


FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129
IN THE RAT

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Safety Assessment Project Number 2448

Department of Product Safety Assessment


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DEPARTMENT OF PRODUCT SAFETY ASSESSMENT

G. D. Searle & Co., Skokie, IL

Title: Four Week Dietary Admix Toxicity Study of SC-19129
in the Rat

Author(s): David E. Semler, Stuart Levin, and Linda Gorman

Study No: S.A. 2448

Date: January 14, 1985

Type of Report: Final

Summary:

SC-19129 was administered by dietary admix for four weeks to Charles River CD rats (10 to 15/sex/group) at intended dosages of 250, 500, and 1000 mg/kg. Based on weekly body weight and food consumption measurements, the dosages received were within 9% of those intended. The control group received Purina Certified Rodent Chow 5002 (meal). Ten animals/sex/group were sacrificed after 4 weeks of dosing. The remaining 5 control and high dose animals per sex were sacrificed 4 weeks after termination of dosing.

No animals died.

There were no test article-related clinical observations or ophthalmic changes.

There were no test article-related effects on body weights, feed consumption, clinical laboratory parameters, or organ weights or ratios.

No test article-related changes were noted in the gross or microscopic examinations.

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129
IN THE RAT

INTRODUCTION

SC-19129 was administered by dietary admix to Charles River CD rats of both sexes for four weeks. The purpose of this study was to determine toxic effects as evidenced by clinical signs and specific organ damage and to assess reversal of any effects observed.

MATERIALS AND METHODS

Materials

The chemical name of SC-19129 is N-L- β -aspartyl-L-phenylalanine, l-methyl ester. The identity, strength, purity, and composition of the test article (lot number 84K-047-101) have been determined. Samples were taken to determine the homogeneity and concentration of test article in carrier. These samples were frozen and will be analyzed at a future date. A summary of the existing analytical data is in Appendix I. A summary of the analytical data for compound stability and the stability, homogeneity, and concentration of test article in carrier will be appended to this report.

SC-19129 was mixed with Purina Certified Rodent Chow 5002 (meal). Separate diets were prepared for each sex and treatment group every time animals were weighed. The concentration of SC-19129 in the diet was adjusted at each diet preparation interval based on estimated food consumption and

body weight to provide the intended dosages. Control animals received chow without SC-19129. Actual dosages, based on individual body weight and feed consumption, are summarized in Table 4.3.

Animals, housing and feed

Charles River CD rats, 52 males and 53 females, 21 days old upon arrival were acclimated to laboratory conditions (72 \pm 5°F temperature, 25% or greater humidity, and a 12-hour light, 12-hour dark cycle) for 13 days before the study began. Purina Certified Rodent Chow 5002 (meal) and tap water (municipal water supply) were available ad libitum. The animals were individually housed in stainless steel cages. Animals used in the study (50 males and 50 females) were selected on the basis of weight change, feed consumption, and physical examination findings. Healthy animals in excess of those needed were deleted by a random process.

Animals used in the study were identified with numbered ear tags.

Experimental design

Group Name	Number	Intended ¹ Dosage (mg/kg/day)	Number of animals/sex	Sacrifice Animals/Sex ²	
				Week 5	Week 9
Control	1	0	15	10	5
Low	2	250	10	10	0
Medium	3	500	10	10	0
High	4	1000	15	10	5

¹The calculated dosage, based on food consumption measurement, and body weights, is presented in Table 4.3.

²Dosing of reversal animals was discontinued on day 28.

To distribute animals into treatment groups, animals of each sex were ranked by weight using the last pretreatment body weight. Animals were then assigned to groups in a random fashion using the following method: 1) the list was divided into blocks equal to the number of animals in the group to be selected; 2) one animal was randomly selected from each block and assigned to the group; 3) the same procedure was used for each of the remaining groups.

Food admixed with SC-19129 was first administered on October 3, 1984. The admix was available ad libitum until the start of fasting on October 30 or 31, 1984. The main group animals were sacrificed on October 31 or November 1, 1984. Reversal animals were sacrificed on November 28, 1984. A copy of the protocol and amendments is Appendix J.

Clinical observations and physical and ophthalmic examinations

Physical examinations were done on day -6 and once weekly during the treatment and reversal periods. Daily evaluations of general appearance and behavior were made during the treatment period in the morning on weekdays that physical exams were not performed. Animals were checked at least once daily for survival and moribundity.

Body and feeder weights were measured on days -7, -1, 1, 3, 6, 8, 10, 15, 22, 28, 36, 43, 50, and 56. Final body weights were taken the day of sacrifice.

An ophthalmic examination was performed on all animals on day 27.

Clinical laboratory determinations

On day 29 or 30, animals to be sacrificed were anesthetized with ether after an overnight fast and blood was collected from the abdominal aorta. The blood obtained was used to determine the following parameters: hematocrit, hemoglobin concentration, total red blood cell count, total white blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, differential smear evaluation, prothrombin time, platelet count, alanine aminotransferase activity, aspartate aminotransferase activity, alkaline phosphatase activity, glucose concentration, sodium concentration, potassium concentration, calcium concentration, chloride concentration, urea concentration, cholesterol concentration, total bilirubin concentration, total protein concentration,

albumin concentration, globulin concentration (calculated), and albumin/globulin ratio (calculated). Bone marrow smears were prepared for possible future evaluation.

Urine was collected on day 28 or 29 from animals scheduled to be sacrificed on day 29 or 30, respectively. The urine obtained was used to determine the following parameters: volume, pH, refractive index, glucose, bilirubin, protein, ketones, occult blood, urobilinogen, and microscopic examination of centrifuged sediment.

Postmortem procedures

At the end of the treatment and reversal periods, all appropriately assigned rats were anesthetized, exsanguinated, and then necropsied.

The following organs were weighed in their fresh state during the week 5 sacrifice: adrenal, brain, epididymis, heart, kidney, liver, ovary, pituitary, prostate, submaxillary salivary gland, spleen, testis, thymus, thyroid¹, and uterus. No organ weights were measured for reversal animals.

Representative samples of the following organs were taken for microscopic examination: adrenal gland, aorta, bone marrow and bone (sternum and femur), brain, epididymis, esophagus, eye, heart, small and large intestine (duodenum, jejunum, ileum, cecum, rectum, and colon) kidney, lacrimal (Harderian) gland, liver, lung, lymph node (submaxillary

¹The parathyroid was weighed with the thyroid and was examined histologically when included in the section of the thyroid.

and mesenteric), mammary gland (females), ovary, pancreas, peripheral nerve, pituitary, prostate, parathyroid¹, spinal cord, salivary gland, skin, skeletal muscle, spleen, stomach, seminal vesicle, testis, thyroid gland, thymus, tongue, trachea, urinary bladder, uterus, and vagina. The testes were preserved in Bouin's fixative and the eyes and Harderian glands were preserved in Zenkers fixative. All other tissues were preserved in Carson's fixative (buffered 10% formalin). After fixation, the tissues were embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Microscopic examination was done on all tissues of the control and high dose animals killed at the end of the treatment period (week 5). Selected tissues of low and medium dose animals numbered 84-1903, 84-1921, 84-1922, and 84-1933 were examined to evaluate the lesions seen at necropsy.

Statistical procedures

Means and standard deviations were calculated for all quantitative parameters. The following variables were selected for further statistical analysis: body weights, body weight changes, organ weights, organ/brain weight ratios, organ/body weight ratios, feed consumption, hematocrit, hemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, total red blood cell count, total white blood cell count, platelet count, prothrombin time, percent mature neutrophils and lymphocytes, alkaline phosphatase activity,

¹The parathyroid was weighed with the thyroid and was examined histologically when included in the section of the thyroid.

urea concentration, glucose concentration, alanine aminotransferase activity, aspartate aminotransferase activity, sodium concentration, potassium concentration, chloride concentration, calcium concentration, cholesterol concentration, total bilirubin concentration, total protein concentration, albumin concentration, globulin concentration, albumin/globulin ratio, and urine refractive index.

The statistical inferences were derived from one-way analysis of variance (Winer, 1971) performed for each sex at each sampling interval. If the F-test among groups was significant ($p < 0.05$), two-tailed t-tests of each treated group versus the control group were performed using the pooled error term from the one-way analysis of variance. A homogeneity-of-variance test using the Bartlett-Box method was also performed (Box, 1949). No compensation was made for heterogeneity of variance in calculating the statistics. Significant ($p < 0.05$) t-tests, one-way analyses of variance, and Bartlett-Box tests have been indicated in Tables 2 through 8.

Data storage

The protocol and related documents, raw data, specimens, and final report are stored at G. D. Searle & Co., Skokie, IL.

Quality assurance statement

The Quality Assurance Statement is in Appendix K.

Professionals

The following professionals were involved in the conduct of this study:

Study Director	D. Semler
Study Pathologist	S. Levin
Analytical Coordinator	K. Pilipauskas
Clinical Chemistry	J. North
Clinical Hematology	R. Leonard
Data Assessment	G. Kirby
Histology	P. Hemmer
Laboratory Animal Resources	J. Erickson
Study Supervisor	L. Gorman
Statistics	P. Sanders
Product Development	
Analytical Department	J. Jiu
Ophthalmology	Dr. W. Vestre
	School of Veterinary
	Medicine
	Purdue University

RESULTS AND DISCUSSION

Quality and integrity of the data

There were no known circumstances that may have affected the quality or integrity of the data.

Mortality and clinical observations

No animals died.

Watery stools, dermal ulcerations, hair loss, or a crust around the eye were seen in one or a few animals (Table 1). These signs were not considered test article-related.

Body weights and feed consumption

There were no test article-related effects on body weights or feed consumption (Figures 1 and 2, Tables 2 through 4, and Appendices A and B).

Ophthalmic examinations

There were no test article-related ophthalmic changes (Appendix F).

Clinical laboratory determinations

There were no test article-related changes in the hematology, clinical chemistry, and urinalysis parameters examined (Tables 5 through 7, and Appendices C through E).

Pathology and organ weights

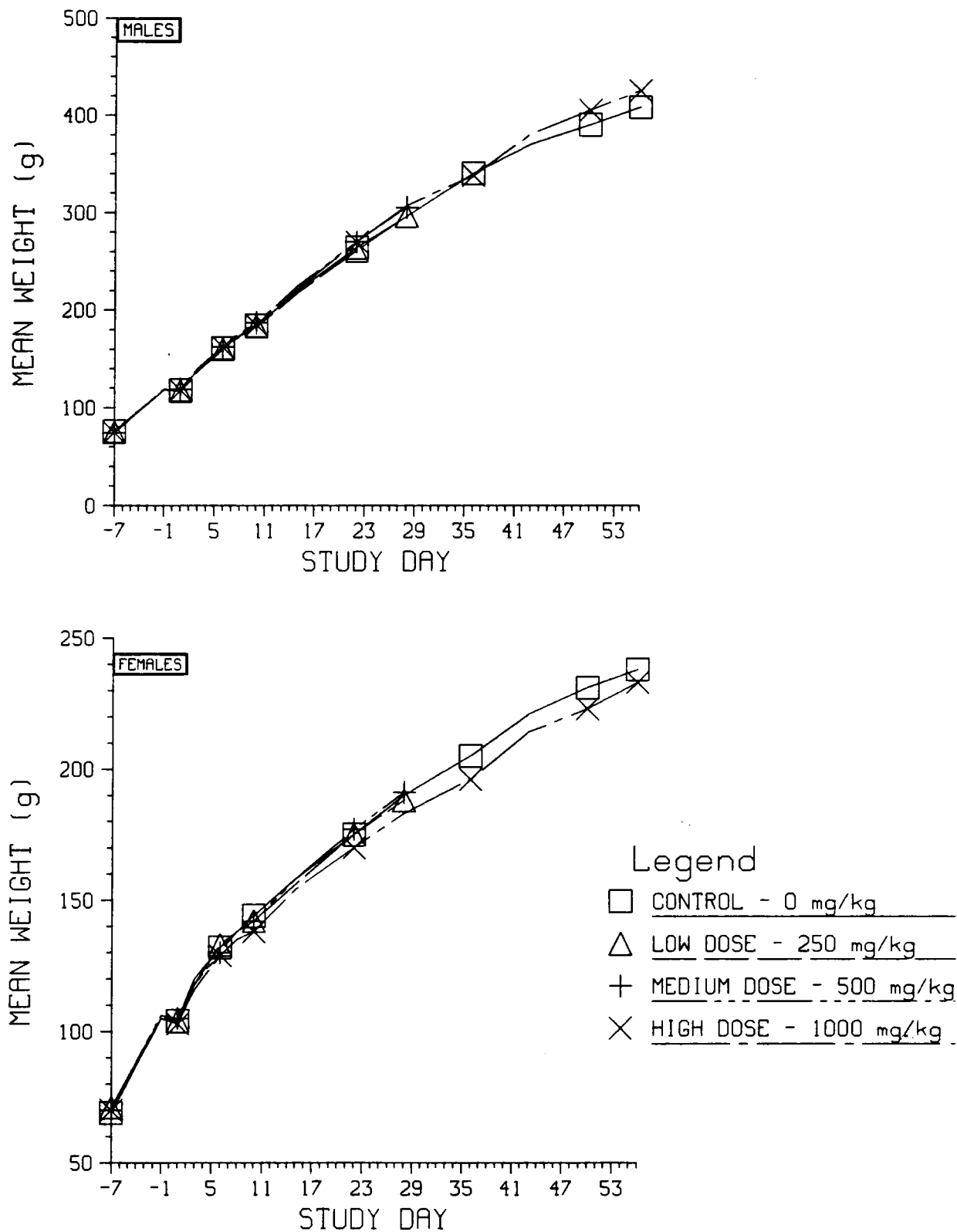
There were no test article-related changes in organ weights or ratios (Table 8 and Appendix G).

