liver
Gallbladder
Spleen
Kidneys
Adrenals
Stomach
Pancreas
Cecum, colon
Duodenum, jejunum, ileum
Mesenteric lymph nodes
Urinary bladder
Testes with epididymides
Prostate
Ovaries
Uterus
Bone (femur)
Bone marrow (sternum)
Nerve muscle (skeletal)
Lesions (if present)

Statistical Analyses

Absolute body weights, total food consumption, clinical pathology data (except leukocyte differentials, erythrocyte morphology, and urinalysis), and organ weight data of the control group were compared statistically against the data of the compound-treated groups of the same sex. Absolute body weights were evaluated at initiation and at Week 4; total food consumption was evaluated from initiation through Week 4.

Analyses of the above data were performed in the following order. Levene's test for homogeneity of variances (Levene, 1960; Draper and Hunter, 1969) was performed and if the variances proved to be homogeneous, the data were analyzed by one-way classification analysis of variance

(ANOVA) (Winer, 1971). If the variances proved to be heterogeneous, a series of transformations was performed until variance homogeneity was achieved. These transformations were: $\log_{10}$, square (X^2), square root ($X^{1/2}$), reciprocal (1/X), angular (arcsine $X^{1/2}$), and rank, in that order. If rank transformation was ineffective in removing variance heterogeneity, ANOVA of ranked data was completed. If ANOVA of untransformed or transformed data was significant, Dunnett's t-test (Dunnett, 1955 and 1964) was used for control vs. compound-treated group mean comparisons. If ANOVA was not significant, the analysis was complete.

Data transformations are designated throughout this report.

Tests for homogeneity of variances and ANOVA were evaluated at the 5.0% one-tailed probability level. Control vs. compound-treated group mean comparisons of the above data were evaluated at the 5.0% two-tailed probability level. In addition to the above data, cumulative survival values were analyzed using the National Cancer Institute Package (Thomas, Breslow, and Gart, 1977). Trend analysis of survival was evaluated at the 5.0% one-tailed probability level while control vs. compound-treated group comparisons of survival were evaluated at the 5.0% two-tailed level.

Statistical references are appended to this report, and statistically significant differences, as indicated by the aforementioned

tests, are designated throughout this report by the term "significant" and/or as follows:

S+ = Significantly higher than the control value.

S- = Significantly lower than the control value.

Specimen, Raw Data, and Final Report Storage

All specimens, raw data, and the final report are stored in the archives of Hazleton Laboratories America, Inc.

RESULTS

Mortality and Clinical Signs

Cumulative survival data are presented in Table 1. The only unscheduled deaths occurred during Week 1, when two males and six females, all from Group 6, were found dead.

Cumulative survival analysis revealed a significant trend towards decreased survival in both the males and females. Group comparisons showed a significantly higher mortality in the Group 6 females.

Treatment-related clinical signs noted during this study included a hunched position, thinness, a rough haircoat, and polypnea at the Week 1 observation, primarily in the two highest dose groups of both sexes. There were no other significant clinical signs noted in this study until Week 4, when observations again included a hunched position for Group 5 animals.

Body Weights and Food Consumption

Weekly mean body weights and food consumption values are presented in Tables 1 and 2, respectively. Individual body weights and food consumption values are presented in Appendices 1 and 2, respectively. Weekly mean compound consumption is presented in Table 3.

The mean body weights of Groups 3, 4, 5, and 6 of both sexes were lower following one week of treatment than at initiation, and were lower than their control groups throughout the study. Statistical analysis revealed a significantly depressed group mean body weight

at Week 4 for males and females of Groups 4, 5, and 6 when compared to the control animals.

Statistical analysis of the total food consumption through Week 4 revealed a significantly lower value for the high-dose males.

Mean compound consumption generally decreased from week to week except for the Groups 5 and 6 males from Weeks 1 to 2, when it increased.

Clinical Pathology

Mean hematology and clinical chemistry data are presented in Tables 4 and 5, respectively. These data are presented individually in Appendices 3 and 4, respectively. The percent inhibition of acetylcholinesterase values is summarized in Text Table 1.

Among the hematology parameters evaluated, the only statistically significant values occurred in the data for the Group 4 females at Week 4. For this group, the mean leukocyte value was significantly higher than the control value, and the erythrocyte count, hemoglobin, and hematocrit values were all significantly lower than the corresponding control values.

Among the clinical chemistry parameters evaluated, the only statistically significant data were in the brain cholinesterase values, where all treated groups at Week 4 for both sexes had statistically significantly lower values than the control groups. The biologically significant values for the cholinesterase data are considered to be those

that are more than 25% inhibited when compared to the controls. Using this criterion, the brain cholinesterase values for all treated groups were biologically as well as statistically significant. These values are presented in the text table on the following page.

Gross Pathology

Gross pathology findings are summarized in Tables 6A (animals sacrificed at termination) and 6B (animals with unscheduled deaths).

The terminally sacrificed animals had few gross necropsy findings noted. An enlarged spleen was noted in one Group 1 female and one Group 5 male and female. At least one female in each group had a uterus which was distended, dark, and/or filled with clear fluid. The eye findings noted were most probably due to the orbital sinus bleeding procedure.

The animals that had unscheduled deaths (i.e., animals found dead or sacrificed in a moribund condition) had gross necropsy findings commonly present in such animals.

Organ Weights

Mean organ weight and organ to terminal body weight ratio data are presented in Table 7.

Among the terminally sacrificed animals (Table 7), the weights on page 15 were significantly different than those of the control group.

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Text Table 1
Percent Inhibition of Acetylcholinesterase Values
Four-Week Dietary Study of UC-54229 in Mice

Group and Dose Level	% Inhibitation Relative to Control Values		
	PCHE-COL	RCHE-COL	BCHE-COL
	Males		
2 375 ppm	8	0	30
3 750 ppm	3	0	33
4 1500 ppm	0	10	43
5 3000 ppm	0	13	48
6 6000 ppm	0	7	73
	Females		
2 375 ppm	2	0	38
3 750 ppm	9	7	34
4 1500 ppm	0	0	39
5 3000 ppm	0	11	45
6 6000 ppm	19	0	68

NOTE: All samples were obtained after four weeks of compound administration. All values at or below zero are presented as zero.

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Absolute Organ Weight			
Organ	Group	Sex	Significantly higher or lower than control
Kidney	4, 5	Male	Lower
Heart	4, 5, 6	Male	Lower
Liver	3, 4, 5, 6	Male	Lower
	2, 4, 5, 6	Female	Lower
Ovaries	5	Female	Lower
Testes	5	Male	Lower

Relative Organ Weight			
Organ	Group	Sex	Significantly higher or lower than control
Brain	4, 5, 6	Male	Higher
	3, 4, 5, 6	Female	Higher
Liver	6	Female	Lower
Terminal Body Weight	4, 5	Male	Lower
	3, 4, 5, 6	Female	Lower

CONCLUSION

Feeding UC-54229 to CD-1® mice for four weeks provided preliminary data useful in setting dose levels for a subchronic toxicity study. The most sensitive parameter measured was brain acetylcholinesterase, as all treated groups showed significant (greater than 25%) depression. Other parameters, including mortality, body weight, organ weights, and organ-to-body weight ratios, were also affected.

Key to Table 1

S- = Value is significantly lower than control when evaluated at the week indicated.

A = Data analyzed following $\log_{10}$ transformation.

F = Data analyzed following rank transformation.

S400688

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** MALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY						
START	MEAN (GRAMS)	31.5	32.2	31.3	30.4	31.1
	S.D.	2.41	1.88	2.44	1.88	2.21
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
1	MEAN (GRAMS)	32.9	33.1	30.9	29.7	28.0
	S.D.	2.63	1.65	2.62	2.19	2.76
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
2	MEAN (GRAMS)	34.3	34.6	32.2	30.6	29.4
	S.D.	2.52	1.39	2.90	1.87	2.77
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
3	MEAN (GRAMS)	34.6	34.9	32.6	30.9	30.6
	S.D.	2.53	1.32	2.86	1.97	2.93
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
4	MEAN (GRAMS)	34.2	36.2	33.5	30.6 S-	30.2 S-
	S.D.	3.77	1.29	2.70	3.25	2.92
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10

S400658

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** MALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (GRAMS)	30.8
	S.D.	1.77
	ADJUSTED SURVIVAL	10/ 10
1	MEAN (GRAMS)	24.2
	S.D.	2.07
	ADJUSTED SURVIVAL	8/ 10
2	MEAN (GRAMS)	27.1
	S.D.	1.79
	ADJUSTED SURVIVAL	8/ 10
3	MEAN (GRAMS)	28.6
	S.D.	1.67
	ADJUSTED SURVIVAL	8/ 10
4	MEAN (GRAMS)	30.1S-
	S.D.	1.45
	ADJUSTED SURVIVAL	8/ 10

S400658

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY						
	MEAN (GRAMS)	24.5	23.6	22.8	23.1	23.6
START	S.D.	2.17	1.97	2.47	1.75	1.95
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	25.5	24.2	22.7	23.0	21.0
1	S.D.	2.52	1.74	2.06	1.70	2.03
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	26.7	24.8	24.3	23.8	22.8
2	S.D.	2.77	1.61	2.85	2.01	2.92
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	27.1	25.1	24.5	24.3	23.3
3	S.D.	2.71	1.95	2.76	2.10	3.41
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10
	MEAN (GRAMS)	27.9	26.2	25.4	24.3 S-	23.1 S-
4	S.D.	2.05	1.66	2.86	2.25	2.84
	ADJUSTED SURVIVAL	10/ 10	10/ 10	10/ 10	10/ 10	10/ 10

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STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 1

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (GRAMS)	23.8
	S.D.	2.23
	ADJUSTED SURVIVAL	10/ 10
1	MEAN (GRAMS)	18.2
	S.D.	1.31
	ADJUSTED SURVIVAL	4/ 10
2	MEAN (GRAMS)	20.9
	S.D.	1.94
	ADJUSTED SURVIVAL	4/ 10
3	MEAN (GRAMS)	22.4
	S.D.	1.87
	ADJUSTED SURVIVAL	4/ 10
4	MEAN (GRAMS)	23.5 S-
	S.D.	1.63
	ADJUSTED SURVIVAL	4/ 10

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STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** MALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY						
START	MEAN (GM/WEEK)	.0	.0	.0	.0	.0
	S.D.	.00	.00	.00	.00	.00
	SAMPLE SIZE	10	10	10	10	10
1	MEAN (GM/WEEK)	41.0	41.4	40.0	38.7	37.3
	S.D.	2.12	2.55	4.51	4.39	4.51
	SAMPLE SIZE	10	10	10	10	10
2	MEAN (GM/WEEK)	41.0	40.8	39.0	38.5	43.1
	S.D.	2.52	2.17	3.65	1.51	4.44
	SAMPLE SIZE	10	10	10	10	10
3	MEAN (GM/WEEK)	40.3	39.9	37.8	36.7	38.4
	S.D.	1.49	2.48	1.76	1.59	2.55
	SAMPLE SIZE	10	10	10	10	10
4	MEAN (GM/WEEK)	36.9	40.2	38.9	34.7	36.0
	S.D.	2.45	1.99	2.06	4.79	3.50
	SAMPLE SIZE	10	10	10	10	10

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** MALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (GM/WEEK)	.0
	S.D.	.00
	SAMPLE SIZE	10
1	MEAN (GM/WEEK)	29.3
	S.D.	9.25
	SAMPLE SIZE	8
2	MEAN (GM/WEEK)	40.3
	S.D.	2.04
	SAMPLE SIZE	8
3	MEAN (GM/WEEK)	38.1
	S.D.	4.25
	SAMPLE SIZE	8
4	MEAN (GM/WEEK)	37.8 S-[a]
	S.D.	4.03
	SAMPLE SIZE	8

[a] Although the Week 4, Group 6 food consumption value is higher than the comparable control value, the total food consumption (Weeks 1 through 4) value is lower than control.

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STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY						
START	MEAN (GM/WEEK)	.0	.0	.0	.0	.0
	S.D.	.00	.00	.00	.00	.00
	SAMPLE SIZE	10	10	10	10	10
1	MEAN (GM/WEEK)	37.9	38.2	37.7	37.9	39.1
	S.D.	3.49	4.13	5.31	5.60	8.30
	SAMPLE SIZE	10	10	10	10	10
2	MEAN (GM/WEEK)	37.5	34.5	39.0	39.2	42.0
	S.D.	5.38	12.54	5.49	4.61	6.38
	SAMPLE SIZE	10	10	10	10	10
3	MEAN (GM/WEEK)	38.5	36.8	37.9	36.0	36.8
	S.D.	8.26	4.06	5.96	2.50	6.55
	SAMPLE SIZE	10	10	10	10	10
4	MEAN (GM/WEEK)	35.9	38.3	38.3	35.4	35.7
	S.D.	3.94	4.91	5.64	5.20	8.33
	SAMPLE SIZE	10	10	10	10	10

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STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 2

MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS

***** FEMALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (GM/WEEK)	.0
	S.D.	.00
	SAMPLE SIZE	10
1	MEAN (GM/WEEK)	35.7
	S.D.	5.25
	SAMPLE SIZE	4
2	MEAN (GM/WEEK)	37.2
	S.D.	2.00
	SAMPLE SIZE	4
3	MEAN (GM/WEEK)	37.0
	S.D.	3.02
	SAMPLE SIZE	4
4	MEAN (GM/WEEK)	37.2
	S.D.	1.02
	SAMPLE SIZE	4

S400658

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** MALES *****

GROUP		1	2	3	4	5
LEVEL (PPM)		.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY						
START	MEAN (MG/DAY/KG)	.00	.00	.00	.00	.00
1	MEAN (MG/DAY/KG)	.00	67.02	138.51	279.03	571.89
2	MEAN (MG/DAY/KG)	.00	63.09	129.63	269.70	628.43
3	MEAN (MG/DAY/KG)	.00	61.13	124.34	254.03	537.92
4	MEAN (MG/DAY/KG)	.00	59.41	124.33	243.19	510.26

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** MALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (MG/DAY/KG)	.00
1	MEAN (MG/DAY/KG)	1041.16
2	MEAN (MG/DAY/KG)	1274.44
3	MEAN (MG/DAY/KG)	1141.49
4	MEAN (MG/DAY/KG)	1075.87

S400653

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** FEMALES *****

GROUP	1	2	3	4	5
LEVEL (PPM)	.000	375.000	750.000	1500.000	3000.000
WEEKS ON STUDY					
START MEAN (MG/DAY/KG)	.00	.00	.00	.00	.00
1 MEAN (MG/DAY/KG)	.00	84.32	178.02	353.50	798.14
2 MEAN (MG/DAY/KG)	.00	74.47	172.44	352.56	789.26
3 MEAN (MG/DAY/KG)	.00	78.65	165.76	317.16	676.57
4 MEAN (MG/DAY/KG)	.00	78.49	161.22	312.33	664.23

S400638

STUDY TITLE FOUR-WEEK DIETARY STUDY IN MICE
COMPOUND TITLE UC-54229

TABLE 3

MEAN COMPOUND CONSUMPTION

***** FEMALES *****

GROUP		6
LEVEL (PPM)		6000.000
WEEKS ON STUDY		
START	MEAN (MG/DAY/KG)	.00
1	MEAN (MG/DAY/KG)	1684.81
2	MEAN (MG/DAY/KG)	1522.79
3	MEAN (MG/DAY/KG)	1416.44
4	MEAN (MG/DAY/KG)	1353.05

Table 4
Mean Clinical Hematology Values with Standard Deviations
Four-Week Dietary Study of UC-54229 in Mice

Interval	Group and Dose Level		WBC (th/μL)	RBC (mi/μL)	HGB (gm/dl)	HCT (%)	PLATELET (th/μL)
			Males				
Initial	Untreated	Mean	6.3	10.00	17.6	51.0	1304
		S.D.	1.16	0.400	0.56	3.02	67.1
		N	10	10	10	10	10
Week 4	1 Control	Mean	6.9	10.75	18.8	55.2	1239
		S.D.	2.06	0.409	0.99	3.72	71.8
		N	5	5	5	5	5
	4 1500 ppm	Mean	7.8	10.13	17.3	51.0	1164
		S.D.	2.06	1.095	2.18	6.83	83.4
		N	5	5	5	5	5
	5 3000 ppm	Mean	8.2	10.52	18.0	54.6	1236
		S.D.	1.55	0.292	0.53	3.00	134.7
		N	5	5	5	5	5
			Females				
Initial	Untreated	Mean	6.0	10.00	17.7	52.3	1175
		S.D.	1.72	0.432	0.65	3.85	89.7
		N	10	10	10	10	10
Week 4	1 Control	Mean	8.3	10.76	19.1	55.2	1121
		S.D.	1.54	0.491	1.08	4.00	106.5
		N	5	5	5	5	5
	4 1500 ppm	Mean	11.1^{S+}	9.71^{S-}	17.3^{S-}	48.3^{S-}	1145
		S.D.	0.95	0.220	0.50	2.41	68.4
		N	5	5	5	5	5
	5 3000 ppm	Mean	6.9	10.46	18.3	53.7	1128
		S.D.	1.63	0.505	0.56	4.22	63.1
		N	5	5	5	5	5

Table 5
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Mice
Males

Interval	Group and Dose Level		PCHE-COL (mcm/ml)	RCHE-COL (mcm/ml)	BCHE-COL (mcm/ml)
Initial	Untreated	Mean	21.7	2.5	51.3
		S.D.	2.99	0.54	5.33
		N	10	10	10
Week 4	1 Control	Mean	19.8	3.0	64.1
		S.D.	2.59	0.71	6.56
		N	5	5	5
	2 375 ppm	Mean	18.2	3.9	44.9[S-]
		S.D.	2.67	1.04	11.26
		N	5	5	5
	3 750 ppm	Mean	19.2	3.1	43.1[S-]
		S.D.	3.65	0.52	7.98
		N	5	5	5
	4 1500 ppm	Mean	23.0	2.7	36.8[S-]
		S.D.	1.90	0.52	7.10
		N	5	5	5
	5 3000 ppm	Mean	23.7	2.6	33.5[S-]
		S.D.	3.91	0.61	11.00
		N	5	5	5
	6 6000 ppm	Mean	22.1	2.8	17.3[S-]
		S.D.	3.60	0.59	4.93
		N	5	5	5

Table 5 - Continued
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Mice
Females

	Group and Dose Level		PCHE-COL (mcm/ml)	RCHE-COL (mcm/ml)	BCHE-COL (mcm/ml)
Initial	Untreated	Mean	26.1	2.7	51.9
		S.D.	1.69	0.42	2.87
		N	10	8	10
Week 4	1 Control	Mean	29.0	2.8	70.4
		S.D.	4.88	0.62	11.06
		N	5	5	5
	2 375 ppm	Mean	28.4	2.8	43.5[S-]
		S.D.	3.86	0.38	7.54
		N	5	5	5
	3 750 ppm	Mean	26.5	2.6	46.4[S-]
		S.D.	3.35	0.24	17.40
		N	5	5	5
	4 1500 ppm	Mean	29.5	2.9	43.2[S-]
		S.D.	2.77	0.35	5.15
		N	5	4	5
	5 3000 ppm	Mean	29.9	2.5	38.6[S-]
		S.D.	3.13	0.33	7.29
		N	5	5	5
	6 6000 ppm	Mean	23.5	2.8	22.3[S-]
		S.D.	4.19	0.56	6.06
		N	5	5	5

Table 5 - Continued
Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Mice
Males

Interval	Group and Dose Level		T PROT (gm/dl)	BUN (mg/dl)	GLUCOSE[FF] (mg/dl)	AST (IU/l)
Initial	Untreated	Mean	5.7	23.6	106	133
		S.D.	0.35	2.59	17.6	60.3
		N	10	10	10	10
Week 4	1 Control	Mean	5.8	28.0	75	78
		S.D.	0.49	8.29	8.6	23.6
		N	2	4	3	4
	4 1500 ppm	Mean	5.5	38.0	70	76
		S.D.	0.42	28.00	14.7	25.7
		N	4	5	4	4
	5 3000 ppm	Mean	5.5	23.6	88	72
		S.D.	0.40	2.79	11.0	17.4
		N	3	5	4	4
			Females			
Initial	Untreated	Mean	5.4	24.1	100	175
		S.D.	0.26	3.78	11.6	172.4
		N	10	10	9	10
Week 4	1 Control	Mean	5.8	25.4	67	85
		S.D.	0.00	4.83	4.4	9.8
		N	2	5	3	4
	4 1500 ppm	Mean	5.1	21.4	77	63
		S.D.	0.10	3.97	6.1	10.5
		N	3	5	3	5
	5 3000 ppm	Mean	5.1	20.0	84	98
		S.D.	0.76	3.08	25.5	49.9
		N	3	5	4	5

FF = Female data analyzed following rank transformation.