Individual animal gross and microscopic findings are in Appendix H. No test article-related changes were noted in either the gross (Table 9) or microscopic (Table 10) examinations. Slight variations in the incidence of specific findings between groups were ascribed to chance. Generally, the types of changes seen in this study were similar to those regularly seen in this strain of rat.

FIGURE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

BODY WEIGHTS



S.A. 2448

FIGURE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEED CONSUMPTION

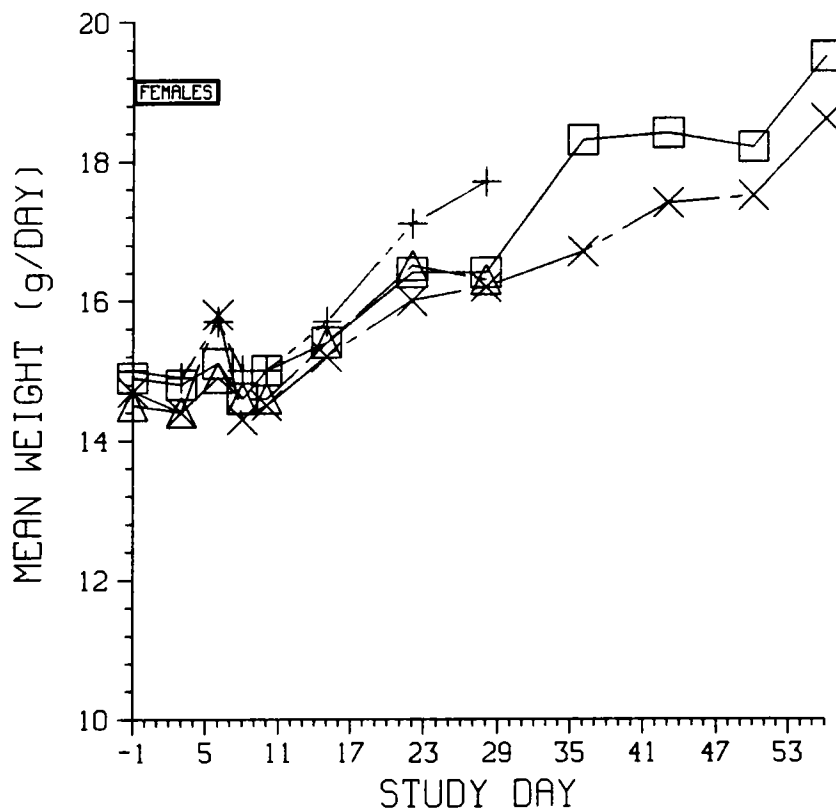
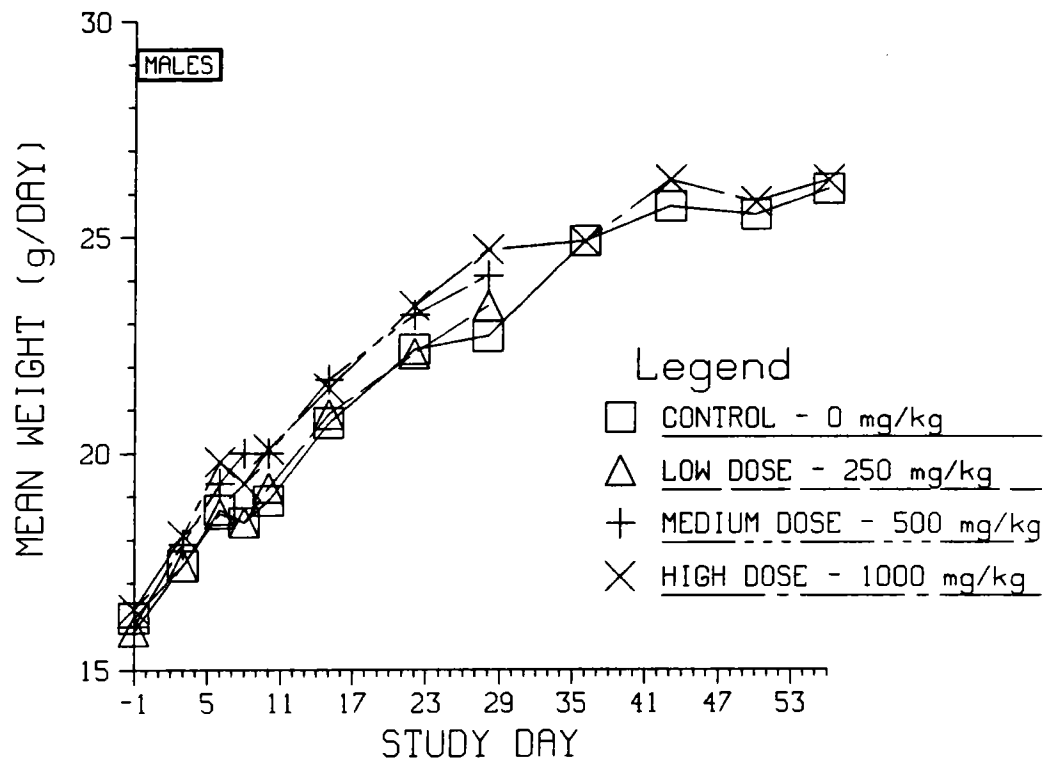


TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129
IN THE RATClinical Observations¹Number of Animals Displaying Signs per
Dose Group (20 to 30 Animals/Group)

Observations	Treatment Groups			
	Control	Low	Medium	High
Dermal ulceration	1	1	0	1
Hair loss	1	1	0	2
Watery stools	0	0	0	1
Crust around eye	1	1	0	0

¹ Summary of observations made during the daily observations and during the physical examinations. Sexes have been pooled.

TABLE 2.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE BODY WEIGHTS (g)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-7	-1	1	3	6	8	10
CONTROL	76.	118.	118.	138.	161.	173.	184.
0 mg/kg	4.8	7.2	8.4	9.2	10.9	12.8	15.3
	15	15	15	15	15	15	15
LOW DOSE	75.	118.	117.	137.	160.	173.	183.
250 mg/kg	4.2	6.6	7.0	8.0	10.3	12.7	14.0
	10	10	10	10	10	10	10
MEDIUM DOSE	74.	119.	119.	140.	162.	176.	187.
500 mg/kg	5.3	7.8	8.5	9.4	10.1	11.8	12.9
	10	10	10	10	10	10	10
HIGH DOSE	75.	118.	118.	137.	162.	174.	185.
1000 mg/kg	4.9	8.7	9.3	11.3	13.5	15.1	17.6
	15	15	15	15	15	15	15

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL
NRA : NO REMAINING ANIMALS

TABLE 2.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE BODY WEIGHTS (g)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	15	22	28	36	43	50	56
CONTROL	220.	264.	296.	340.	370.	390.	408.
0 mg/kg	19.7	24.2	30.1	37.7	41.2	42.4	42.4
	15	15	15	5	5	5	5
LOW DOSE	218.	261.	296.	NRA	NRA	NRA	NRA
250 mg/kg	17.8	21.5	25.6				
	10	10	10				
MEDIUM DOSE	225.	270.	305.	NRA	NRA	NRA	NRA
500 mg/kg	15.9	18.6	21.7				
	10	10	10				
HIGH DOSE	222.	270.	307.	338.	381.	405.	425.
1000 mg/kg	21.5	29.0	35.3	33.6	56.4	60.7	57.9
	15	15	15	5	5	5	5

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TABLE 2.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE BODY WEIGHTS (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-7	-1	1	3	6	8	10
CONTROL	69.	105.	104.	120.	132.	138.	144.
0 mg/kg	3.5	6.4	6.6	7.6	8.4	8.8	10.1
	15	15	15	15	15	15	15
LOW DOSE	71.	105.	104.	118.	133.	138.	142.
250 mg/kg	4.0	9.1	10.8	12.8	14.1	16.6	17.8
	10	10	10	10	10	10	10
MEDIUM DOSE	70.	106.	105.	118.	130.	138.	142.
500 mg/kg	4.4	6.9	8.4	8.4	9.1	10.1	9.8
	10	10	10	10	10	10	10
HIGH DOSE	70.	105.	103.	116.	129.	135.	138.
1000 mg/kg	5.0	8.4	8.3	10.0	10.3	11.3	12.2
	15	15	15	15	15	15	15

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TABLE 2.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE BODY WEIGHTS (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	15	22	28	36	43	50	56
CONTROL	158.	175.	190.	205.	221.	231.	238.
0 mg/kg	10.9	13.6	14.2	20.3	23.5	21.4	27.4
	15	15	15	5	5	5	5
LOW DOSE	156.	175.	188.	NRA	NRA	NRA	NRA
250 mg/kg	19.0	21.9	24.8				
	10	10	10				
MEDIUM DOSE	158.	177.	191.	NRA	NRA	NRA	NRA
500 mg/kg	11.3	11.4	14.1				
	10	10	10				
HIGH DOSE	154.	170.	183.	196.	214.	223.	233.
1000 mg/kg	13.7	17.5	19.1	19.5	20.7	23.9	26.5
	15	15	15	5	5	5	5

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TABLE 3.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	3	6	8	10	15	22
CONTROL	19.	23.	12.	11.	36.	44.
0 mg/kg	1.9	3.2	3.7	3.4	5.0	9.3
	15	15	15	15	15	15
LOW DOSE	20.	22.	13.	11.	35.	43.
250 mg/kg	2.0	2.9	3.3	2.9	4.4	6.3
	10	10	10	10	10	10
MEDIUM DOSE	21.	23.	14.	11.	38.	45.
500 mg/kg	1.8	2.8	3.1	2.2	3.6	4.9
	10	10	10	10	10	10
HIGH DOSE	19.	25.	13.	11.	36.	48.
1000 mg/kg	3.1	3.6	3.3	3.0	5.3	8.5
	15	15	15	15	15	15

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MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	28	36	43	50	56
CONTROL	33.	36.	30. B	20.	18.
0 mg/kg	8.5	7.3	4.2	4.8	2.3
	15	5	5	5	5
LOW DOSE	35.	NRA	NRA	NRA	NRA
250 mg/kg	5.6				
	10				
MEDIUM DOSE	36.	NRA	NRA	NRA	NRA
500 mg/kg	4.0				
	10				
HIGH DOSE	37.	28.	43.	24.	20.
1000 mg/kg	8.0	15.7	24.8	7.6	4.8
	15	5	5	5	5

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TABLE 3.2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	3	6	8	10	15	22
CONTROL	15. B	13.	6.	6.	14.	17.
0 mg/kg	2.5	3.8	3.3	2.5	3.0	5.7
	15	15	15	15	15	15
LOW DOSE	14.	15.	5.	4.	14.	19.
250 mg/kg	3.3	3.6	3.1	3.2	3.1	4.8
	10	10	10	10	10	10
MEDIUM DOSE	13.	13.	8.	4.	16.	19.
500 mg/kg	1.3	4.1	2.4	2.7	2.9	5.1
	10	10	10	10	10	10
HIGH DOSE	13.	13.	5.	4.	16.	16.
1000 mg/kg	3.4	2.1	3.0	3.0	3.2	5.4
	15	15	15	15	15	15

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 NRA : NO REMAINING ANIMALS

TABLE 3.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	28	36	43	50	56
CONTROL	15.	17.	16.	10.	7.
0 mg/kg	3.7	6.0	5.7	3.1	8.3
	15	5	5	5	5
LOW DOSE	13.	NRA	NRA	NRA	NRA
250 mg/kg	3.8				
	10				
MEDIUM DOSE	14.	NRA	NRA	NRA	NRA
500 mg/kg	4.8				
	10				
HIGH DOSE	13.	11.	19.	9.	10.
1000 mg/kg	4.2	7.0	14.5	4.8	5.5
	15	5	5	5	5

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NRA : NO REMAINING ANIMALS

TABLE 4.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE FEED CONSUMPTION (g/DAY)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-1	3	6	8	10	15
CONTROL	16.2	17.4	18.7	18.4	18.9	20.7
0 mg/kg	0.99	1.42	1.44	1.70	2.17	2.11
	15	15	15	15	15	15
LOW DOSE	15.9	17.4	18.6	18.4	19.2	20.9
250 mg/kg	0.74	1.00	1.13	1.43	1.67	1.82
	10	10	10	10	10	10
MEDIUM DOSE	16.0	17.9	19.3	20.0	20.0	21.7
500 mg/kg	1.11	1.20	1.39	1.41	1.89	1.79
	10	10	10	10	10	10
HIGH DOSE	16.4	18.1	19.8	19.3	20.1	21.5
1000 mg/k	0.96	1.40	1.64	1.89	1.99	2.27
	15	15	15	15	14	15

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TABLE 4.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE FEED CONSUMPTION (g/DAY)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22	28	36	43	50	56
CONTROL	22.4	22.7	24.9	25.7	25.5	26.1
0 mg/kg	2.26	2.69	2.91	3.17	3.45	2.62
	15	15	5	5	5	5
LOW DOSE	22.3	23.4	NRA	NRA	NRA	NRA
250 mg/kg	1.90	2.12				
	10	10				
MEDIUM DOSE	23.2	24.1	NRA	NRA	NRA	NRA
500 mg/kg	1.71	1.89				
	10	10				
HIGH DOSE	23.4	24.7	24.9	26.3	25.8	26.3
1000 mg/k	2.66	2.82	2.20	4.84	3.26	2.78
	15	15	5	5	5	5

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NRA : NO REMAINING ANIMALS

TABLE 4.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE FEED CONSUMPTION (g/DAY)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-1	3	6	8	10	15
CONTROL	14.9	14.8	15.1	14.6	15.0	15.4
0 mg/kg	0.86	2.41	1.01	1.33	1.60	1.34
	15	15	15	15	15	15
LOW DOSE	14.5	14.4	14.9	14.6	14.6	15.4
250 mg/kg	1.31	1.74	1.55	2.01	2.08	1.72
	10	10	10	10	10	10
MEDIUM DOSE	15.0	14.9	15.7	15.0	15.0	15.7
500 mg/kg	1.12	1.17	1.00	1.18	1.05	0.95
	10	10	10	10	10	10
HIGH DOSE	14.7	14.4	15.8	14.3	14.5	15.2
1000 mg/k	1.21	1.47	1.62	1.71	1.66	1.45
	15	15	15	15	15	15

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TABLE 4.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE FEED CONSUMPTION (g/DAY)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22	28	36	43	50	56
CONTROL	16.4	16.4	18.3	18.4	18.2	19.5
0 mg/kg	1.42	1.67	1.43	1.71	2.13	1.51
	15	15	5	5	5	5
LOW DOSE	16.5	16.3	NRA	NRA	NRA	NRA
250 mg/kg	1.65	1.87				
	10	10				
MEDIUM DOSE	17.1	17.7	NRA	NRA	NRA	NRA
500 mg/kg	0.91	1.02				
	10	10				
HIGH DOSE	16.0	16.2	16.7	17.4	17.5	18.6
1000 mg/k	1.34	1.44	0.99	1.34	1.90	1.64
	15	15	5	5	5	5

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TABLE 4.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
DOSAGE (mg/kg/day)
ARITHMETIC MEANS, PERCENT OF INTENDED DOSE AND CONCENTRATION

STUDY DAY	1-3	3-6	6-8	8-10	10-15	15-22	22-28
MALES							
LOW DOSE	240.46	257.51	251.23	259.87	259.06	266.31	260.09
% intended dose	96.	103.	100.	104.	104.	107.	104.
CONCENTRATION (g/kg)	1.762	2.050	2.273	2.407	2.487	2.859	3.089
MEDIUM DOSE	488.16	512.01	525.31	495.58	517.01	538.50	524.91
% intended dose	98.	102.	105.	99.	103.	108.	105.
CONCENTRATION (g/kg)	3.524	4.015	4.442	4.489	4.901	5.739	6.261
HIGH DOSE	999.83	1039.04	964.24	1025.39	1092.45	1088.37	1057.51
% intended dose	100.	104.	96.	103.	109.	109.	106.
CONCENTRATION (g/kg)	7.048	7.828	8.411	9.244	10.370	11.454	12.368
FEMALES							
LOW DOSE	253.95	245.85	262.15	242.96	258.85	262.54	241.65
% intended dose	102.	98.	105.	97.	104.	105.	97.
CONCENTRATION (g/kg)	1.953	2.063	2.434	2.326	2.500	2.622	2.688
MEDIUM DOSE	523.63	522.76	496.25	499.67	509.93	539.38	517.28
% intended dose	105.	105.	99.	100.	102.	108.	103.
CONCENTRATION (g/kg)	3.906	4.125	4.438	4.658	4.869	5.273	5.369
HIGH DOSE	1030.96	1049.46	935.04	994.47	1020.44	1044.77	995.42
% intended dose	103.	105.	94.	99.	102.	104.	100.
CONCENTRATION (g/kg)	7.813	8.125	8.650	9.363	9.797	10.563	10.824

TABLE 5.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE CLINICAL CHEMISTRY, STUDY DAYS 29-30
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	AST U/L	ALT U/L	AP U/L	GLUCOSE mmol/L	UREA mmol/L	TOT BILI mmol/L	CHOL mmol/L
CONTROL	105.	18. B	118. B	5.6	4.4	2.3	1.1
0 mg/kg	21.4	8.7	35.0	0.72	0.40	0.89	0.23
	9	9	9	9	9	9	9
LOW DOSE	91.	17.	111.	6.4	4.7	1.9	1.1
250 mg/kg	20.3	4.8	21.8	1.09	0.74	0.70	0.14
	10	10	10	10	10	10	10
MEDIUM DOSE	91.	20.	118.	5.7	4.1	1.8	1.0
500 mg/kg	20.1	5.7	11.4	1.09	0.54	1.04	0.28
	10	10	10	10	10	10	10
HIGH DOSE	95.	17.	117.	5.4	4.2	2.1	1.2
1000 mg/kg	30.2	3.0	21.3	1.04	0.63	0.81	0.33
	9	9	9	9	9	9	9

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TABLE 5.1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE CLINICAL CHEMISTRY, STUDY DAYS 29-30

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	NA mmol/L	K mmol/L	CL mmol/L	CA mmol/L	T PRO g/L	ALB g/L	GLOB g/L	A/G
CONTROL	149.	5.2 B	111.	2.42	58.	33.	24.	1.37
0 mg/kg	2.4	0.19	3.8	0.089	1.5	1.5	1.5	0.131
	9	9	9	9	9	9	9	9
LOW DOSE	148.	5.0	109.	2.43	58.	33.	24.	1.38
250 mg/kg	3.3	0.41	2.8	0.097	2.7	0.8	2.8	0.158
	10	10	10	10	10	10	10	10
MEDIUM DOSE	149.	5.2	109.	2.42	57.	34.	23.	1.50
500 mg/kg	3.5	0.25	3.5	0.109	3.8	2.0	3.1	0.196
	10	10	10	10	10	10	10	10
HIGH DOSE	148.	5.3	110.	2.41	55.	33.	23.	1.45
1000 mg/kg	2.9	0.50	2.7	0.099	2.6	1.1	3.0	0.220
	9	9	9	9	9	9	9	9

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TABLE 5.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE CLINICAL CHEMISTRY, STUDY DAYS 29-30
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	AST U/L	ALT U/L	AP U/L	GLUCOSE mmol/L	UREA mmol/L	TOT BILI mmol/L	CHOL mmol/L
CONTROL	87.	16. B	84.	5.7	5.0	2.4	1.4
0 mg/kg	17.4	4.4	15.8	1.27	0.78	0.89	0.18
	10	10	10	10	10	10	10
LOW DOSE	92.	20.	78.	5.2	5.0	2.0	1.2
250 mg/kg	20.7	10.7	20.5	0.81	0.87	0.58	0.37
	10	10	10	10	10	10	10
MEDIUM DOSE	95.	18.	83.	5.7	5.1	1.9	1.3
500 mg/kg	25.6	11.4	11.5	1.14	0.83	0.81	0.40
	10	10	10	10	10	10	10
HIGH DOSE	86.	15.	84.	5.3	4.5	1.9	1.2
1000 mg/kg	30.1	3.6	16.0	0.68	0.61	0.76	0.33
	10	10	10	10	10	10	10

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TABLE 5.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE CLINICAL CHEMISTRY, STUDY DAYS 29-30
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	NA mmol/L	K mmol/L	CL mmol/L	CA mmol/L	T PRO g/L	ALB g/L	GLOB g/L	A/G
CONTROL	149.	4.8	112.	2.43	60.	35.	25.	1.42
0 mg/kg	4.4	0.69	3.7	0.108	3.5	1.9	3.3	0.212
	10	10	10	10	10	10	10	10
LOW DOSE	147.	4.8	111.	2.40	58.	34.	24.	1.45
250 mg/kg	2.9	0.48	3.3	0.089	2.9	1.4	2.5	0.155
	10	10	10	10	10	10	10	10
MEDIUM DOSE	147.	4.8	112.	2.40	58.	34.	23.	1.50
500 mg/kg	3.5	0.60	2.6	0.077	3.0	1.3	2.8	0.178
	10	10	10	10	10	10	10	10
HIGH DOSE	147.	4.9	110.	2.42	58.	35.	23.	1.57
1000 mg/kg	2.4	0.45	2.4	0.085	2.3	2.8	2.9	0.278
	10	10	10	10	10	10	10	10

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TABLE 6.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE HEMATOLOGY, STUDY DAYS 29-30
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	HGB g/dL	HCT L/L	RBC X10E12/L	MCV fL	MCH pg	MCHC g/dL	PT SECONDS	PLAT X10E9/L
CONTROL	14.9	0.429	7.36	58.2	20.2	34.7	11.8	1315.
0 mg/kg	0.67	0.0205	0.302	1.81	0.64	0.47	0.34	209.4
	9	9	9	9	9	9	8	9
LOW DOSE	15.3	0.445	7.60	58.5	20.1	34.4	12.0	1253.
250 mg/kg	0.68	0.0263	0.497	1.59	0.75	0.80	0.30	89.1
	9	9	9	9	9	9	10	9
MEDIUM DOSE	15.4	0.448	7.61	58.9	20.3	34.4	11.8	1386.
500 mg/kg	0.44	0.0168	0.376	1.72	0.83	0.87	0.50	151.8
	10	10	10	10	10	10	8	10
HIGH DOSE	15.1	0.436	7.54	57.8	20.0	34.6	11.7	1296.
1000 mg/kg	0.70	0.0280	0.436	0.94	0.64	0.91	0.45	203.0
	10	10	10	10	10	10	9	10

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TABLE 6.1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE HEMATOLOGY, STUDY DAYS 29-30

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	WBC X10E9/L	INEU + %	MNEU %	LYM %	MON + %	EOS + %	BAS + %
CONTROL	6.6	0.	8.	87.	5.	0.	0.
0 mg/kg	4.62	0.0	4.0	6.2	3.3	0.5	0.0
	9	9	9	9	9	9	9
LOW DOSE	7.8	0.	7.	89.	3.	0.	0.
250 mg/kg	2.70	0.0	2.7	3.9	3.1	0.4	0.0
	9	9	9	9	9	9	9
MEDIUM DOSE	7.6	0.	9.	87.	3.	0.	0.
500 mg/kg	4.46	0.0	6.2	6.2	1.5	0.5	0.0
	10	10	10	10	10	10	10
HIGH DOSE	7.5	0.	11.	84.	3.	1.	0.
1000 mg/kg	2.49	0.0	6.6	6.0	2.2	1.0	0.0
	10	10	10	10	10	10	10

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 + : DATA NOT STATISTICALLY ANALYZED

TABLE 6.2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE HEMATOLOGY, STUDY DAYS 29-30