Table 6A
Gross Pathology Observations Incidence Summary
Four-Week Dietary Study of UC-54229 in Mice
Animals Sacrificed at Termination

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

PRINTED: 14-OCT-83
PAGE: 1

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400653

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T,1;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER-OF-ANIMALS-AFFECTED ---											
	SEX:	----------MALE----------						----------FEMALE----------					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
** TOP OF LIST **													
BRAIN (BR)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
SOFT		0	0	0	0	0	0	0	0	0	0	0	0
THOR SPINAL CORD (TC)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
LUM SPINAL CORD (LC)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
PITUITARY (PI)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK		0	0	0	0	0	0	0	0	0	0	0	0
DARK FOCUS(I)		0	0	0	0	0	0	0	0	1	0	0	0
ADRENALS (AD)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	0
DARK		0	0	0	0	0	0	0	0	0	0	0	0
THYROID (TY)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
PARATHYROIDS (PT)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
ESOPHAGUS (ES)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
TRACHEA (TR)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
LUNG (LU)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK FOCUS(I)/AREA(S)		0	0	1	0	0	0	0	0	1	0	0	0
HEART (HT)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
SPLEEN (SP)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
ENLARGED		0	0	0	0	1	0	1	0	0	0	1	0
LIVER (LI)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK		0	0	0	0	0	0	0	0	0	0	0	0
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	0	0	0	0	0	0	0

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

PRINTED: 14-OCT-83
PAGE: 2

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T,1;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER-OF-ANIMALS-AFFECTED ---											
	SEX:	----------MALE----------						----------FEMALE----------					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
GALL BLADDER (GB)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DISTENDED WITH FLUID		0	0	0	0	0	0	0	0	0	0	0	0
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	0
KIDNEYS (KD)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DILATED PELVIS(ES)		1	0	0	0	0	0	0	0	0	0	0	0
CYST(S)		0	0	0	0	0	0	0	0	0	1	0	0
STOMACH (ST)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	0	0	0	0	0	0	0
MUCOSA,DARK		0	0	0	0	0	0	0	0	0	0	0	0
DUODENUM (DU)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
SMALL MASS(ES)		0	0	0	0	0	0	0	0	0	0	1	0
JEJUNUM (JE)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
ILEUM (IL)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
SMALL MASS(ES)		0	0	0	0	0	0	1	0	0	0	0	0
PANCREAS (PA)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
SMALL MASS(ES)		0	0	0	0	1	0	0	0	0	0	0	0
CECUM (CE)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
PROMINENT VESSELS		0	0	0	0	0	0	0	1	0	0	0	0
WALLS REDDENED		0	0	0	0	0	1	0	0	0	0	0	0
COLON (CO)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
MESENTERIC L.N. (MS)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK		0	0	0	0	0	0	0	0	0	0	0	0
TESTES W/EPIDID (TP)	NUMBER EXAMINED:	9	10	10	10	10	8	0	0	0	0	0	0
PROSTATE (PR)	NUMBER EXAMINED:	9	10	10	10	10	8	0	0	0	0	0	0

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T,1;SUBSET=ALL

		--- NUMBER-OF-ANIMALS-AFFECTED ---											
	SEX:	----------MALE----------						----------FEMALE----------					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
URINARY BLADDER (UB)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
OVARIES (OV)	NUMBER EXAMINED:	0	0	0	0	0	0	10	10	10	10	10	4
CYST(S)		0	0	0	0	0	0	1	0	1	0	0	0
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0	0	0	10	10	10	10	10	4
DISTENDED		0	0	0	0	0	0	1	3	1	0	2	1
INTRALUMINAL CLEAR FLUID		0	0	0	0	0	0	1	3	1	1	2	1
DARK		0	0	0	0	0	0	0	0	0	0	1	0
SALIVARY GLD.(S) (SG)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
THYMUS (TH)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	0	0	0	1	0	0	0
EYE(S) (EY)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
UNEQUAL SIZE		0	0	0	0	0	0	0	0	0	0	0	0
GLOBE RUPTURED ANTE MORTEM		0	0	0	0	0	0	0	0	0	0	0	0
OPAQUE		0	0	1	1	2	0	1	0	1	0	1	0
WHITE INTRAOCULAR MATERIAL		0	0	0	0	0	0	0	1	0	0	0	0
PROTRUDING		0	0	0	1	0	0	0	0	0	0	0	0
SKELETAL MUSCLE (SM)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
STERNUM W/MARROW (SE)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
FEMUR (FE)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
PERITONEAL CAVIT (PC)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
THORACIC CAVITY (TA)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4
CRANIAL CAVITY (CC)	NUMBER EXAMINED:	9	10	10	10	10	8	10	10	10	10	10	4

** END OF LIST **

Table 6B
Gross Pathology Observations Incidence Summary
Four-Week Dietary Study of UC-54229 in Mice
Animals with Unscheduled Deaths

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

PRINTED: 22-FEB-83
PAGE: 1

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=D,M,A;SUBSET=ALL

		--- NUMBER OF ANIMALS AFFECTED ---											
	SEX:	MALE						FEMALE					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	1	0	0	0	0	2	0	0	0	0	0	6
** TOP OF LIST **													
BRAIN (BR)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
SOFT		0	0	0	0	0	0	0	0	0	0	0	2
THOR SPINAL CORD (TC)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
LUM SPINAL CORD (LC)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
PITUITARY (PI)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK		1	0	0	0	0	0	0	0	0	0	0	0
DARK FOCUS(I)		0	0	0	0	0	0	0	0	0	0	0	0
ADRENALS (AD)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	1
DARK		0	0	0	0	0	0	0	0	0	0	0	1
THYROID (TY)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
PARATHYROIDS (PT)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
ESOPHAGUS (ES)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
TRACHEA (TR)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
LUNG (LU)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	1	0	0	0	0	0	0
HEART (HT)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
SPLEEN (SP)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	0
LIVER (LI)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK		0	0	0	0	0	1	0	0	0	0	0	0
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	1	0	0	0	0	0	0

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=D,M,A;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER OF ANIMALS AFFECTED ---											
	SEX:	MALE						FEMALE					
	GROUP:	-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
	NUMBER:	1	0	0	0	0	2	0	0	0	0	0	6
GALL BLADDER (GB)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DISTENDED WITH FLUID		0	0	0	0	0	0	0	0	0	0	0	1
ENLARGED		0	0	0	0	0	0	0	0	0	0	0	1
KIDNEYS (KD)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DILATED PELVIS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
CYST(S)		0	0	0	0	0	0	0	0	0	0	0	0
STOMACH (ST)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	2	0	0	0	0	0	5
MUCOSA,DARK		1	0	0	0	0	0	0	0	0	0	0	1
DUODENUM (DU)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
SMALL MASS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
JEJUNUM (JE)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
ILEUM (IL)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
SMALL MASS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
PANCREAS (PA)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
SMALL MASS(ES)		0	0	0	0	0	0	0	0	0	0	0	0
CECUM (CE)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
PROMINENT VESSELS		0	0	0	0	0	0	0	0	0	0	0	0
WALLS REDDENED		0	0	0	0	0	0	0	0	0	0	0	0
COLON (CO)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
MESENTERIC L.N. (MS)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK		1	0	0	0	0	0	0	0	0	0	0	0
TESTES W/EPIDID (TP)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	0
PROSTATE (PR)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	0

OBSERVATIONS INCIDENCE SUMMARY

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=D,M,A;SUBSET=ALL

ORGAN AND KEYWORD(S) OR PHRASE		--- NUMBER OF ANIMALS AFFECTED ---											
SEX:		MALE						FEMALE					
GROUP:		-1-	-2-	-3-	-4-	-5-	-6-	-1-	-2-	-3-	-4-	-5-	-6-
NUMBER:		1	0	0	0	0	2	0	0	0	0	0	6
URINARY BLADDER (UB)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
OVARIES (OV)	NUMBER EXAMINED:	0	0	0	0	0	0	0	0	0	0	0	6
CYST(S)		0	0	0	0	0	0	0	0	0	0	0	0
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0	0	0	0	0	0	0	0	6
DISTENDED		0	0	0	0	0	0	0	0	0	0	0	0
INTRALUMINAL CLEAR FLUID		0	0	0	0	0	0	0	0	0	0	0	0
DARK		0	0	0	0	0	0	0	0	0	0	0	0
SALIVARY GLD.(S) (SG)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
THYMUS (TH)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
DARK FOCUS(I)/AREA(S)		0	0	0	0	0	0	0	0	0	0	0	0
EYE(S) (EY)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
UNEQUAL SIZE		1	0	0	0	0	0	0	0	0	0	0	0
GLOBE RUPTURED ANTE MORTEM		1	0	0	0	0	0	0	0	0	0	0	0
OPAQUE		0	0	0	0	0	0	0	0	0	0	0	0
WHITE INTRAOCULAR MATERIAL		0	0	0	0	0	0	0	0	0	0	0	0
PROTRUDING		0	0	0	0	0	0	0	0	0	0	0	0
SKELETAL MUSCLE (SM)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
STERNUM W/MARROW (SE)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
FEMUR (FE)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
PERITONEAL CAVIT (PC)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
THORACIC CAVITY (TA)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6
CRANIAL CAVITY (CC)	NUMBER EXAMINED:	1	0	0	0	0	2	0	0	0	0	0	6

** END OF LIST **

Explanation of Footnotes for Table 7

AF = Female data analyzed following $\log_{10}$ transformation.

BF = Female data analyzed following square (X^2) transformation.

FF = Female data analyzed following rank transformation.

FM = Male data analyzed following rank transformation.

DF = Female data analyzed following reciprocal (1/X) transformation.