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	HGB g/dL	HCT L/L	RBC X10E12/L	MCV fL	MCH pg	MCHC g/dL	PT SECONDS	PLAT X10E9/L
CONTROL	15.2	0.430	7.54	57.0 F	20.2 F	35.4	12.1	1257.
0 mg/kg	0.62	0.0187	0.399	1.56	0.58	0.74	0.40	108.6
	9	9	9	9	9	9	9	9
LOW DOSE	15.2	0.430	7.57	56.8	20.1	35.3	11.9	1195.
250 mg/kg	0.55	0.0196	0.317	1.27	0.51	1.15	0.76	89.4
	10	10	10	10	10	10	9	10
MEDIUM DOSE	15.0	0.424	7.32	57.9	20.5	35.3	12.1	1324.
500 mg/kg	0.63	0.0210	0.450	2.01	0.53	0.70	0.59	148.6
	9	9	9	9	9	9	9	9
HIGH DOSE	14.9	0.422	7.57	55.8	19.7	35.4	12.1	1298.
1000 mg/kg	0.57	0.0174	0.242	1.59	0.56	0.56	0.78	138.5
	10	10	10	10	10	10	10	10

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TABLE 6.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE HEMATOLOGY, STUDY DAYS 29-30
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	WBC X10E9/L	INEU + %	MNEU %	LYM %	MON + %	EOS + %	BAS + %
CONTROL	5.7	0.	8.	89.	2.	1.	0.
0 mg/kg	3.63	0.0	7.9	9.1	1.8	0.7	0.0
	9	9	9	9	9	9	9
LOW DOSE	6.1	0.	7.	89.	3.	1.	0.
250 mg/kg	1.90	0.0	4.5	5.6	2.6	1.2	0.0
	10	10	10	10	10	10	10
MEDIUM DOSE	6.0	0.	8.	88.	3.	1.	0.
500 mg/kg	3.67	0.0	6.4	7.8	3.0	0.9	0.0
	9	9	9	9	9	9	9
HIGH DOSE	6.0	0.	7.	88.	4.	1.	0.
1000 mg/kg	4.09	0.0	4.9	5.7	1.5	1.5	0.0
	10	10	10	10	10	10	10

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Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
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** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL
+ : DATA NOT STATISTICALLY ANALYZED

TABLE 7.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE URINALYSIS, STUDY DAYS 28-29
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	REFR INDEX a	pH + b	PROTEIN + c	GLUCOSE + c	KETONES + d	BILI + d	OC BL + d	UROB + e
CONTROL	1.346	7.8	1.	0.	0.	0.	0.	0.4
0 mg/kg	0.0047	0.46	0.4	0.0	0.5	0.0	0.0	0.47
	8	8	8	8	8	8	8	8
LOW DOSE	1.349	7.2	1.	0.	0.	0.	0.	0.7
250 mg/kg	0.0059	0.44	0.4	0.0	0.5	0.0	0.0	0.45
	9	9	9	9	9	9	9	9
MEDIUM DOSE	1.352	7.3	1.	0.	0.	0.	0.	0.9
500 mg/kg	0.0036	0.67	0.4	0.0	0.4	0.0	0.3	0.30
	9	9	9	9	9	9	9	9
HIGH DOSE	1.348	7.5	1.	0.	1.	0.	0.	0.6
1000 mg/kg	0.0057	0.58	0.0	0.0	0.5	0.0	0.4	0.48
	7	7	7	7	7	7	7	7

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL
a : REFRACTIVITY X10E-4 + 1.333
b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)
c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1
d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)
e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)
+ : DATA NOT STATISTICALLY ANALYZED

TABLE 7.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE URINALYSIS, STUDY DAYS 28-29
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	CASTS + f	CRYS + g	RBC + h	WBC + h	BACT + g	VOLUME ++ mL
CONTROL	0.	1.	0.	0.	1.	28.
0 mg/kg	0.0	0.5	0.0	0.4	0.0	24.1
	8	8	8	8	8	10
LOW DOSE	0.	1.	0.	0.	1.	19.
250 mg/kg	0.0	0.3	0.0	0.4	0.0	15.1
	9	9	9	9	9	10
MEDIUM DOSE	0.	1.	0.	0.	1.	32.
500 mg/kg	0.0	0.7	0.0	0.0	0.3	19.7
	9	9	9	9	9	10
HIGH DOSE	0.	1.	0.	0.	1.	24.
1000 mg/kg	0.0	0.4	0.0	0.0	0.0	15.8
	7	7	7	7	7	10

+ : DATA NOT STATISTICALLY ANALYZED
++ : DATA NOT STATISTICALLY ANALYZED BECAUSE DATA CONTAINS TRUNCATED VALUES
f : CASTS PER LOW POWER FIELD
g : VALUE REPRESENTS A GRADING SYSTEM BASED ON A SUBJECTIVE MICROSCOPIC DETERMINATION OF THE NUMBER PRESENT (FEW TO MANY) IN A SAMPLE
h : CELLS PER HIGH POWER FIELD

TABLE 7.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE URINALYSIS, STUDY DAYS 28-29
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	REFR INDEX a	pH + b	PROTEIN + c	GLUCOSE + c	KETONES + d	BILI + d	OC BL + d	UROB + e
CONTROL	1.347 F	7.6	1.	0.	0.	0.	0.	1.0
0 mg/kg	0.0037	0.82	0.0	0.0	0.0	0.0	0.0	0.00
	8	8	8	8	8	8	8	8
LOW DOSE	1.346	7.4	1.	0.	0.	0.	0.	0.7
250 mg/kg	0.0044	0.69	0.0	0.0	0.0	0.0	0.0	0.47
	8	8	8	8	8	8	8	8
MEDIUM DOSE	1.351 *	6.9	1.	0.	0.	0.	0.	0.8
500 mg/kg	0.0044	0.99	0.4	0.0	0.0	0.0	0.0	0.42
	8	8	8	8	8	8	8	8
HIGH DOSE	1.345	7.4	1.	0.	0.	0.	0.	0.4
1000 mg/kg	0.0033	0.73	0.0	0.0	0.0	0.0	0.0	0.44
	7	7	7	7	7	7	7	7

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL
o : REFRACTIVITY X10E-4 + 1.333
b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)
c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1
d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)
e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)
+ : DATA NOT STATISTICALLY ANALYZED

TABLE 7.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE URINALYSIS, STUDY DAYS 28-29
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	CASTS + f	CRYS + g	RBC + h	WBC + h	BACT + g	VOLUME ++ mL
CONTROL	0.	0.	0.	0.	1.	6.
0 mg/kg	0.0	0.5	0.0	0.0	0.0	4.7
	8	8	8	8	8	8
LOW DOSE	0.	1.	0.	0.	1.	16.
250 mg/kg	0.0	0.5	0.0	0.4	0.5	20.6
	8	8	8	8	8	9
MEDIUM DOSE	0.	1.	0.	0.	1.	15.
500 mg/kg	0.0	0.5	0.0	0.0	0.0	20.8
	8	8	8	8	8	10
HIGH DOSE	0.	0.	0.	0.	1.	12.
1000 mg/kg	0.0	0.5	0.0	0.0	0.4	5.6
	7	7	7	7	7	10

+ : DATA NOT STATISTICALLY ANALYZED
++ : DATA NOT STATISTICALLY ANALYZED BECAUSE DATA CONTAINS TRUNCATED VALUES
f : CASTS PER LOW POWER FIELD
g : VALUE REPRESENTS A GRADING SYSTEM BASED ON A SUBJECTIVE MICROSCOPIC DETERMINATION OF THE NUMBER PRESENT (FEW TO MANY) IN A SAMPLE
h : CELLS PER HIGH POWER FIELD

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	B R A I N		H E A R T		
		WT	ORG/FBW X10E-3	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	267.	1.95	7.4	1.06	4.0	5.4
0 mg/kg	26.9	0.082	0.71	0.177	0.44	0.85
	10	10	10	10	10	10
LOW DOSE	268.	1.98	7.4	1.00	3.7	5.1
250 mg/kg	22.6	0.078	0.60	0.096	0.24	0.50
	10	10	10	10	10	10
MEDIUM DOSE	279.	2.01	7.2	1.02	3.6	5.0
500 mg/kg	18.2	0.089	0.35	0.116	0.30	0.55
	10	10	10	10	10	10
HIGH DOSE	278.	1.97	7.1	1.09	3.9	5.5
1000 mg/kg	26.1	0.052	0.64	0.138	0.21	0.70
	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	L I V E R			K I D N E Y		
		WT	ORG/FBW X10E-2	ORG/BRN	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	267.	7.74	2.9 B	4.0	2.26	8.5	11.6
0 mg/kg	26.9	0.982	0.13	0.42	0.242	0.37	0.99
	10	10	10	10	10	10	10
LOW	268.	8.06	3.0	4.1	2.24	8.3	11.3
250 mg/kg	22.6	1.056	0.22	0.51	0.208	0.38	0.97
	10	10	10	10	10	10	10
MEDIUM	279.	8.27	3.0	4.1	2.35	8.4	11.7
500 mg/kg	18.2	0.771	0.13	0.33	0.201	0.43	0.95
	10	10	10	10	10	10	10
HIGH	278.	8.73	3.1	4.4	2.35	8.4	12.0
1000 mg/kg	26.1	1.492	0.35	0.79	0.284	0.77	1.56
	10	10	10	10	10	10	10

F : ONEDAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	WT	A D R E N A L		WT	T H Y R O I D	
			ORG/FBW X10E-4	ORG/ERN X10E-2		ORG/FBW X10E-5	ORG/ERN X10E-3
CONTROL	267.	0.055	2.1	2.8	0.019	7.1	9.6
0 mg/kg	26.9	0.0058	0.23	0.25	0.0024	1.02	0.96
	10	10	10	10	10	10	10
LOW DOSE	268.	0.052	2.0	2.7	0.017	6.5	8.8
250 mg/kg	22.6	0.0042	0.22	0.24	0.0035	1.36	1.82
	10	10	10	10	9	9	9
MEDIUM DOSE	279.	0.053	1.9	2.6	0.020	7.1	9.8
500 mg/kg	18.2	0.0070	0.21	0.27	0.0032	1.20	1.52
	10	10	10	10	10	10	10
HIGH DOSE	278.	0.054	2.0	2.8	0.019	6.9	9.8
1000 mg/kg	26.1	0.0099	0.31	0.48	0.0048	1.73	2.34
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	P I T U I T A R Y		S P L E E N			
		WT	ORG/FBW X10E-5	ORG/BRN X10E-3	WT	ORG/FBW X10E-4	ORG/BRN X10E-1
CONTROL	267.	0.010	3.6	5.0	0.51	19.0	2.6
0 mg/kg	26.9	0.0019	0.58	0.83	0.048	1.44	0.22
	10	10	10	10	10	10	10
LOW DOSE	268.	0.009	3.5	4.7	0.52	19.6	2.6
250 mg/kg	22.6	0.0015	0.38	0.71	0.047	1.82	0.23
	10	10	10	10	10	10	10
MEDIUM DOSE	279.	0.011	3.8	5.3	0.55	19.7	2.7
500 mg/kg	18.2	0.0011	0.40	0.55	0.042	1.83	0.24
	10	10	10	10	10	10	10
HIGH DOSE	278.	0.010	3.6	5.1	0.50	18.3	2.6
1000 mg/kg	26.1	0.0012	0.38	0.63	0.042	2.22	0.20
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	THYMUS WT	ORG/FBW X10E-3	ORG/BRN X10E-1	SALIVARY GL WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	267.	0.54	2.0	2.8	0.63	2.4	3.2
0 mg/kg	26.9	0.110	0.33	0.56	0.141	0.40	0.66
	10	10	10	10	10	10	10
LOW DOSE	268.	0.54	2.0	2.7	0.61	2.3	3.1
250 mg/kg	22.6	0.084	0.21	0.42	0.096	0.35	0.50
	10	10	10	10	10	10	10
MEDIUM DOSE	279.	0.56	2.0	2.8	0.64	2.3	3.2
500 mg/kg	18.2	0.124	0.47	0.67	0.072	0.27	0.35
	10	10	10	10	10	10	10
HIGH DOSE	278.	0.52	1.9	2.7	0.62	2.2	3.2
1000 mg/kg	26.1	0.091	0.33	0.51	0.098	0.37	0.47
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	TESTIS			PROSTATE			EPIDIDYMIS		
		WT	ORG/FBW X10E-3	ORG/BRN	WT	ORG/FBW X10E-4	ORG/BRN X10E-1	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	267.	2.84	10.8	1.5	0.40	14.7	2.0	0.93	3.5	4.8
0 mg/kg	26.9	0.178	1.41	0.10	0.117	3.62	0.58	0.096	0.54	0.41
	10	10	10	10	10	10	10	10	10	10
LOW DOSE	268.	2.88	10.8	1.5	0.38	14.2	1.9	0.92	3.4	4.6
250 mg/kg	22.6	0.224	0.86	0.10	0.091	3.73	0.50	0.157	0.52	0.84
	10	10	10	10	10	10	10	10	10	10
MEDIUM DOSE	279.	2.86	10.3	1.4	0.40	14.3	2.0	0.93	3.3	4.6
500 mg/kg	18.2	0.239	0.92	0.12	0.104	3.20	0.48	0.121	0.36	0.53
	10	10	10	10	10	10	10	10	10	10
HIGH DOSE	278.	2.82	10.2	1.4	0.33	12.0	1.7	0.88	3.2	4.5
1000 mg/kg	26.1	0.224	0.96	0.13	0.079	2.88	0.40	0.106	0.47	0.54
	10	10	10	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	B R A I N		H E A R T		
		WT	ORG/FBW X10E-3	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	171.	1.84	10.8	0.75	4.4	4.1
0 mg/kg	14.3	0.091	0.88	0.085	0.45	0.46
	10	10	10	10	10	10
LOW DOSE	170.	1.82	10.8	0.70	4.1	3.8
250 mg/kg	22.0	0.083	1.38	0.090	0.33	0.44
	10	10	10	10	10	10
MEDIUM DOSE	175.	1.82	10.4	0.74	4.2	4.1
500 mg/kg	12.4	0.094	0.62	0.071	0.30	0.43
	10	10	10	10	10	10
HIGH DOSE	168.	1.83	11.1	0.69	4.1	3.8
1000 mg/kg	18.9	0.049	1.39	0.057	0.52	0.35
	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	L I V E R			K I D N E Y		
		WT	ORG/FBW X10E-2	ORG/BRN	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	171.	5.42	3.2	2.9	1.60	9.4	8.7
0 mg/kg	14.3	0.506	0.14	0.33	0.137	0.77	0.63
	10	10	10	10	10	10	10
LOW	170.	5.11	3.0	2.8	1.53	9.1	8.4
250 mg/kg	22.0	0.701	0.27	0.34	0.160	1.00	0.67
	10	10	10	10	10	10	10
MEDIUM	175.	5.49	3.1	3.0	1.56	8.9	8.6
500 mg/kg	12.4	0.637	0.28	0.34	0.099	0.48	0.56
	10	10	10	10	10	10	10
HIGH	168.	5.17	3.1	2.8	1.56	9.4	8.5
1000 mg/kg	18.9	0.556	0.14	0.30	0.119	0.86	0.65
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	A D R E N A L			T H Y R O I D		
		WT	ORG/FBW X10E-4	ORG/BRN X10E-2	WT	ORG/FBW X10E-5	ORG/BRN X10E-3
CONTROL 0 mg/kg	171.	0.068	3.9	3.7	0.015	8.9	8.2
	14.3	0.0125	0.55	0.70	0.0033	1.91	1.92
	10	10	10	10	10	10	10
LOW DOSE 250 mg/kg	170.	0.060	3.5	3.3	0.015	8.7	8.2
	22.0	0.0136	0.70	0.72	0.0036	1.81	2.17
	10	10	10	10	10	10	10
MEDIUM DOSE 500 mg/kg	175.	0.064	3.6	3.5	0.016	9.3	9.0
	12.4	0.0086	0.33	0.49	0.0031	1.52	1.53
	10	10	10	10	10	10	10
HIGH DOSE 1000 mg/kg	168.	0.061	3.7	3.3	0.015	9.2	8.2
	18.9	0.0068	0.77	0.40	0.0043	3.18	2.26
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	P I T U I T A R Y			S P L E E N		
		WT	ORG/FBW X10E-5	ORG/BRN X10E-3	WT	ORG/FBW X10E-4	ORG/BRN X10E-1
CONTROL 0 mg/kg	171.	0.010	6.1	5.7	0.36	20.9	1.9
	14.3	0.0018	0.70	1.00	0.052	2.18	0.27
	10	10	10	10	10	10	10
LOW DOSE 250 mg/kg	170.	0.010	5.7	5.3	0.35	20.6	1.9
	22.0	0.0020	1.10	1.11	0.071	3.50	0.39
	10	10	10	10	10	10	10
MEDIUM DOSE 500 mg/kg	175.	0.009	5.3	5.1	0.37	21.4	2.1
	12.4	0.0024	1.22	1.36	0.057	3.05	0.34
	10	10	10	10	10	10	10
HIGH DOSE 1000 mg/kg	168.	0.010	5.9	5.5	0.35	20.8	1.9
	18.9	0.0026	1.50	1.42	0.047	1.55	0.25
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	T H Y M U S			— S A L I V A R Y G L —		
		WT	ORG/FBW X10E-3	ORG/BRN X10E-1	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	171.	0.40	2.3	2.2	0.48	2.8	2.6
0 mg/kg	14.3	0.053	0.25	0.27	0.060	0.37	0.34
	10	10	10	10	10	10	10
LOW DOSE	170.	0.43	2.5	2.4	0.42	2.5	2.3
250 mg/kg	22.0	0.097	0.52	0.59	0.084	0.53	0.45
	10	10	10	10	10	10	10
MEDIUM DOSE	175.	0.41	2.3	2.3	0.45	2.5	2.5
500 mg/kg	12.4	0.107	0.54	0.63	0.064	0.21	0.35
	10	10	10	10	10	10	10
HIGH DOSE	168.	0.40	2.4	2.2	0.41	2.5	2.2
1000 mg/kg	18.9	0.079	0.31	0.44	0.073	0.49	0.40
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 8.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT	O V A R Y		U T E R U S			
		WT	ORG/FBW X10E-4	ORG/BRN X10E-2	WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL 0 mg/kg	171.	0.10	5.7 B	5.4	0.41	2.4 B	2.2
	14.3	0.043	2.54	2.45	0.083	0.36	0.48
	10	10	10	10	10	10	10
LOW DOSE 250 mg/kg	170.	0.09	5.3	5.0	0.46	2.7	2.5
	22.0	0.027	1.34	1.48	0.116	0.67	0.60
	10	10	10	10	10	10	10
MEDIUM DOSE 500 mg/kg	175.	0.10	5.7	5.6	0.45	2.5	2.5
	12.4	0.029	1.43	1.63	0.083	0.38	0.46
	10	10	10	10	10	10	10
HIGH DOSE 1000 mg/kg	168.	0.10	6.4	5.6	0.45	2.7	2.5
	18.9	0.038	3.04	2.11	0.130	0.83	0.67
	10	10	10	10	10	10	10

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
X : INSUFFICIENT DATA FOR STATISTICAL ANALYSIS
Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 1% LEVEL
*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 9.1

SEARLE RESEARCH & DEVELOPMENT		INCIDENCE SUMMARY REPORT FOR GROSS NECROPSY OBSERVATIONS				PRINTED: 7-JAN-85	
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448				PAGE: 1	
SKOKIE, ILLINOIS 60077		REPORT FOR INTERIM SACRIFICE NUMBER 1					
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84				STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
NOTE: CTLs = CONTROLS		ANIMAL SEX:		— MALES —		— FEMALES —	
FROM GROUP(S): 1		GROUP:		CTLs		CTLs	
		NO. IN GROUP:		10 2 3 4		10 2 3 4	
				10 10 10 10		10 10 10 10	
WHOLE BODY							
NORMAL				8 8 8 8		9 9 9 10	
SKIN							
CRUST				1 0 0 0		0 0 0 0	
KIDNEY							
HYDRONEPHROSIS				1 1 2 2		1 0 0 0	
TESTIS							
SMALL				0 1 0 0			
LIVER							
DISCOLORATION, PALE				0 0 0 0		0 1 0 0	
LYMPH NODE							
DISCOLORED				0 0 0 0		0 0 1 0	

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TABLE 9.2

SEARLE RESEARCH & DEVELOPMENT		INCIDENCE SUMMARY REPORT FOR GROSS NECROPSY OBSERVATIONS		PRINTED: 7-JAN-85	
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 1	
SKOKIE, ILLINOIS 60077		REPORT FOR FINAL SACRIFICE			
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
NOTE: CTLS = CONTROLS		ANIMAL SEX:			
FROM GROUP(S): 1		GROUP:			
NO. IN GROUP:		CTLS		CTLS	
		5 0 0 0 5		5 0 0 0 5	
		CTLS		CTLS	
		4 0 0 0 5		4 0 0 0 5	
		1 0 0 0 0		1 0 0 0 0	
WHOLE BODY					
NORMAL					
KIDNEY					
HYDRONEPHROSIS					

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SEARLE RESEARCH & DEVELOPMENT										LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)										PRINTED: 7-JAN-85									
PRODUCT SAFETY ASSESSMENT										STUDY NUMBER: SA2448										PAGE: 1									
SKOKIE, ILLINOIS 60077										PATHOLOGIST(S): STUART LEVIN, DVM, PHD																			
SPECIES: RAT/CHARLES RIVER CD										STUDY START DATE: 03-OCT-84										STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX									
NOTES: ANIMALS = INTERIM SACRIFICE 1										— A N I M A L S										A F F E C T E D —									
CTLS = CONTROLS FROM GROUP(S): 1										— MALES —										— FEMALES —									
T I S S U E S W I T H F I N D I N G S										CTLS 2 3 4										CTLS 2 3 4									
										10 10 10 10										10 10 10 10									

TABLE 10

SEARLE RESEARCH & DEVELOPMENT										LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)										PRINTED: 7-JAN-85									
PRODUCT SAFETY ASSESSMENT										STUDY NUMBER: SA2448										PAGE: 2									
SKOKIE, ILLINOIS 60077										PATHOLOGIST(S): STUART LEVIN, DVM, PHD																			
SPECIES: RAT/CHARLES RIVER CD										STUDY START DATE: 03-OCT-84										STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX									
NOTES: ANIMALS = INTERIM SACRIFICE 1										— A N I M A L S A F F E C T E D —																			
CTLS = CONTROLS FROM GROUP(S): 1										— MALES —										— FEMALES —									
T I S S U E S W I T H F I N D I N G S										CTLS 2 3 4										CTLS 2 3 4									
										10 10 10 10										10 10 10 10									

SEARLE RESEARCH & DEVELOPMENT										LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)										PRINTED: 7-JAN-85									
PRODUCT SAFETY ASSESSMENT										STUDY NUMBER: SA2448										PAGE: 4									
SKOKIE, ILLINOIS 60077										PATHOLOGIST(S): STUART LEVIN, DVM, PHD																			
SPECIES: RAT/CHARLES RIVER CD										STUDY START DATE: 03-OCT-84										STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX									
NOTES: ANIMALS = INTERIM SACRIFICE 1																													
CTLS = CONTROLS FROM GROUP(S): 1																													
T I S S U E S W I T H F I N D I N G S										— A N I M A L S										A F F E C T E D —									
										— M A L E S —										— F E M A L E S —									
										CTLS 2 3 4										CTLS 2 3 4									
										10 10 10 10										10 10 10 10									
S P L E E N										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
S T O M A C H										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
S E M I N A L V E S I C L E										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
T E S T I S										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
T H Y R O I D G L A N D										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
T H Y M U S										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
T O N G U E										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
T R A C H E A										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
U R I N A R Y B L A D D E R										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
U T E R U S										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									
V A G I N A										NUMBER EXAMINED:										10 0 0 10									
																				10 0 0 10									

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REFERENCES

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Winer, B. J. (1971). Statistical Principles in Experimental Design, 2nd edition. McGraw-Hill, New York. pp. 149-185, 210-219.

APPENDIX A, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	-7	-1	1	3	6	8	10
CONTROL - 0 mg/kg							
84-1864	80.	127.	126.	147.	171.	186.	201.
84-1865	77.	123.	127.	146.	174.	190.	204.
84-1866	66.	105.	104.	123.	150.	158.	171.
84-1867	81.	121.	124.	141.	163.	178.	194.
84-1868	77.	118.	124.	144.	170.	183.	196.
84-1869	74.	113.	107.	126.	141.	146.	148.
84-1870	71.	109.	109.	127.	150.	164.	177.
84-1871	76.	120.	121.	136.	159.	175.	184.
84-1872	83.	128.	130.	152.	174.	187.	198.
84-1873	73.	115.	116.	135.	158.	171.	184.
84-1874	79.	125.	123.	145.	170.	174.	185.
84-1875	76.	120.	120.	140.	166.	179.	192.
84-1876	67.	106.	105.	123.	143.	153.	161.
84-1877	77.	123.	121.	142.	168.	178.	189.
84-1878	76.	121.	119.	138.	160.	172.	182.
LOW DOSE - 250 mg/kg							
84-1894	81.	129.	128.	151.	176.	192.	201.
84-1895	76.	121.	122.	142.	165.	178.	188.
84-1896	71.	114.	112.	130.	147.	154.	160.
84-1897	80.	122.	123.	141.	165.	178.	192.
84-1898	79.	125.	124.	144.	168.	181.	194.
84-1899	73.	117.	115.	137.	158.	171.	178.
84-1900	71.	107.	106.	123.	143.	153.	162.
84-1901	69.	113.	114.	133.	156.	174.	186.
84-1902	77.	118.	120.	140.	166.	183.	196.
84-1903	77.	112.	110.	132.	151.	162.	176.
MEDIUM DOSE - 500 mg/kg							
84-1914	80.	120.	122.	140.	160.	178.	189.
84-1915	79.	126.	128.	150.	174.	188.	198.
84-1916	74.	121.	119.	143.	160.	170.	179.
84-1917	68.	109.	106.	126.	146.	160.	167.
84-1918	67.	110.	112.	131.	157.	170.	181.
84-1919	83.	134.	135.	157.	182.	199.	212.
84-1920	72.	116.	114.	133.	156.	164.	176.
84-1921	70.	113.	115.	135.	160.	174.	189.
84-1922	74.	115.	115.	136.	160.	172.	182.
84-1923	76.	124.	124.	146.	169.	185.	197.