Table 7
Absolute Organ Weight Means and
Organ to Terminal Body Weight Ratio Means
Four-Week Dietary Study of UC-54229 in Mice
Fasted and Nonfasted Animals

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

MEAN ABSOLUTE ORGAN WEIGHTS (g)

PRINTED: 23-APR-84
PAGE: 1

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
FM))) TERMINAL BODY WEIGHT (g) (((BF												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	36.4	36.6	34.1	31.6 S-	31.7 S-	30.0 S-	28.7	26.4	25.5 S-	25.3 S-	24.4 S-	23.6 S-
STAND DEV:	2.0	1.1	2.8	2.2	3.1	1.6	2.3	1.4	2.9	2.0	2.9	2.0
MINIMUM:	34.3	34.6	29.7	28.0	28.7	28.0	24.9	23.8	22.5	22.0	20.2	21.8
MAXIMUM:	39.3	38.3	36.6	35.1	37.2	32.7	32.0	28.4	30.7	28.7	27.9	26.4
))) BRAIN (((												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	.506	.522	.497	.500	.505	.494	.480	.488	.477	.474	.485	.501
STAND DEV:	.020	.020	.024	.025	.029	.018	.037	.038	.031	.040	.043	.036
MINIMUM:	.481	.493	.459	.465	.464	.471	.410	.424	.408	.422	.412	.460
MAXIMUM:	.537	.552	.540	.541	.562	.516	.534	.544	.516	.528	565	.536
))) TESTES W/EPIDID (((												
# IN GRP.:	9	10	10	10	10	8	0	0	0	0	0	0
MEAN:	.404	.394	.393	.367	.341 S-	.379						
STAND DEV:	.053	.029	.034	.045	.047	.046						
MINIMUM:	.315	.333	.328	.292	.282	.309						
MAXIMUM:	.451	.429	.446	.435	.409	.466						
))) KIDNEYS (((FF												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	.624	.624	.564	.534 S-	.525 S-	.540	.389	.373	.356	.340	342	.335
STAND DEV:	.066	.077	.085	.089	.047	.042	.051	.030	.049	.035	.048	.018
MINIMUM:	.546	.535	.452	.467	.462	.500	.283	.339	.305	.284	.255	.310
MAXIMUM:	.742	.765	.693	.755	.612	.616	.454	.420	.421	.395	.395	.352
))) HEART (((FF												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	.158	.155	150	.137 S-	.131 S-	.127 S-	.124	.115	.114	.108	.109	.104
STAND DEV:	.011	.013	.028	.011	.013	.015	.017	.006	.010	.011	.029	.012
MINIMUM:	.140	.134	.121	.119	.109	.100	.096	.103	.089	.090	.073	.088
MAXIMUM:	.176	.178	.220	.153	.157	.148	.148	.122	.125	.125	.172	.114

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

MEAN ABSOLUTE ORGAN WEIGHTS (g)

PRINTED: 23-APR-84
PAGE: 2

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
>>> LIVER <<<												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	2.17	2.12	1.93 S-	1.78 S-	1.74 S-	1.60 S-	1.60	1.44 S-	1.44	1.29 S-	1.30 S-	1.20 S-
STAND DEV:	.23	.14	.28	.15	.24	.09	.16	.08	.22	.16	.26	.12
MINIMUM:	1.94	1.86	1.30	1.51	1.42	1.46	1.39	1.33	1.20	1.03	.94	1.11
MAXIMUM:	2.63	2.28	2.30	2.00	2.13	1.73	1.87	1.55	1.81	1.52	1.65	1.38
>>> OVARIES <<<												
# IN GRP.:	0	0	0	0	0	0	10	10	10	10	10	4
MEAN:							.0251	.0255	.0241	.0209	.0197 S-	.0210
STAND DEV:							.0059	.0044	.0023	.0026	.0030	.0014
MINIMUM:							.0160	.0200	.0190	.0180	.0150	.0190
MAXIMUM:							.0340	.0330	.0270	.0260	.0260	.0220

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

PRINTED: 23-APR-84
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MEAN ORGAN/TERMINAL BODY WEIGHT RATIOS (%)

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
FM)))) TERMINAL BODY WEIGHT (g) ((((BF												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	36.4	36.6	34.1	31.6 S-	31.7 S-	30.0	28.7	26.4	25.5 S-	25.3 S-	24.4 S-	23.6 S-
STAND DEV:	2.0	1.1	2.8	2.2	3.1	1.6	2.3	1.4	2.9	2.0	2.9	2.0
MINIMUM:	34.3	34.6	29.7	28.0	28.7	28.0	24.9	23.8	22.5	22.0	20.2	21.8
MAXIMUM:	39.3	38.3	36.6	35.1	37.2	32.7	32.0	28.4	30.7	28.7	27.9	26.4
))))) BRAIN ((((AF												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	1.3941	1.4281	1.4615	1.5859 S+	1.6038 S+	1.6466 S+	1.6794	1.8459	1.8853 S+	1.8847 S+	2.0037 S+	2.1439 S+
STAND DEV:	.0816	.0607	.0809	.0869	.1205	.0733	.1053	.1108	.1605	.1794	.1590	.3170
MINIMUM:	1.2570	1.3003	1.3661	1.4411	1.4310	1.5780	1.4467	1.7300	1.6189	1.6850	1.7991	1.7424
MAXIMUM:	1.5318	1.5041	1.6296	1.7107	1.7317	1.8036	1.7985	2.0853	2.1330	2.2455	2.2921	2.4128
FM)))) TESTES W/EPIDID ((((												
# IN GRP.:	9	10	10	10	10	8	0	0	0	0	0	0
MEAN:	1.1202	1.0774	1.1535	1.1678	1.0836	1.2615						
STAND DEV:	.1990	.0864	.0803	.1898	.1658	.1305						
MINIMUM:	.8015	.9624	1.0601	.8902	.8701	1.0510						
MAXIMUM:	1.3149	1.1983	1.3300	1.4548	1.4007	1.4429						
))))) KIDNEYS ((((												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	1.7187	1.7050	1.6516	1.6837	1.6642	1.7976	1.3527	1.4117	1.3954	1.3454	1.4023	1.4267
STAND DEV:	.1930	.1986	.1930	.2009	.1535	.0751	.1029	.0681	.0953	.0608	.0762	.1240
MINIMUM:	1.3893	1.4504	1.2732	1.4758	1.3391	1.6835	1.1365	1.3452	1.3093	1.2348	1.2624	1.2803
MAXIMUM:	2.0320	2.1074	1.9304	2.1510	1.9356	1.8838	1.4754	1.5273	1.5421	1.4228	1.5481	1.5642
))))) HEART ((((												
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	.4357	.4255	.4406	.4337	.4156	.4229	.4311	.4353	.4498	.4268	.4435	.4422
STAND DEV:	.0393	.0366	.0691	.0316	.0293	.0440	.0429	.0248	.0519	.0332	.0699	.0614
MINIMUM:	.3766	.3727	.3770	.3879	.3733	.3390	.3700	.4068	.3704	.3913	.3614	.3713
MAXIMUM:	.5044	.5042	.6128	.4949	.4658	.4983	.4883	.4790	.5279	.5045	.6165	.5156

HAZLETON LABORATORIES AMERICA, INC
DEPARTMENT OF PATHOLOGY
VIENNA, VIRGINIA

*** PATH/TOX SYSTEM OUTPUT ***
FOUR-WEEK DIETARY STUDY IN MICE

PRINTED: 23-APR-84
PAGE: 2

MEAN ORGAN/TERMINAL BODY WEIGHT RATIOS (%)

STUDY NUMBER: 400658

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER:	9	10	10	10	10	8	10	10	10	10	10	4
					FM))) LIVER (((FF							
# IN GRP.:	9	10	10	10	10	8	10	10	10	10	10	4
MEAN:	5.967	5.798	5.645	5.641	5.500	5.315	5.576	5.469	5.638	5.127	5.297	5.067 S-
STAND DEV:	.516	.320	.616	.416	.455	.206	.336	.276	.388	.571	.660	.151
MINIMUM:	5.231	5.258	4.384	5.000	4.892	4.986	5.077	5.053	5.150	4.167	4.653	4.861
MAXIMUM:	6.913	6.289	6.404	6.193	6.034	5.551	6.017	5.840	6.117	6.070	6.620	5.223
					))) OVARIES (((							
# IN GRP.:	0	0	0	0	0	0	10	10	10	10	10	4
MEAN:							.0869	.0966	.0954	.0831	.0813	.0896
STAND DEV:							.0154	.0162	.0121	.0118	.0107	.0113
MINIMUM:							.0586	.0760	.0782	.0679	.0628	.0795
MAXIMUM:							.1104	.1269	.1164	.1045	.0932	.1009

Appendix 1
Individual Body Weights (grams)
Four-Week Dietary Study of UC-54229 in Mice

APPENDIX - 1

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

KEY TO SYMBOLS: * DEAD ANIMAL

GROUP 1 - CONTROL

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5261	32.1	32.8	34.3	33.9	33.7	
5262	29.3	31.3	33.5	33.4	34.6	
5263	29.9	30.8	32.5	33.0	33.9	
5264	34.6	36.9	37.5	38.6	38.6	
5265	31.4	33.4	33.8	34.9	36.1	
5266	28.2	28.9	31.0	31.2	31.8	
5267	32.9	34.1	35.1	36.1	34.7	
5268	33.0	34.8	36.3	36.5	36.4	
5269	34.9	36.1	38.0	37.3	37.5	
5270	28.6	30.1	30.6	31.1	25.1	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 1 - CONTROL
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5271	20.2	20.2	21.1	21.8	23.7	
5272	24.5	25.5	26.5	27.0	27.9	
5273	27.0	27.4	29.6	29.8	30.7	
5274	23.2	24.1	26.0	25.8	27.2	
5275	22.3	23.3	23.0	23.7	25.9	
5276	24.7	26.3	28.7	28.9	29.1	
5277	26.6	27.1	28.6	29.0	28.0	
5278	27.0	29.3	29.2	30.3	30.4	
5279	25.0	25.5	27.2	27.2	28.0	
5280	24.8	26.5	27.6	27.8	28.2	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 2 - 375.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5281	33.8	34.7	35.1	36.2	37.2	
5282	33.0	33.3	34.3	35.7	36.5	
5283	28.9	31.3	34.0	34.6	36.0	
5284	34.2	35.2	36.3	36.0	37.2	
5285	33.0	34.8	36.2	36.2	37.2	
5286	34.2	34.0	36.3	35.4	38.3	
5287	33.0	33.9	35.2	35.8	36.1	
5288	31.6	31.4	32.9	33.3	35.0	
5289	29.9	31.4	33.0	32.6	34.8	
5290	30.5	31.1	33.0	33.7	34.2	

APPENDIX - 1 CONTINUED
INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 2 - 375.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5291	25.7	26.4	26.8	27.4	28.2	
5292	23.7	24.3	24.5	25.5	26.1	
5293	23.9	25.8	26.1	26.4	27.5	
5294	27.1	26.8	27.1	27.9	28.1	
5295	22.2	23.1	23.8	24.7	26.6	
5296	19.7	21.1	21.8	21.4	22.7	
5297	23.5	23.7	25.0	25.3	26.6	
5298	22.9	23.1	23.4	23.9	25.0	
5299	23.6	23.5	25.0	25.0	25.8	
5300	24.2	24.7	24.4	23.1	25.0	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