APPENDIX A, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	-7	-1	1	3	6	8	10
HIGH DOSE - 1000 mg/kg							
84-1934	68.	106.	104.	121.	142.	152.	162.
84-1935	86.	138.	139.	165.	194.	210.	226.
84-1936	78.	124.	125.	145.	171.	189.	206.
84-1937	76.	118.	118.	132.	157.	171.	185.
84-1938	78.	122.	123.	141.	170.	182.	193.
84-1939	72.	114.	113.	135.	156.	172.	184.
84-1940	75.	117.	114.	132.	154.	163.	169.
84-1941	74.	114.	116.	133.	154.	168.	178.
84-1942	69.	111.	109.	129.	150.	165.	174.
84-1943	80.	126.	124.	146.	171.	185.	197.
84-1944	76.	113.	114.	130.	149.	161.	170.
84-1945	70.	114.	116.	136.	162.	171.	179.
84-1946	73.	116.	111.	132.	159.	165.	175.
84-1947	72.	111.	110.	126.	156.	166.	175.
84-1948	81.	133.	132.	153.	181.	195.	209.

APPENDIX A, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	15	22	28	36	43	50	56
CONTROL - 0 mg/kg							
84-1864	239.	285.	317.	DEAD			
84-1865	248.	300.	335.	374.	408.	427.	444.
84-1866	201.	247.	282.	DEAD			
84-1867	236.	285.	322.	DEAD			
84-1868	238.	257.	305.	DEAD			
84-1869	174.	204.	217.	DEAD			
84-1870	211.	255.	292.	329.	357.	385.	400.
84-1871	221.	272.	308.	DEAD			
84-1872	236.	287.	320.	363.	392.	411.	430.
84-1873	222.	272.	308.	DEAD			
84-1874	217.	250.	272.	DEAD			
84-1875	228.	276.	305.	DEAD			
84-1876	193.	234.	255.	279.	304.	319.	338.
84-1877	226.	274.	314.	353.	388.	408.	429.
84-1878	212.	258.	292.	DEAD			
LOW DOSE - 250 mg/kg							
84-1894	241.	280.	310.	DEAD			
84-1895	226.	264.	300.	DEAD			
84-1896	193.	231.	257.	DEAD			
84-1897	226.	271.	307.	DEAD			
84-1898	230.	275.	314.	DEAD			
84-1899	213.	265.	302.	DEAD			
84-1900	187.	221.	253.	DEAD			
84-1901	223.	266.	305.	DEAD			
84-1902	235.	289.	332.	DEAD			
84-1903	207.	248.	275.	DEAD			
MEDIUM DOSE - 500 mg/kg							
84-1914	230.	279.	316.	DEAD			
84-1915	240.	287.	328.	DEAD			
84-1916	218.	256.	292.	DEAD			
84-1917	201.	241.	268.	DEAD			
84-1918	217.	267.	304.	DEAD			
84-1919	256.	307.	347.	DEAD			
84-1920	211.	258.	294.	DEAD			
84-1921	228.	272.	304.	DEAD			
84-1922	215.	257.	293.	DEAD			
84-1923	234.	272.	306.	DEAD			

APPENDIX A, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	15	22	28	36	43	50	56
HIGH DOSE - 1000 mg/kg							
84-1934	192.	232.	266.	299.	328.	353.	373.
84-1935	270.	335.	384.	386.	473.	504.	517.
84-1936	249.	304.	344.	DEAD			
84-1937	222.	265.	295.	331.	361.	373.	391.
84-1938	231.	283.	320.	DEAD			
84-1939	218.	269.	311.	354.	391.	421.	445.
84-1940	203.	233.	257.	DEAD			
84-1941	213.	257.	290.	318.	350.	374.	399.
84-1942	207.	252.	281.	DEAD			
84-1943	242.	296.	352.	DEAD			
84-1944	200.	248.	283.	DEAD			
84-1945	221.	274.	313.	DEAD			
84-1946	203.	240.	271.	DEAD			
84-1947	214.	263.	301.	DEAD			
84-1948	244.	297.	334.	DEAD			

APPENDIX A, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	-7	-1	1	3	6	8	10
CONTROL - 0 mg/kg							
84-1879	69.	106.	104.	120.	134.	137.	143.
84-1880	68.	107.	107.	122.	131.	141.	146.
84-1881	64.	96.	97.	111.	127.	137.	142.
84-1882	75.	117.	120.	133.	153.	158.	168.
84-1883	69.	108.	107.	123.	138.	143.	144.
84-1884	64.	101.	102.	121.	136.	145.	152.
84-1885	71.	103.	100.	117.	134.	135.	145.
84-1886	66.	102.	101.	115.	124.	134.	136.
84-1887	75.	113.	112.	133.	141.	147.	154.
84-1888	66.	95.	96.	110.	121.	125.	130.
84-1889	70.	104.	103.	119.	130.	138.	143.
84-1890	72.	108.	106.	123.	137.	147.	154.
84-1891	68.	102.	99.	111.	124.	128.	134.
84-1892	69.	98.	99.	111.	122.	126.	130.
84-1893	73.	114.	113.	128.	134.	135.	139.
LOW DOSE - 250 mg/kg							
84-1904	71.	102.	99.	109.	123.	126.	131.
84-1905	70.	108.	106.	124.	132.	140.	140.
84-1906	75.	114.	114.	130.	143.	148.	155.
84-1907	71.	106.	106.	115.	134.	140.	145.
84-1908	67.	101.	100.	112.	123.	128.	125.
84-1909	67.	98.	95.	111.	125.	128.	133.
84-1910	73.	106.	106.	121.	138.	142.	147.
84-1911	70.	104.	103.	118.	135.	141.	147.
84-1912	66.	88.	86.	97.	112.	110.	116.
84-1913	79.	122.	126.	144.	164.	173.	180.
MEDIUM DOSE - 500 mg/kg							
84-1924	63.	99.	101.	116.	133.	142.	141.
84-1925	76.	116.	120.	132.	144.	151.	158.
84-1926	69.	102.	99.	113.	129.	133.	138.
84-1927	68.	102.	98.	112.	125.	130.	138.
84-1928	72.	108.	105.	117.	128.	135.	141.
84-1929	75.	111.	112.	124.	140.	151.	153.
84-1930	75.	116.	114.	128.	135.	143.	144.
84-1931	71.	105.	102.	116.	123.	134.	138.
84-1932	66.	96.	92.	103.	112.	118.	122.
84-1933	66.	102.	104.	116.	134.	143.	147.

APPENDIX A, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	-7	-1	1	3	6	8	10
HIGH DOSE - 1000 mg/kg							
84-1949	70.	105.	104.	119.	132.	141.	145.
84-1950	70.	106.	102.	116.	130.	136.	140.
84-1951	79.	119.	113.	128.	137.	135.	137.
84-1952	69.	103.	105.	116.	127.	130.	136.
84-1953	74.	113.	110.	124.	138.	144.	143.
84-1954	69.	100.	97.	103.	115.	119.	120.
84-1955	61.	88.	88.	98.	110.	113.	115.
84-1956	65.	96.	99.	109.	124.	129.	137.
84-1957	69.	102.	100.	113.	127.	137.	141.
84-1958	75.	111.	112.	125.	140.	145.	150.
84-1959	65.	95.	89.	102.	113.	117.	123.
84-1960	66.	100.	99.	114.	129.	137.	143.
84-1961	78.	117.	118.	133.	144.	151.	157.
84-1962	69.	109.	104.	124.	141.	149.	157.
84-1963	73.	105.	101.	119.	131.	135.	133.

APPENDIX A, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	15	22	28	36	43	50	56
CONTROL - 0 mg/kg							
84-1879	157.	171.	182.	DEAD			
84-1880	159.	177.	192.	DEAD			
84-1881	153.	172.	185.	DEAD			
84-1882	181.	205.	221.	DEAD			
84-1883	163.	183.	193.	216.	232.	239.	248.
84-1884	170.	195.	213.	233.	249.	258.	271.
84-1885	159.	166.	189.	199.	219.	232.	233.
84-1886	155.	182.	199.	DEAD			
84-1887	165.	178.	193.	DEAD			
84-1888	142.	154.	171.	DEAD			
84-1889	160.	174.	185.	DEAD			
84-1890	170.	181.	198.	DEAD			
84-1891	148.	166.	181.	DEAD			
84-1892	140.	153.	168.	179.	185.	199.	196.
84-1893	150.	170.	178.	199.	219.	227.	244.
LOW DOSE - 250 mg/kg							
84-1904	142.	161.	172.	DEAD			
84-1905	148.	164.	175.	DEAD			
84-1906	172.	184.	195.	DEAD			
84-1907	162.	178.	187.	DEAD			
84-1908	140.	158.	171.	DEAD			
84-1909	145.	163.	174.	DEAD			
84-1910	164.	190.	210.	DEAD			
84-1911	164.	186.	201.	DEAD			
84-1912	130.	143.	153.	DEAD			
84-1913	195.	221.	240.	DEAD			
MEDIUM DOSE - 500 mg/kg							
84-1924	157.	184.	206.	DEAD			
84-1925	175.	194.	209.	DEAD			
84-1926	155.	168.	180.	DEAD			
84-1927	148.	165.	175.	DEAD			
84-1928	156.	181.	193.	DEAD			
84-1929	169.	190.	211.	DEAD			
84-1930	160.	172.	187.	DEAD			
84-1931	151.	174.	180.	DEAD			
84-1932	136.	158.	174.	DEAD			
84-1933	168.	183.	197.	DEAD			

APPENDIX A, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHTS (g)

INDIVIDUAL VALUES

STUDY DAY	15	22	28	36	43	50	56
HIGH DOSE - 1000 mg/kg							
84-1949	160.	181.	194.	207.	219.	224.	233.
84-1950	153.	162.	181.	DEAD			
84-1951	148.	162.	178.	DEAD			
84-1952	155.	174.	187.	186.	228.	236.	255.
84-1953	160.	173.	188.	DEAD			
84-1954	132.	143.	147.	DEAD			
84-1955	131.	143.	154.	169.	178.	182.	188.
84-1956	154.	175.	193.	DEAD			
84-1957	160.	178.	194.	DEAD			
84-1958	165.	184.	197.	DEAD			
84-1959	132.	140.	149.	DEAD			
84-1960	161.	183.	193.	DEAD			
84-1961	174.	186.	204.	220.	227.	240.	249.
84-1962	174.	201.	209.	DEAD			
84-1963	153.	169.	183.	197.	220.	235.	240.

APPENDIX A, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	3	6	8	10	15	22
CONTROL - 0 mg/kg						
84-1864	21.	24.	15.	15.	38.	46.
84-1865	19.	28.	16.	14.	44.	52.
84-1866	19.	27.	8.	13.	30.	46.
84-1867	17.	22.	15.	16.	42.	49.
84-1868	20.	26.	13.	13.	42.	19.
84-1869	19.	15.	5.	2.	26.	30.
84-1870	18.	23.	14.	13.	34.	44.
84-1871	15.	23.	16.	9.	37.	51.
84-1872	22.	22.	13.	11.	38.	51.
84-1873	19.	23.	13.	13.	38.	50.
84-1874	22.	25.	4.	11.	32.	33.
84-1875	20.	26.	13.	13.	36.	48.
84-1876	18.	20.	10.	8.	32.	41.
84-1877	21.	26.	10.	11.	37.	48.
84-1878	19.	22.	12.	10.	30.	46.
LOW DOSE - 250 mg/kg						
84-1894	23.	25.	16.	9.	40.	39.
84-1895	20.	23.	13.	10.	38.	38.
84-1896	18.	17.	7.	6.	33.	38.
84-1897	18.	24.	13.	14.	34.	45.
84-1898	20.	24.	13.	13.	36.	45.
84-1899	22.	21.	13.	7.	35.	52.
84-1900	17.	20.	10.	9.	25.	34.
84-1901	19.	23.	18.	12.	37.	43.
84-1902	20.	26.	17.	13.	39.	54.
84-1903	22.	19.	11.	14.	31.	41.
MEDIUM DOSE - 500 mg/kg						
84-1914	18.	20.	18.	11.	41.	49.
84-1915	22.	24.	14.	10.	42.	47.
84-1916	24.	17.	10.	9.	39.	38.
84-1917	20.	20.	14.	7.	34.	40.
84-1918	19.	26.	13.	11.	36.	50.
84-1919	22.	25.	17.	13.	44.	51.
84-1920	19.	23.	8.	12.	35.	47.
84-1921	20.	25.	14.	15.	39.	44.
84-1922	21.	24.	12.	10.	33.	42.
84-1923	22.	23.	16.	12.	37.	38.