GROUP 3 - 750.0000 (PPM)

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5301	34.0	32.9	35.0	35.1	35.7	
5302	31.5	31.1	32.9	33.8	34.6	
5303	27.9	27.4	28.8	28.7	29.7	
5304	28.4	28.1	28.2	29.1	30.1	
5305	33.5	33.2	33.6	34.2	35.7	
5306	32.7	33.1	34.9	34.6	35.4	
5307	32.5	32.8	34.7	35.0	35.2	
5308	32.6	30.8	32.1	32.9	34.5	
5309	27.4	26.7	27.7	27.9	29.2	
5310	32.4	33.4	34.2	34.6	35.2	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

GROUP 3 - 750.0000 (PPM)

FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5311	19.9	20.1	20.5	21.8	22.4	
5312	21.5	20.7	21.9	22.3	23.8	
5313	22.6	22.2	22.7	22.3	23.1	
5314	21.1	21.1	22.1	21.8	22.4	
5315	20.5	21.2	22.6	23.0	24.5	
5316	23.4	23.5	26.2	26.7	27.1	
5317	28.3	25.5	27.9	28.2	29.2	
5318	22.0	22.7	23.6	24.5	24.7	
5319	23.3	23.6	25.9	25.2	26.5	
5320	25.1	26.3	29.1	29.3	30.7	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 4 - 1500.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5321	30.7	28.4	29.4	29.1	30.7	
5322	33.2	32.7	32.3	32.1	33.3	
5323	32.7	33.1	32.6	33.0	34.3	
5324	32.2	31.4	33.0	33.9	36.2	
5325	29.5	28.0	29.6	29.8	31.7	
5326	30.1	27.5	29.5	30.3	27.2	
5327	29.9	29.8	30.4	31.6	28.4	
5328	30.4	30.8	32.6	32.7	30.2	
5329	27.2	27.8	28.4	28.7	27.7	
5330	28.4	27.4	28.1	28.3	26.5	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 4 - 1500.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5331	25.8	25.7	26.6	27.2	27.8	
5332	21.1	20.3	21.0	20.9	22.5	
5333	22.8	22.9	22.9	23.2	25.2	
5334	23.5	22.9	24.6	25.6	26.9	
5335	22.6	22.4	24.4	24.3	25.0	
5336	25.5	24.9	26.6	27.2	25.1	
5337	24.3	23.3	24.0	24.9	24.4	
5338	22.2	22.9	22.8	22.9	21.9	
5339	23.2	23.8	24.8	25.3	23.3	
5340	20.3	20.4	20.8	22.0	20.5	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

GROUP 5 - 3000.0000 (PPM)

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5341	30.1	29.3	29.4	31.8	32.0	
5342	28.6	26.9	26.9	28.2	28.9	
5343	28.9	25.7	26.9	27.9	30.1	
5344	29.3	24.5	25.1	26.2	29.1	
5345	33.7	32.4	33.7	34.9	36.4	
5346	30.3	28.0	29.1	29.6	27.1	
5347	35.6	31.3	33.3	34.6	32.7	
5348	30.7	24.0	28.6	28.9	26.7	
5349	31.5	28.2	29.8	31.2	28.3	
5350	32.0	29.3	31.2	32.8	30.9	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)
S400658

GROUP 5 - 3000.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5351	22.2	17.9	19.4	17.8	19.8	
5352	25.6	23.8	26.4	27.2	28.5	
5353	23.5	19.6	20.2	19.6	22.1	
5354	23.3	21.6	24.0	25.9	26.2	
5355	20.2	18.9	19.1	20.4	21.1	
5356	26.3	24.3	27.2	27.8	25.2	
5357	23.7	20.0	20.1	21.0	19.6	
5358	21.5	20.9	23.8	24.0	22.1	
5359	24.5	22.0	23.4	24.7	22.5	
5360	25.6	20.9	24.3	24.9	23.5	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

GROUP 6 - 6000.0000 (PPM)

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5361	28.6	*	*	*	*	
5362	29.3	24.0	26.5	27.8	28.8	
5363	30.6	22.7	26.3	28.3	29.7	
5364	32.1	21.1	25.8	27.8	29.4	
5365	28.4	24.5	26.7	27.4	29.0	
5366	33.0	27.8	31.3	32.0	32.5	
5367	33.3	26.2	27.4	30.4	32.3	
5368	30.2	23.6	25.7	27.3	29.3	
5369	30.1	*	*	*	*	
5370	32.1	23.4	27.0	28.1	30.0	

APPENDIX - 1 CONTINUED

INDIVIDUAL BODY WEIGHTS (GRAMS)

S400658

GROUP 6 - 6000.0000 (PPM)

FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5371	28.6	*	*	*	*	
5372	23.1	*	*	*	*	
5373	22.1	18.2	19.2	20.8	22.3	
5374	23.0	*	*	*	*	
5375	24.0	*	*	*	*	
5376	20.4	*	*	*	*	
5377	22.3	17.5	20.6	21.3	22.4	
5378	24.8	20.0	23.7	25.0	25.8	
5379	25.1	*	*	*	*	
5380	24.8	17.0	20.2	22.4	23.7	

Appendix 2
Individual Food Consumption (grams)
Four-Week Dietary Study of UC-54229 in Mice

APPENDIX - 2

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400658

KEY TO SYMBOLS: * DEAD ANIMAL, ** INVALID FOOD VALUE

GROUP 1 - CONTROL

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5261	.0	42.3	41.3	40.8	39.1	
5262	.0	41.2	44.0	41.2	41.4	
5263	.0	38.4	38.5	37.9	37.0	
5264	.0	41.7	41.8	41.0	38.5	
5265	.0	41.0	39.0	40.4	38.0	
5266	.0	36.6	37.3	38.2	35.0	
5267	.0	40.5	38.4	38.7	34.1	
5268	.0	41.8	43.0	41.4	34.7	
5269	.0	42.0	43.6	41.2	36.9	
5270	.0	44.2	43.4	42.2	33.9	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 1 - CONTROL
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5271	.0	31.4	31.0	32.2	35.2	
5272	.0	34.6	31.8	31.4	35.6	
5273	.0	38.5	39.7	38.9	37.2	
5274	.0	36.7	36.9	37.4	37.4	
5275	.0	36.9	33.8	32.7	33.1	
5276	.0	42.6	49.6	60.1	45.6	
5277	.0	36.2	34.8	34.9	30.5	
5278	.0	41.6	38.2	41.3	34.5	
5279	.0	39.3	38.2	39.2	34.9	
5280	.0	41.5	41.0	37.2	34.8	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400658

GROUP 2 - 375.0000 (PPM)

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5281	.0	43.0	41.4	41.9	41.8	
5282	.0	40.8	40.1	42.1	40.1	
5283	.0	40.1	42.6	40.5	41.5	
5284	.0	44.0	40.5	38.2	38.2	
5285	.0	45.4	42.0	40.4	40.5	
5286	.0	40.9	41.1	38.9	39.3	
5287	.0	39.3	39.1	39.1	41.3	
5288	.0	37.6	36.8	36.5	37.3	
5289	.0	39.1	39.4	36.8	38.2	
5290	.0	44.0	44.8	44.4	43.8	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400658

GROUP 2 - 375.0000 (PPM)

FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5291	.0	35.8	.0	33.7	36.4	
5292	.0	34.3	34.7	36.0	35.0	
5293	.0	36.4	36.0	36.6	38.5	
5294	.0	40.9	40.9	39.6	39.4	
5295	.0	46.3	43.8	47.3	51.1	
5296	.0	42.1	41.4	34.0	34.8	
5297	.0	38.9	40.3	35.5	38.1	
5298	.0	36.8	35.7	34.2	37.2	
5299	.0	32.0	33.9	35.9	33.5	
5300	.0	38.2	37.9	35.1	39.3	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 3 - 750.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5301	.0	41.4	41.4	39.2	40.0	
5302	.0	39.3	38.7	38.9	39.1	
5303	.0	38.8	38.5	36.4	37.6	
5304	.0	33.8	31.3	35.2	36.0	
5305	.0	49.0	42.1	40.6	43.0	
5306	.0	41.9	44.1	38.8	40.4	
5307	.0	43.8	41.0	37.1	37.0	
5308	.0	35.7	39.2	39.0	39.5	
5309	.0	35.3	35.2	35.5	37.0	
5310	.0	41.1	38.2	37.5	39.5	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 3 - 750.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5311	.0	38.4	50.2	36.7	36.2	
5312	.0	47.1	44.0	49.8	51.6	
5313	.0	30.2	37.5	33.2	33.6	
5314	.0	36.7	35.4	37.8	40.1	
5315	.0	36.3	34.4	35.0	35.0	
5316	.0	42.6	37.2	34.0	37.6	
5317	.0	42.0	43.3	46.8	41.8	
5318	.0	32.1	32.2	31.5	31.4	
5319	.0	32.3	35.3	35.0	35.8	
5320	.0	39.3	40.8	39.4	39.7	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 4 - 1500.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5321	.0	41.0	39.1	36.2	36.1	
5322	.0	47.6	39.4	37.3	40.6	
5323	.0	36.7	36.3	35.2	35.0	
5324	.0	39.5	39.3	36.8	40.2	
5325	.0	37.7	41.1	39.9	41.8	
5326	.0	40.6	38.8	37.4	28.6	
5327	.0	33.5	37.5	35.0	30.8	
5328	.0	40.6	38.9	37.6	33.3	
5329	.0	31.8	36.1	34.4	30.0	
5330	.0	37.6	38.5	37.1	31.1	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 4 - 1500.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5331	.0	36.1	36.8	35.2	35.7	
5332	.0	38.5	40.6	37.7	45.2	
5333	.0	35.5	33.4	35.1	38.4	
5334	.0	40.7	41.3	37.6	40.6	
5335	.0	42.5	43.2	33.6	32.1	
5336	.0	32.9	36.7	36.2	31.1	
5337	.0	38.3	42.4	38.7	38.4	
5338	.0	34.5	40.8	35.3	29.6	
5339	.0	49.8	46.0	39.7	32.8	
5340	.0	29.8	31.2	31.3	29.7	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400658

GROUP 5 - 3000.0000 (PPM)

MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5341	.0	35.8	38.5	39.6	38.6	
5342	.0	35.6	37.9	35.3	36.1	
5343	.0	35.3	40.9	36.3	34.2	
5344	.0	30.5	46.8	40.6	40.8	
5345	.0	35.2	39.8	38.5	40.3	
5346	.0	45.5	40.3	34.3	30.4	
5347	.0	42.1	44.8	42.1	34.9	
5348	.0	33.2	51.7	37.5	37.9	
5349	.0	39.0	43.4	39.0	31.3	
5350	.0	40.9	47.0	41.0	35.3	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 5 - 3000.0000 (PPM)
FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5351	.0	34.5	43.8	37.7	43.5	
5352	.0	54.8	57.4	52.5	56.8	
5353	.0	25.1	37.5	28.7	31.6	
5354	.0	36.2	41.0	40.7	35.2	
5355	.0	44.4	34.1	31.2	30.8	
5356	.0	44.2	39.3	36.3	31.5	
5357	.0	37.0	40.0	37.5	31.3	
5358	.0	31.7	44.0	33.0	30.6	
5359	.0	44.9	44.9	37.3	32.6	
5360	.0	38.1	37.7	33.4	33.5	

APPENDIX - 2 CONTINUED
INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)
S400658

GROUP 6 - 6000.0000 (PPM)
MALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5361	.0	*	*	*	*	
5362	.0	28.5	39.9	35.6	35.6	
5363	.0	20.7	36.6	35.5	37.3	
5364	.0	15.6	43.4	43.1	41.1	
5365	.0	43.9	41.4	37.5	36.1	
5366	.0	29.5	40.8	33.6	31.3	
5367	.0	40.0	41.6	46.0	42.9	
5368	.0	26.5	39.7	38.0	42.5	
5369	.0	*	*	*	*	
5370	.0	30.1	38.8	35.8	35.7	

APPENDIX - 2 CONTINUED

INDIVIDUAL FOOD CONSUMPTION (GRAMS PER WEEK)

S400658

GROUP 6 - 6000.0000 (PPM)

FEMALES

ANIMAL NUMBER	INTERVALS 0	1	2	3	4	5
5371	.0	*	*	*	*	
5372	.0	*	*	*	*	
5373	.0	29.5	36.0	35.6	36.8	
5374	.0	*	*	*	*	
5375	.0	*	*	*	*	
5376	.0	*	*	*	*	
5377	.0	39.5	39.9	38.5	38.7	
5378	.0	33.3	37.4	33.5	36.5	
5379	.0	*	*	*	*	
5380	.0	40.6	35.4	40.3	36.7	

Explanation of Footnote for Appendix 3

A = Data analyzed following $\log_{10}$ transformation.

400-658

Standard Key to Hematology

Leukocyte Differentials

BLAST = Blast Cells
BAND = Band Neutrophils
LYMPH = Lymphocytes
EOSIN = Eosinophils
META = Metamyelocytes
SEG = Segmented Neutrophils
MONO = Monocytes
BASO = Basophils

Erythrocyte and Leukocyte Morphology

ANISO = Anisocytes
ECHINO = Echinocytes
TARGET = Target Cells
HYPO = Hypochromic Cells
MICRO = Microcytes
BURR = Burr Cells
POIK = Poikilocytes
ACANTH = Acanthocytes
BASOSTIP = Basophilic Stippled Cells
POLY = Polychromatophilic Cells
MACRO = Macrocytes
CRENATED = Crenated Cells

Presence of the above cell types are indicated as:

- = No finding noted
T = Trace numbers present
1 = Slight numbers present
2 = Moderate numbers present
3 = Marked numbers present
4 = Severe numbers present

HJBODY = Howell-Jolly Bodies
TOXIC = Toxic Granulation
SMUDGE = Smudge Cells
PLTCLUMP = Platelet Clumps
RECTRBC = Rectangular RBC's
FILARIA = Microfilaria
DOHLE = Dohle Bodies

Presence of the above cell types are indicated as:

- = No cells present
F = Few cells present
M = Many cells present

or

- = No cells present
P = Cells present (not quantitated)

NRBC = Nucleated RBC's
IM LYMPH = Immature Lymphocytes
REACTLYM = Reactive Lymphocytes
PLASMA = Plasma Cells

Presence of the above cell types are indicated as a percentage of 100 white blood cells counted.

400-658

Standard Key to Serum Hemolysis

HT = Trace Hemolysis

H1 = Slight Hemolysis

H2 = Moderate Hemolysis

H3 = Marked Hemolysis

H4 = Severe Hemolysis

Appendix 3
Individual and Mean Clinical Hematology Values
Four-Week Dietary Study of UC-54229 in Mice

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 0 PAGE: 1

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
A009-1	5.2	10.33	17.8	53.5	1410
A010-1	5.2	10.39	17.8	54.8	1230
A011-2	7.2	10.22	18.3	51.3	1270
A014-1	5.2	10.08	17.8	53.1	1404
A015-2	6.3	9.48	16.6	46.4	1288
A022-2	7.0	10.49	18.2	53.8	1265
A029-2	7.9	10.17	18.0	52.5	1317
A038-1	7.5	9.93	17.5	49.0	1227
A041-2	4.6	9.56	17.5	49.2	1360
A042-2	6.8	9.38	16.8	46.7	1264
MEAN	6.3	10.00	17.6	51.0	1304
S.D.	1.16	.400	.56	3.02	67.1

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 0 PAGE: 1

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
A003-2	3.7	9.27	16.2	47.8	1322
A004-2	5.3	9.94	17.7	50.1	1036
A007-2	7.0	10.41	17.8	52.9	1066
A009-1	6.6	9.96	18.2	50.3	1181
A009-2	10.2	9.79	17.9	53.9	1131
A012-1	5.4	10.22	18.2	50.8	1294
A022-2	5.0	10.62	18.0	59.3	1200
A026-1	6.1	9.58	17.1	51.0	1210
A030-1	5.6	10.50	18.4	58.4	1176
A034-2	5.5	9.73	17.6	48.9	1135
MEAN	6.0	10.00	17.7	52.3	1175
S.D.	1.72	.432	.65	3.85	89.7

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	WBC TH/UL	RBC MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM		
A05266	6.3	11.18	20.3	60.9	1183
A05267	10.1	10.44	18.4	54.3	1298
A05268	7.0	10.74	18.3	52.9	1313
A05269	6.5	10.25	17.8	51.4	1254
A05270	4.4	11.12	19.3	56.7	1148
MEAN	6.9	10.75	18.8	55.2	1239
S.D.	2.06	.409	.99	3.72	71.8
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM		
A05326	8.1	10.42	18.3	50.1	1231
A05327	5.3	8.35	13.7	40.0	1094
A05328	11.0	10.00	17.0	51.7	1229
A05329	7.2	10.58	18.5	55.1	1210
A05330	7.5	11.28	19.2	57.9	1054
MEAN	7.8	10.13	17.3	51.0	1164
S.D.	2.06	1.095	2.18	6.83	83.4
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM		
A05346	9.9	10.61	18.2	54.2	1089
A05347	7.4	10.08	17.1	50.7	1336
A05348	5.9	10.89	18.1	59.0	1410
A05349	9.0	10.49	18.0	53.7	1136
A05350	8.6	10.55	18.5	55.2	1210
MEAN	8.2	10.52	18.0	54.6	1236
S.D.	1.55	.292	.53	3.00	134.7

APPENDIX 3
INDIVIDUAL & MEAN CLINICAL HEMATOLOGY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	WBC TH/UL	RBC[A] MI/UL	HGB GM/DL	HCT %	PLATELET TH/UL
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM		
A05276	7.8	10.26	18.2	50.2	1179
A05277	7.3	11.04	18.8	58.4	1278
A05278	7.1	10.27	18.0	51.8	1084
A05279	10.9	11.38	20.5	59.2	1040
A05280	8.5	10.86	19.9	56.3	1024
MEAN	8.3	10.76	19.1	55.2	1121
S.D.	1.54	.491	1.08	4.00	106.5
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM		
A05336	12.1	9.78	17.6	50.7	1088
A05337	11.9	9.80	17.2	50.9	1258
A05338	10.9	9.80	18.0	47.9	1143
A05339	9.8	9.85	16.9	45.9	1093
A05340	10.6	9.32	16.8	46.1	1142
MEAN	11.1 S+	9.71 S-	17.3 S-	48.3 S-	1145
S.D.	.95	.220	.50	2.41	68.4
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM		
A05356	4.0	9.93	17.5	48.4	1187
A05357	8.1	10.11	18.0	56.0	1187
A05358	7.2	10.94	18.9	54.9	1126
A05359	7.5	11.05	18.7	58.8	1102
A05360	7.5	10.26	18.3	50.5	1037
MEAN	6.9	10.46	18.3	53.7	1128
S.D.	1.63	.505	.56	4.22	63.1

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 0 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

MALES WEEK : 0

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A010-1	0	0	1	30	66	3	0	0
A011-2	0	0	1	15	84	0	0	0
A014-1	0	0	0	30	70	0	0	0
A015-2	0	0	0	25	74	0	1	0
A022-2	0	0	0	14	86	0	0	0
A029-2	0	0	0	14	85	0	1	0
A038-1	0	0	0	13	84	3	0	0
A041-2	0	0	0	22	78	0	0	0
A042-2	0	0	0	11	86	0	3	0
A09-1	0	0	0	22	78	0	0	0

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 0 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

FEMALES WEEK : 0

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A012-1	0	0	0	11	89	0	0	0
A022-2	0	0	0	9	85	2	4	0
A026-1	0	0	0	27	73	0	0	0
A03-2	0	0	0	50	49	0	1	0
A030-1	0	0	0	33	67	0	0	0
A034-2	0	0	0	14	84	1	1	0
A04-2	0	0	0	13	87	0	0	0
A07-2	0	0	0	28	70	0	2	0
A09-1	0	0	0	16	82	0	0	0
A09-2	0	0	0	17	83	0	0	0

PROJECT: S400652 SPECIES: MOUSE SEX: MALES WEEK : 0 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

MALES WEEK : 0

ANIMAL	ECHINO	TARGET	POLY	HJBODY	NRBC
A010-1	T	T	1	-	1
A011-2	1	-	1	F	-
A014-1	2	-	1	-	-
A015-2	3	-	1	-	-
A022-2	2	-	1	F	-
A029-2	2	-	1	-	-
A038-1	2	-	1	F	-
A041-2	3	-	1	F	-
A042-2	3	-	1	F	-
A09-1	1	-	1	-	-

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 0 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY UC-54229 IN MICE