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APPENDIX A, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	3	6	8	10	15	22
HIGH DOSE - 1000 mg/kg						
84-1934	17.	21.	10.	10.	30.	40.
84-1935	26.	29.	16.	16.	44.	65.
84-1936	20.	26.	18.	17.	43.	55.
84-1937	14.	25.	14.	14.	37.	43.
84-1938	18.	29.	12.	11.	38.	52.
84-1939	22.	21.	16.	12.	34.	51.
84-1940	18.	22.	9.	6.	34.	30.
84-1941	17.	21.	14.	10.	35.	44.
84-1942	20.	21.	15.	9.	33.	45.
84-1943	22.	25.	14.	12.	45.	54.
84-1944	16.	19.	12.	9.	30.	48.
84-1945	20.	26.	9.	8.	42.	53.
84-1946	21.	27.	6.	10.	28.	37.
84-1947	16.	30.	10.	9.	39.	49.
84-1948	21.	28.	14.	14.	35.	53.

APPENDIX A, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	28	36	43	50	56
CONTROL - 0 mg/kg					
84-1864	32.	DEAD			
84-1865	35.	39.	34.	19.	17.
84-1866	35.	DEAD			
84-1867	37.	DEAD			
84-1868	48.	DEAD			
84-1869	13.	DEAD			
84-1870	37.	37.	28.	28.	15.
84-1871	36.	DEAD			
84-1872	33.	43.	29.	19.	19.
84-1873	36.	DEAD			
84-1874	22.	DEAD			
84-1875	29.	DEAD			
84-1876	21.	24.	25.	15.	19.
84-1877	40.	39.	35.	20.	21.
84-1878	34.	DEAD			
LOW DOSE - 250 mg/kg					
84-1894	30.	DEAD			
84-1895	36.	DEAD			
84-1896	26.	DEAD			
84-1897	36.	DEAD			
84-1898	39.	DEAD			
84-1899	37.	DEAD			
84-1900	32.	DEAD			
84-1901	39.	DEAD			
84-1902	43.	DEAD			
84-1903	27.	DEAD			
MEDIUM DOSE - 500 mg/kg					
84-1914	37.	DEAD			
84-1915	41.	DEAD			
84-1916	36.	DEAD			
84-1917	27.	DEAD			
84-1918	37.	DEAD			
84-1919	40.	DEAD			
84-1920	36.	DEAD			
84-1921	32.	DEAD			
84-1922	36.	DEAD			
84-1923	34.	DEAD			

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APPENDIX A, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	28	36	43	50	56
HIGH DOSE - 1000 mg/kg					
84-1934	34.	33.	29.	25.	20.
84-1935	49.	2.	87.	31.	13.
84-1936	40.	DEAD			
84-1937	30.	36.	30.	12.	18.
84-1938	37.	DEAD			
84-1939	42.	43.	37.	30.	24.
84-1940	24.	DEAD			
84-1941	33.	28.	32.	24.	25.
84-1942	29.	DEAD			
84-1943	56.	DEAD			
84-1944	35.	DEAD			
84-1945	39.	DEAD			
84-1946	31.	DEAD			
84-1947	38.	DEAD			
84-1948	37.	DEAD			

APPENDIX A, TABLE 4

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	3	6	8	10	15	22
CONTROL - 0 mg/kg						
84-1879	16.	14.	3.	6.	14.	14.
84-1880	15.	9.	10.	5.	13.	18.
84-1881	14.	16.	10.	5.	11.	19.
84-1882	13.	20.	5.	10.	13.	24.
84-1883	16.	15.	5.	1.	19.	20.
84-1884	19.	15.	9.	7.	18.	25.
84-1885	17.	17.	1.	10.	14.	7.
84-1886	14.	9.	10.	2.	19.	27.
84-1887	21.	8.	6.	7.	11.	13.
84-1888	14.	11.	4.	5.	12.	12.
84-1889	16.	11.	8.	5.	17.	14.
84-1890	17.	14.	10.	7.	16.	11.
84-1891	12.	13.	4.	6.	14.	18.
84-1892	12.	11.	4.	4.	10.	13.
84-1893	15.	6.	1.	4.	11.	20.
LOW DOSE - 250 mg/kg						
84-1904	10.	14.	3.	5.	11.	19.
84-1905	18.	8.	8.	0.	8.	16.
84-1906	16.	13.	5.	7.	17.	12.
84-1907	9.	19.	6.	5.	17.	16.
84-1908	12.	11.	5.	-3.	15.	18.
84-1909	16.	14.	3.	5.	12.	18.
84-1910	15.	17.	4.	5.	17.	26.
84-1911	15.	17.	6.	6.	17.	22.
84-1912	11.	15.	-2.	6.	14.	13.
84-1913	18.	20.	9.	7.	15.	26.
MEDIUM DOSE - 500 mg/kg						
84-1924	15.	17.	9.	-1.	16.	27.
84-1925	12.	12.	7.	7.	17.	19.
84-1926	14.	16.	4.	5.	17.	13.
84-1927	14.	13.	5.	8.	10.	17.
84-1928	12.	11.	7.	6.	15.	25.
84-1929	12.	16.	11.	2.	16.	21.
84-1930	14.	7.	8.	1.	16.	12.
84-1931	14.	7.	11.	4.	13.	23.
84-1932	11.	9.	6.	4.	14.	22.
84-1933	12.	18.	9.	4.	21.	15.

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APPENDIX A, TABLE 4

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	3	6	8	10	15	22
HIGH DOSE - 1000 mg/kg						
84-1949	15.	13.	9.	4.	15.	21.
84-1950	14.	14.	6.	4.	13.	9.
84-1951	15.	9.	-2.	2.	11.	14.
84-1952	11.	11.	3.	6.	19.	19.
84-1953	14.	14.	6.	-1.	17.	13.
84-1954	6.	12.	4.	1.	12.	11.
84-1955	10.	12.	3.	2.	16.	12.
84-1956	10.	15.	5.	8.	17.	21.
84-1957	13.	14.	10.	4.	19.	18.
84-1958	13.	15.	5.	5.	15.	19.
84-1959	13.	11.	4.	6.	9.	8.
84-1960	15.	15.	8.	6.	18.	22.
84-1961	15.	11.	7.	6.	17.	12.
84-1962	20.	17.	8.	8.	17.	27.
84-1963	18.	12.	4.	-2.	20.	16.

APPENDIX A, TABLE 4

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	28	36	43	50	56
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CONTROL - 0 mg/kg

84-1879	11.	DEAD			
84-1880	15.	DEAD			
84-1881	13.	DEAD			
84-1882	16.	DEAD			
84-1883	10.	23.	16.	7.	9.
84-1884	18.	20.	16.	9.	13.
84-1885	23.	10.	20.	13.	1.
84-1886	17.	DEAD			
84-1887	15.	DEAD			
84-1888	17.	DEAD			
84-1889	11.	DEAD			
84-1890	17.	DEAD			
84-1891	15.	DEAD			
84-1892	15.	11.	6.	14.	-3.
84-1893	8.	21.	20.	8.	17.

LOW DOSE - 250 mg/kg

84-1904	11.	DEAD
84-1905	11.	DEAD
84-1906	11.	DEAD
84-1907	9.	DEAD
84-1908	13.	DEAD
84-1909	11.	DEAD
84-1910	20.	DEAD
84-1911	15.	DEAD
84-1912	10.	DEAD
84-1913	19.	DEAD

MEDIUM DOSE - 500 mg/kg

84-1924	22.	DEAD
84-1925	15.	DEAD
84-1926	12.	DEAD
84-1927	10.	DEAD
84-1928	12.	DEAD
84-1929	21.	DEAD
84-1930	15.	DEAD
84-1931	6.	DEAD
84-1932	16.	DEAD
84-1933	14.	DEAD

APPENDIX A, TABLE 4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE BODY WEIGHT CHANGE (g) FROM PRECEDING PERIOD

INDIVIDUAL VALUES					
STUDY DAY	28	36	43	50	56
HIGH DOSE - 1000 mg/kg					
84-1949	13.	13.	12.	5.	9.
84-1950	19.	DEAD			
84-1951	16.	DEAD			
84-1952	13.	-1.	42.	8.	19.
84-1953	15.	DEAD			
84-1954	4.	DEAD			
84-1955	11.	15.	9.	4.	6.
84-1956	18.	DEAD			
84-1957	16.	DEAD			
84-1958	13.	DEAD			
84-1959	9.	DEAD			
84-1960	10.	DEAD			
84-1961	18.	16.	7.	13.	9.
84-1962	8.	DEAD			
84-1963	14.	14.	23.	15.	5.

APPENDIX B, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	-1	3	6	8	10	15
CONTROL - 0 mg/kg						
84-1864	16.8	19.0	20.0	20.5	21.5	23.8
84-1865	16.5	18.0	21.3	21.0	22.0	23.4
84-1866	13.7	15.0	18.3	17.5	18.5	19.4
84-1867	16.2	17.0	19.0	19.0	21.0	23.2
84-1868	16.0	17.5	19.0	18.5	19.5	22.0
84-1869	16.0	16.0	16.7	14.0	13.5	16.2
84-1870	15.0	16.0	17.0	18.5	18.0	19.4
84-1871	17.2	16.5	17.0	19.0	18.0	20.6
84-1872	17.2	19.5	20.0	19.5	20.5	22.2
84-1873	15.7	18.0	18.3	18.5	19.0	20.6
84-1874	17.3	19.5	20.3	18.5	19.0	19.8
84-1875	17.0	18.0	19.0	19.0	20.5	22.2
84-1876	15.2	15.5	16.7	16.0	16.5	18.4
84-1877	16.5	18.5	19.7	18.5	18.0	20.4
84-1878	16.2	17.0	18.0	17.5	17.5	19.0
LOW DOSE - 250 mg/kg						
84-1894	16.3	19.0	19.7	20.5	19.5	21.8
84-1895	16.5	16.5	18.7	18.0	19.0	21.4
84-1896	16.0	17.5	18.0	16.5	17.0	18.8
84-1897	16.2	16.5	19.0	19.0	20.5	21.2
84-1898	16.7	18.0	20.0	19.0	21.5	23.0
84-1899	15.3	17.5	18.7	17.5	17.0	19.0
84-1900	14.3	15.5	16.0	16.0	17.0	17.6
84-1901	16.7	18.0	19.0	20.0	20.5	22.6
84-1902	15.5	17.0	19.3	19.0	20.5	22.4
84-1903	15.5	18.0	18.0	18.0	19.5	21.2
MEDIUM DOSE - 500 mg/kg						
84-1914	16.0	16.5	18.3	19.0	19.5	21.6
84-1915	16.8	19.5	21.0	21.0	20.0	22.4
84-1916	15.7	18.5	18.7	19.0	17.5	20.4
84-1917	16.3	17.5	17.7	19.5	18.0	20.0
84-1918	15.2	16.5	18.7	19.5	20.0	20.8
84-1919	18.2	20.0	22.0	23.0	24.0	25.4
84-1920	15.0	17.0	18.0	18.0	19.0	20.0
84-1921	14.8	17.5	19.0	21.0	21.5	22.8
84-1922	15.0	17.5	19.0	19.5	19.5	20.4
84-1923	17.2	18.5	20.3	20.5	21.5	23.6

APPENDIX B, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	-1	3	6	8	10	15
HIGH DOSE - 1000 mg/kg						
84-1934	14.2	16.5	17.3	16.5	ND	18.6
84-1935	18.2	21.5	22.7	22.5	24.0	25.2
84-1936	16.5	19.0	21.3	23.0	24.0	25.6
84-1937	16.5	18.0	19.3	19.0	21.0	22.0
84-1938	16.8	17.5	20.3	19.5	20.5	21.6
84-1939	15.5	17.5	19.3	19.5	19.0	20.8
84-1940	15.8	17.5	18.3	18.0	18.0	19.2
84-1941	16.3	17.5	18.7	19.0	19.0	20.0
84-1942	15.5	18.0	19.0	18.5	19.0	20.2
84-1943	16.7	19.5	21.7	20.5	20.0	23.2
84-1944	16.0	16.0	17.3	16.5	17.5	18.0
84-1945	17.0	18.5	21.0	18.0	19.5	22.2
84-1946	17.3	18.0	19.3	19.5	19.5	20.0
84-1947	16.2	16.5	19.7	18.0	19.0	21.6
84-1948	17.5	19.5	22.0	21.0	22.0	23.8