FEMALES WEEK : 0

ANIMAL	ECHINO	TARGET	POLY	HJBODY	REACTLYM
A012-1	1	-	1	F	-
A022-2	1	-	1	-	-
A026-1	2	-	1	-	-
A03-2	1	-	1	F	1
A030-1	2	-	1	F	-
A034-2	2	-	1	F	2
A04-2	1	-	1	F	-
A07-2	T	T	T	F	-
A09-1	2	-	T	-	-
A09-2	T	-	T	F	-

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 4 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

MALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05266	0	0	0	16	81	1	0	0
A05267	0	0	0	14	86	0	0	0
A05268	0	0	0	28	70	0	2	0
A05269	0	0	0	23	74	2	1	0
A05270	0	0	1	13	82	2	2	0

GROUP: 4 DOSE LEVEL: 1500 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05326	0	0	0	19	80	0	1	0
A05327	0	0	0	19	80	0	1	0
A05328	0	0	0	10	88	1	1	0
A05329	0	0	0	23	77	0	0	0
A05330	0	0	0	24	74	0	2	0

GROUP: 5 DOSE LEVEL: 3000 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05347	0	0	0	15	83	2	0	0
A05348	0	0	0	27	66	2	5	0
A05349	0	0	0	27	68	1	4	0
A05350	0	0	0	11	85	2	2	0
A5346	0	0	0	22	74	2	2	0

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 4 PAGE 1

APPENDIX 3
INDIVIDUAL LEUKOCYTE DIFFERENTIALS
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

FEMALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT:

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05276	0	0	0	19	79	1	1	0
A05277	0	0	0	33	60	2	5	0
A05278	0	0	0	24	76	0	0	0
A05279	0	0	0	19	80	0	1	0
A05280	0	0	0	18	79	1	2	0

GROUP: 4 DOSE LEVEL: 1500 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05336	0	0	0	20	79	0	1	0
A05337	0	0	0	8	89	0	3	0
A05338	0	0	0	35	62	1	2	0
A05340	0	0	0	16	81	1	2	0
A5339	0	0	0	12	81	1	6	0
MISTAKE	NO TEST	NO TEST	NO TEST	NO TEST	NO TEST	NO TEST	NO TEST	NO TEST

GROUP: 5 DOSE LEVEL: 3000 DOSAGE UNIT: PPM

ANIMAL NUMBER	BLAST %	META %	BAND %	SEG %	LYMPH %	MONO %	EOSIN %	BASO %
A05356	0	0	0	22	71	3	4	0
A05357	0	0	0	31	68	0	1	0
A05358	0	0	0	37	62	0	1	0
A05359	0	0	0	12	86	1	1	0
A05360	0	0	0	22	75	1	2	0

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 4 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54299 IN MICE

MALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY
A05266	4	-	1	F
A05267	2	T	1	F
A05268	1	T	1	F
A05269	1	T	1	F
A05270	2	T	1	F
MISTAKE	NO TEST	NO TEST	NO TEST	NO TEST

GROUP: 4 DOSE LEVEL: 1500 DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY
A05326	4	T	1	F
A05327	3	-	1	F
A05328	1	-	1	F
A05329	T	-	T	-
A05330	T	-	1	-

GROUP: 5 DOSE LEVEL: 3000 DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY
A05346	1	T	1	F
A05347	2	-	1	F
A05348	1	-	T	F
A05349	1	T	1	F
A05350	1	T	1	F

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 4 PAGE 1

APPENDIX 3
ERYTHROCYTE AND LEUKOCYTE MORPHOLOGY
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

FEMALES WEEK : 4

GROUP: 1 DOSE LEVEL: CONTROL DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY	NRBC	REACTLYM
A05276	3	-	1	F	-	-
A05277	2	T	1	F	-	1
A05278	3	T	1	F	-	-
A05279	2	T	1	F	-	-
A05280	3	-	1	F	-	-

GROUP: 4 DOSE LEVEL: 1500 DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY	NRBC	REACTLYM
A05336	2	-	1	F	-	-
A05337	1	-	1	F	-	-
A05338	4	T	1	F	-	-
A05339	T	T	1	F	-	-
A05340	2	T	1	F	-	-

GROUP: 5 DOSE LEVEL: 3000 DOSAGE UNIT: PPM

ANIMAL	ECHINO	TARGET	POLY	HJBODY	NRBC	REACTLYM
05356	1	-	T	F	-	-
A05357	1	T	1	F	-	-
A05358	1	T	1	-	-	-
A05359	T	T	1	F	-	1
A05360	T	T	1	F	1	-

Explanation of Footnotes for Appendix 4

a = NO TEST indicates the sample contained less than the required amount to perform all tests.

b = Hemolysis notations apply to Red Blood Cell and Plasma Cholinesterase values only.

c = NO TEST indicates sample broke in centrifuge.

F = Data analyzed following rank transformation.

NOTE: All aceytlcholinesterase values are based samples from nonfasted animals.

Appendix 4
Individual and Mean Clinical Chemistry Values
Four-Week Dietary Study of UC-54229 in Mice

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 0 PAGE: 1

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
A009-1HT	5.8	28.0	104	263
A010-1	5.6	22.0	80	198
A011-2	6.0	23.0	110	96
A014-1[a]	6.3	24.0	NO TEST	83
A015-2	5.3	23.0	92	87
A022-2HT	5.9	25.0	111	170
A029-2[a]H1	5.4	19.0	NO TEST	132
A038-1	5.5	23.0	95	76
A041-2	6.1	27.0	135	116
A042-2	5.3	22.0	123	107
MEAN	5.7	23.6	106	133
S.D.	.35	2.59	17.6	60.3

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
A003-2[a]	5.2	26.0	NO TEST	664
A004-2HT	5.9	22.0	90	123
A007-2	5.6	16.0	81	129
A009-1F	5.6	24.0	100	112
A009-2	5.2	21.0	114	150
A012-1	5.3	23.0	98	101
A022-2FHT	5.6	29.0	107	112
A026-1HT	5.2	27.0	106	129
A030-1	5.5	26.0	87	122
A034-2	5.1	27.0	113	108
MEAN	5.4	24.1	100	175
S.D.	.26	3.78	11.6	172.4

F following animal numbers A009-1 and A022-2 is part of the temporary animal number.

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE MG/DL	AST IU/L
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM	
A05266	6.2	20.0	67	98
A05267[a]	NO TEST	37.0	NO TEST	49
A05268	5.5	22.0	73	68
A05269[a] H2	NO TEST	33.0	84	96
A05270[a]	NO TEST	NO TEST	NO TEST	NO TEST
MEAN	5.8	28.0	75	78
S.D.	.49	8.29	8.6	23.6
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM	
A05326	5.5	23.0	56	75
A05327	5.9	88.0	88	45
A05328	4.9	27.0	60	74
A05329[a] HT	NO TEST	27.0	NO TEST	NO TEST
A05330	5.6	25.0	75	108
MEAN	5.5	38.0	70	76
S.D.	.42	28.00	14.7	25.7
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM	
A05346	5.1	26.0	94	87
A05347[a]	NO TEST	21.0	NO TEST	NO TEST
A05348	5.9	23.0	80	70
A05349[a]	NO TEST	27.0	77	82
A05350	5.5	21.0	100	48
MEAN	5.5	23.6	88	72
S.D.	.40	2.79	11.0	17.4

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	T PROT GM/DL	BUN MG/DL	GLUCOSE[F] MG/DL	AST IU/L
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM	
A05276[a] HT	NO TEST	31.0	NO TEST	74
A05277	5.8	19.0	70	88
A05278[a]	NO TEST	27.0	NO TEST	NO TEST
A05279	5.8	28.0	62	97
A05280[a] HT	NO TEST	22.0	69	81
MEAN	5.8	25.4	67	85
S.D.	.00	4.83	4.4	9.8
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM	
A05336	5.2	22.0	84	68
A05337	5.1	24.0	76	61
A05338[a]	NO TEST	16.0	NO TEST	52
A05339	5.0	19.0	72	79
A05340[a]	NO TEST	26.0	NO TEST	57
MEAN	5.1	21.4	77	63
S.D.	.10	3.97	6.1	10.5
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM	
A05356	4.3	23.0	67	183
A05357	5.8	23.0	116	89
A05358[a]	NO TEST	16.0	60	85
A05359	5.3	20.0	92	50
A05360[a]	NO TEST	18.0	NO TEST	84
MEAN	5.1	20.0	84	98
S.D.	.76	3.08	25.5	49.9

PROJECT: S400658 SPECIES: MOUSE SEX: MALES WEEK : 0 PAGE: 1

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	RCHE-COL[b] MCM/ML	PCHE-COL[b] MCM/ML	BCHE-COL MCM/ML
A001-1H1	2.2	19.3	45.7
A006-2H2	2.5	24.3	52.6
A010-2H1	2.2	25.7	51.4
A027-1H1	2.4	21.7	59.4
A027-2HT	2.3	22.9	53.7
A028-2H1	3.3	20.3	56.8
A034-2H1	1.6	25.7	43.1
A036-2HT	3.4	19.7	53.1
A038-2HT	2.2	16.4	44.3
A042-1H2	2.8	21.2	52.6
MEAN	2.5	21.7	51.3
S.D.	.54	2.99	5.33

PROJECT: S400658 SPECIES: MOUSE SEX: FEMALES WEEK : 0 PAGE: 1

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	RCHE-COL[b] MCM/ML	PCHE-COL[b] MCM/ML	BCHE-COL MCM/ML
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM
A013-2[a] H2	2.8	NO TEST	54.3
A015-2HT	3.0	28.3	52.5
A017-2H1	2.0	28.0	51.7
A021-2H1	3.2	27.4	52.6
A025-2H1	2.2	26.3	52.6
A027-2H1	3.3	25.3	50.0
A030-2[a]	2.5	NO TEST	53.4
A032-1H1	2.7	25.4	54.0
A036-1HT	2.4	24.9	44.6
A036-2HT	2.7	23.4	53.7
MEAN	2.7	26.1	51.9
S.D.	.42	1.69	2.87

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	PCHE-COL[b] MCM/ML	RCHE-COL[b] MCM/ML	BCHE-COL MCM/ML
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM
A05261HT	17.1	2.3	64.6
A05262H1	23.1	2.3	71.4
A05263H2	19.4	3.7	57.3
A05264H2	17.6	3.2	57.6
A05265H2	21.7	3.7	69.6
MEAN	19.8	3.0	64.1
S.D.	2.59	.71	6.56
GROUP: 02	DOSE LEVEL: 375		DOSAGE UNIT: PPM
A05281HT	17.6	3.9	42.4
A05282HT	17.8	3.1	50.9
A05283HT	14.3	3.0	51.2
A05284HT	21.5	3.9	53.8
A05285H2	19.6	5.6	26.3
MEAN	18.2	3.9	44.9[S-]
S.D.	2.67	1.04	11.26
GROUP: 03	DOSE LEVEL: 750		DOSAGE UNIT: PPM
A05301HT	19.4	3.5	50.6
A05302H1	14.8	3.5	46.5
A05303H1	18.5	3.3	30.4
A05304H1	24.9	2.5	47.4
A05305H1	18.2	2.5	40.4
MEAN	19.2	3.1	43.1[S-]
S.D.	3.65	.52	7.98
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM
A05321H1	23.1	2.9	40.7
A05322H1	24.9	3.5	24.6
A05323HT	22.6	2.2	37.7
A05324H1	24.5	2.3	42.7
A05325H1	20.1	2.8	38.3
MEAN	23.0	2.7	36.8[S-]
S.D.	1.90	.52	7.10

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	PCHE-COL[b] MCM/ML	RCHE-COL[b] MCM/ML	BCHE-COL MCM/ML
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM
A05341H1	23.1	2.2	34.5
A05342H1	20.8	2.3	29.8
A05343H1	21.7	2.6	38.3
A05344H1	30.5	3.7	47.4
A05345H2	22.2	2.4	17.6
MEAN	23.7	2.6	33.5[S-]
S.D.	3.91	.61	11.00
GROUP: 06	DOSE LEVEL: 6000		DOSAGE UNIT: PPM
A05362HT	23.6	3.6	21.2
A05363H1	25.2	2.2	23.7
A05364H1	17.6	2.8	14.0
A05365HT	25.2	2.3	12.0
A05366HT	18.9	3.2	15.8
MEAN	22.1	2.8	17.3[S-]
S.D.	3.60	.59	4.93

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	PCHE-COL[b] MCM/ML	RCHE-COL[b] MCM/ML	BCHE-COL MCM/ML
GROUP: 01	DOSE LEVEL: CONTROL		DOSAGE UNIT: PPM
A05271H2	28.6	2.2	70.2
A05272H1	23.1	3.2	76.0
A05273H3	31.0	2.4	53.2
A05274HT	36.0	2.6	83.1
A05275H1	26.3	3.7	69.3
MEAN	29.0	2.8	70.4
S.D.	4.88	.62	11.06
GROUP: 02	DOSE LEVEL: 375		DOSAGE UNIT: PPM
A05291H1	22.6	3.2	53.2
A05292H2	27.7	2.8	34.2
A05293H2	33.3	2.3	40.4
A05294H1	28.6	2.5	40.7
A05295H1	29.6	3.1	48.9
MEAN	28.4	2.8	43.5[S-]
S.D.	3.86	.38	7.54
GROUP: 03	DOSE LEVEL: 750		DOSAGE UNIT: PPM
A05311H3	29.1	2.8	48.0
A05312H1	24.0	2.3	29.5
A05313HT	24.0	2.9	73.1
A05314H1	24.2	2.5	32.2
A05315H1	31.0	2.5	49.4
MEAN	26.5	2.6	46.4[S-]
S.D.	3.35	.24	17.40
GROUP: 04	DOSE LEVEL: 1500		DOSAGE UNIT: PPM
A05331[c]HT	29.1	NO TEST	34.8
A05332HT	31.0	2.4	42.4
A05333H2	30.7	3.0	45.0
A05334H1	24.9	3.2	48.3
A05335H1	31.9	3.0	45.6
MEAN	29.5	2.9	43.2[S-]
S.D.	2.77	.35	5.15

APPENDIX 4
INDIVIDUAL & MEAN CLINICAL CHEMISTRY VALUES
FOUR-WEEK DIETARY STUDY OF UC-54229 IN MICE

ANIMAL NUMBER	PCHE-COL MCM/ML	RCHE-COL MCM/ML	BCHE-COL MCM/ML
GROUP: 05	DOSE LEVEL: 3000		DOSAGE UNIT: PPM
A05351H1	27.2	2.3	48.6
A05352H1	28.6	2.9	29.2
A05353H1	30.5	2.8	36.8
A05354H1	28.2	2.5	36.0
A05355H1	35.1	2.1	42.4
MEAN	29.9	2.5	38.6S-
S.D.	3.13	.33	7.29
GROUP: 06	DOSE LEVEL: 6000		DOSAGE UNIT: PPM
A05373H1	20.8	3.0	18.1
A05377H1	21.7	2.6	27.5
A05378H1	21.9	2.2	27.5
A05380H2	29.8	3.5	16.1
MEAN	23.5	2.8	22.3S-
S.D.	4.19	.56	6.06

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Appendix 5
References
Four-Week Dietary Study of UC-54229 in Mice

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Appendix 5 - Continued
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Four-Week Dietary Study of UC-54229 in Mice

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Appendix 5 - Continued
References
Four-Week Dietary Study of UC-54229 in Mice

HEMATOLOGY

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Appendix 5 - Continued
References
Four-Week Dietary Study of UC-54229 in Mice

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Plasma Cholinesterase (P CHE), Fasting Glucose (GLUCOSE), Total Protein (T PROT), and Blood Urea Nitrogen (BUN).

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Four-Week Dietary Study of UC-54229 in Mice

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TYPE: INT. SUPP FLWP

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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:
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0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:
Carbamate chloride, 2,3-dihydro-2,3-dimethyl-7-benzofuranyl-N-(trimethylammoniumacetyl)-N-methyl-

CAS#
unknown ← UC 54229

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	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. OCCC/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 REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 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~~	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

SBTOX

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

COMMENTS

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COMMENT
SUBACUTE ORAL TOXICITY IN RATS IS OF HIGH CONCERN. SPRAGUE-DAWLEY RATS (10/SEX/DOSE) WERE FED DIETARY LEVELS OF 0, 133, 237, 422, 750, OR 1330 PPM (0, 6.65, 11.9, 21.1, 37.5, 66.5 MG/KG/DAY IN FEMALES AND 0, 7.98, 14.2, 25.3, 45.0, 79.8 MG/KG/DAY IN MALES) FOR FOUR WEEKS. PLASMA ACETYLCHOLINESTERASE WAS SIGNIFICANTLY INHIBITED (I.E., MORE THAN 25% INHIBITED COMPARED TO CONTROLS) IN MALES AT ALL DOSE LEVELS. BRAIN ACETYLCHOLINESTERASE WAS SIGNIFICANTLY INHIBITED (I.E., MORE THAN 25% INHIBITED COMPARED TO CONTROLS) IN BOTH SEXES AT ALL DOSE LEVELS. THE FOLLOWING WERE ALSO NOTED: DECREASED BODY WEIGHT (MALES AT 45.0 MG/KG/DAY, (FEMALES AT 21.1 MG/KG/DAY), DECREASED HEART WEIGHT (MALES AT 79.8 MG/KG/DAY), DECREASED LIVER WEIGHT (MALES AT 45.0 MG/KG/DAY, FEMALES AT 66.5 MG/KG/DAY), AND INCREASED RELATIVE BRAIN (MALES AT 45.0 MG/KG/DAY, FEMALES AT 6.65 AND 21.1 MG/KG/DAY), KIDNEY (FEMALES AT 37.5 MG/KG/DAY), HEART (FEMALES AT 21.1 AND 37.5 MG/KG/DAY), AND TESTES (MALES AT 45.0 MG/KG/DAY). DOSE-RELATED EFFECTS WERE NOTED FOR THE INCIDENCE OF CLINICAL SIGNS (HUNCHED POSITION, ROUGH HAIRCOAT, AND HYPERACTIVITY IN BOTH SEXES, PRIMARILY AT TWO HIGHEST DOSE GROUPS) AND POLYPNEA (MALES AND FEMALES IN HIGH-DOSE GROUP). SUBACUTE ORAL TOXICITY IN MICE IS OF HIGH CONCERN. CD-1 MICE (10/SEX/DOSE) WERE FED DIETARY LEVELS OF 0, 375, 750, 1500, 3000, OR 6000 PPM (0, 45, 90, 180, 360, 720 MG/KG/DAY) FOR FOUR WEEKS. AT 720 MG/KG/DAY, MORTALITY WAS 20% IN MALES AND 60% IN FEMALES. BODY WEIGHTS WERE DEPRESSED IN BOTH SEXES AT 90 MG/KG/DAY. BRAIN ACETYLCHOLINESTERASE WAS SIGNIFICANTLY INHIBITED (I.E., MORE THAN 25% INHIBITED COMPARED TO CONTROLS) IN BOTH SEXES AT ALL DOSE LEVELS. THE FOLLOWING DOSE-RELATED EFFECTS WERE ALSO NOTED: DECREASED ABSOLUTE LIVER WEIGHT (MALES AT 90 MG/KG/DAY, FEMALES AT 45 MG/KG/DAY), DECREASED ABSOLUTE HEART WEIGHT (MALES AT 180 MG/KG/DAY), AND INCREASED RELATIVE BRAIN WEIGHT (MALES AT 180 MG/KG/DAY, FEMALES AT 90 MG/KG/DAY). TREATMENT-RELATED CLINICAL SIGNS INCLUDED HUNCHED POSITION, THINNESS, ROUGH HAIRCOAT, AND POLYPNEA, PRIMARILY IN THE TWO HIGHEST DOSE GROUPS (BOTH SEXES). SUBACUTE ORAL TOXICITY IN RATS IS OF MODERATE CONCERN. MALE CD RATS (10/GROUP) WERE EXPOSED TO 0 OR 500 PPM (30 MG/KG/DAY) VIA THE DIET FOR SEVEN DAYS. IN THE TREATMENT GROUP, MEAN BODY WEIGHT, BODY WEIGHT GAIN, AND FOOD CONSUMPTION VALUES WERE REDUCED 10.5%, 57.4%, AND 10.6%, RESPECTIVELY (STATISTICALLY SIGNIFICANT). MEAN ERYTHROCYTE, PLASMA, AND BRAIN CHOLINESTERASE VALUES WERE REDUCED 8%, 50%, AND 55%, RESPECTIVELY, IN TREATED ANIMALS COMPARED TO CONTROLS (STATISTICALLY SIGNIFICANT). THERE WERE NO MORTALITIES, AND PHYSICAL OBSERVATIONS WERE NOT SIGNIFICANTLY DIFFERENT IN TREATED ANIMALS COMPARED TO CONTROLS.