APPENDIX B, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	22	28	36	43	50	56
CONTROL - 0 mg/kg						
84-1864	24.7	24.8	DEAD			
84-1865	26.1	26.8	28.3	30.3	30.4	29.5
84-1866	21.0	22.7	DEAD			
84-1867	25.3	25.8	DEAD			
84-1868	20.9	21.7	DEAD			
84-1869	17.3	16.5	DEAD			
84-1870	22.1	22.3	24.0	24.1	25.0	25.2
84-1871	22.9	23.7	DEAD			
84-1872	23.9	25.3	26.5	26.6	25.7	25.7
84-1873	22.4	23.0	DEAD			
84-1874	20.7	19.7	DEAD			
84-1875	24.4	23.2	DEAD			
84-1876	20.4	19.3	20.5	21.7	20.7	22.5
84-1877	22.6	23.8	25.0	26.0	25.7	27.5
84-1878	22.0	22.5	DEAD			
LOW DOSE - 250 mg/kg						
84-1894	21.3	22.7	DEAD			
84-1895	21.6	23.2	DEAD			
84-1896	20.3	20.2	DEAD			
84-1897	22.6	23.7	DEAD			
84-1898	24.6	25.2	DEAD			
84-1899	22.6	24.0	DEAD			
84-1900	19.0	21.0	DEAD			
84-1901	23.1	24.7	DEAD			
84-1902	25.4	27.5	DEAD			
84-1903	22.4	22.2	DEAD			
MEDIUM DOSE - 500 mg/kg						
84-1914	23.6	24.3	DEAD			
84-1915	24.0	24.8	DEAD			
84-1916	21.3	22.2	DEAD			
84-1917	22.0	21.5	DEAD			
84-1918	22.1	24.2	DEAD			
84-1919	27.0	28.3	DEAD			
84-1920	21.6	22.7	DEAD			
84-1921	24.0	24.8	DEAD			
84-1922	22.3	23.5	DEAD			
84-1923	24.1	24.7	DEAD			

APPENDIX B, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	22	28	36	43	50	56
HIGH DOSE - 1000 mg/kg						
84-1934	19.9	21.0	21.6	22.1	23.0	24.0
84-1935	28.3	29.7	26.5	34.1	31.0	30.0
84-1936	26.6	27.2	DEAD			
84-1937	23.3	23.8	25.6	24.7	24.6	24.3
84-1938	23.6	25.0	DEAD			
84-1939	23.4	25.8	26.9	27.6	26.9	28.5
84-1940	19.9	20.0	DEAD			
84-1941	21.6	23.0	23.6	23.0	23.6	24.5
84-1942	22.3	23.3	DEAD			
84-1943	25.7	27.8	DEAD			
84-1944	20.1	22.2	DEAD			
84-1945	25.3	25.8	DEAD			
84-1946	20.6	21.5	DEAD			
84-1947	24.3	26.0	DEAD			
84-1948	26.0	27.7	DEAD			

APPENDIX B, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	-1	3	6	8	10	15
CONTROL - 0 mg/kg						
84-1879	14.7	7.0	14.7	12.5	14.0	14.8
84-1880	15.5	16.0	15.0	15.5	16.5	15.4
84-1881	13.2	14.0	14.7	15.0	15.0	14.6
84-1882	15.7	17.0	16.7	16.5	17.5	17.4
84-1883	15.2	16.0	15.3	15.5	14.0	15.0
84-1884	15.3	17.0	17.0	16.5	18.5	18.0
84-1885	13.8	15.0	16.0	13.0	14.5	14.2
84-1886	15.3	14.5	15.0	15.0	15.0	16.4
84-1887	16.0	16.5	16.0	15.5	16.0	16.4
84-1888	13.7	14.5	14.3	14.0	13.0	14.0
84-1889	15.2	15.5	14.7	15.0	13.5	15.4
84-1890	15.5	15.5	14.7	15.0	16.0	16.6
84-1891	14.2	14.5	14.7	14.0	14.5	15.4
84-1892	14.2	13.5	13.0	13.0	13.5	13.2
84-1893	15.7	16.0	14.3	12.5	13.5	14.2
LOW DOSE - 250 mg/kg						
84-1904	13.7	13.0	13.7	13.5	14.5	14.6
84-1905	14.5	14.5	15.0	14.5	13.0	14.4
84-1906	16.7	16.5	16.3	16.0	16.5	16.4
84-1907	15.3	13.0	15.3	15.0	15.0	16.4
84-1908	13.7	14.5	13.3	13.5	11.5	12.8
84-1909	13.7	13.0	14.0	13.0	13.5	14.0
84-1910	14.2	15.0	14.0	15.0	16.0	16.2
84-1911	13.8	14.5	15.7	15.0	15.0	16.6
84-1912	12.8	12.5	13.7	11.5	12.5	14.0
84-1913	16.7	18.0	18.3	19.0	18.5	18.6
MEDIUM DOSE - 500 mg/kg						
84-1924	14.2	15.5	17.0	15.5	14.0	15.6
84-1925	15.8	16.5	16.7	16.5	16.5	17.4
84-1926	13.3	13.5	15.7	14.0	15.0	15.8
84-1927	14.2	13.5	15.0	14.5	15.0	14.6
84-1928	15.3	14.5	15.7	15.0	15.5	15.6
84-1929	16.2	15.5	16.0	16.5	16.0	16.0
84-1930	17.0	16.5	16.0	15.0	14.0	15.2
84-1931	15.3	15.5	15.7	15.5	15.5	16.6
84-1932	14.2	13.5	13.3	12.5	13.0	14.0
84-1933	14.7	14.5	16.0	15.0	15.5	15.8

APPENDIX B, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	-1	3	6	8	10	15
HIGH DOSE - 1000 mg/kg						
84-1949	16.8	17.0	18.0	16.0	17.0	17.0
84-1950	14.3	14.0	17.0	14.0	15.0	15.6
84-1951	16.3	15.0	16.0	13.0	13.0	13.8
84-1952	14.8	15.0	15.3	14.0	15.0	15.8
84-1953	14.5	15.0	15.7	14.5	14.5	15.2
84-1954	13.7	11.5	13.0	12.0	12.5	12.6
84-1955	13.2	13.0	14.3	11.5	11.5	13.4
84-1956	13.7	13.5	15.0	14.5	15.5	16.0
84-1957	14.5	15.0	15.3	14.5	15.0	15.4
84-1958	15.0	14.0	17.0	14.5	14.5	16.4
84-1959	12.7	12.5	13.7	12.5	13.5	14.2
84-1960	14.3	14.0	16.0	16.5	15.0	14.8
84-1961	15.0	16.0	17.3	16.0	15.5	16.2
84-1962	16.7	16.5	19.0	17.5	17.5	18.0
84-1963	15.2	14.5	15.0	13.0	12.5	14.0

APPENDIX B, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	22	28	36	43	50	56
CONTROL - 0 mg/kg						
84-1879	15.4	14.5	DEAD			
84-1880	16.0	16.3	DEAD			
84-1881	15.0	14.8	DEAD			
84-1882	19.1	19.0	DEAD			
84-1883	16.0	15.5	18.0	18.3	16.6	20.2
84-1884	19.3	20.2	20.8	20.4	20.3	21.5
84-1885	14.9	16.3	17.9	18.9	20.7	19.5
84-1886	17.9	17.8	DEAD			
84-1887	17.0	18.0	DEAD			
84-1888	15.1	15.5	DEAD			
84-1889	15.9	14.8	DEAD			
84-1890	16.6	16.5	DEAD			
84-1891	16.6	17.0	DEAD			
84-1892	15.3	15.3	17.0	15.7	16.6	17.5
84-1893	15.4	15.0	17.9	18.7	16.7	18.7
LOW DOSE - 250 mg/kg						
84-1904	15.3	14.8	DEAD			
84-1905	15.9	15.2	DEAD			
84-1906	16.9	16.5	DEAD			
84-1907	17.4	16.3	DEAD			
84-1908	14.0	14.5	DEAD			
84-1909	15.3	15.0	DEAD			
84-1910	18.1	18.5	DEAD			
84-1911	17.6	18.2	DEAD			
84-1912	15.3	14.2	DEAD			
84-1913	19.4	19.5	DEAD			
MEDIUM DOSE - 500 mg/kg						
84-1924	17.9	19.3	DEAD			
84-1925	18.1	19.2	DEAD			
84-1926	16.7	17.0	DEAD			
84-1927	15.9	16.7	DEAD			
84-1928	17.7	17.7	DEAD			
84-1929	17.4	18.7	DEAD			
84-1930	16.6	17.3	DEAD			
84-1931	18.1	17.0	DEAD			
84-1932	15.7	17.7	DEAD			
84-1933	16.6	16.5	DEAD			

APPENDIX B, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE FEED CONSUMPTION (g/DAY)

INDIVIDUAL VALUES

STUDY DAY	22	28	36	43	50	56
HIGH DOSE - 1000 mg/kg						
84-1949	17.0	17.0	17.6	17.1	17.1	18.0
84-1950	14.9	15.0	DEAD			
84-1951	15.3	15.7	DEAD			
84-1952	16.7	17.8	16.8	18.9	19.4	20.5
84-1953	15.9	16.0	DEAD			
84-1954	14.1	13.8	DEAD			
84-1955	14.3	14.0	15.5	15.4	14.4	16.8
84-1956	17.1	17.8	DEAD			
84-1957	17.0	17.7	DEAD			
84-1958	16.6	17.3	DEAD			
84-1959	14.3	15.0	DEAD			
84-1960	16.7	15.7	DEAD			
84-1961	16.4	16.7	17.8	18.4	18.0	17.5
84-1962	18.9	18.3	DEAD			
84-1963	15.0	15.3	16.0	17.3	18.4	20.2

APPENDIX C, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE CLINICAL CHEMISTRY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	AST U/L	ALT U/L	AP U/L	GLUCOSE mmol/L	UREA mmol/L	TOT BILI mcmol/L	CHOL mmol/L
CONTROL - 0 mg/kg							
84-1864	102	16	90	6.0	4.7	2.6	1.5
84-1866	96	15	152	5.9	5.1	2.6	1.1
84-1867	ND	ND	ND	ND	ND	ND	ND
84-1868	96	16	116	4.9	4.4	2.2	1.1
84-1869	113	20	192	6.0	4.3	3.1	0.8
84-1871	79	12	122	5.3	4.1	2.1	1.0
84-1873	98	18	81	4.5	4.3	1.7	1.1
84-1874	90	10	92	6.9	4.0	1.8	0.9
84-1875	151	40	100	5.8	4.1	0.9	0.8
84-1878	124	18	114	5.1	5.0	4.0	1.3
LOW DOSE - 250 mg/kg							
84-1894	84	14	145	7.1	6.1	2.9	0.9
84-1895	95	10	146	4.1	4.1	1.5	1.2
84-1896	80	14	129	6.2	5.1	1.5	1.1
84-1897	116	26	93	5.7	4.5	1.4	1.2
84-1898	71	22	89	7.4	5.3	2.2	0.9
84-1899	61	21	106	6.4	4.4	2.1	1.1
84-1900	114	17	100	6.9	5.3	1.8	1.0
84-1901	116	19	115	5.7	3.8	1.3	0.9
84-1902	100	13	99	8.0	4.2	3.2	1.3
84-1903	72	16	90	6.7	4.0	1.1	1.0
MEDIUM DOSE - 500 mg/kg							
84-1914	111	17	110	6.1	4.3	3.7	1.6
84-1915	104	28	138	3.3	4.4	2.0	1.0
84-1916	59	14	120	6.3	3.3	1.1	1.2
84-1917	100	21	117	7.0	4.8	1.1	0.9
84-1918	73	16	131	5.8	3.5	3.1	1.3
84-1919	89	28	103	6.1	3.8	0.4	0.6
84-1920	59	15	112	6.5	4.7	1.9	1.0
84-1921	100	20	105	4.8	3.6	1.2	0.9
84-1922	112	15	128	4.8	4.5	2.4	0.8
84-1923	101	27	115	6.3	3.7	1.0	0.9
HIGH DOSE - 1000 mg/kg							
84-1936	119	17	104	6.4	5.6	3.3	1.8
84-1938	73	17	103	5.9	4.2	1.7	1.6
84-1940	76	15	106	6.1	4.8	3.0	1.0
84-1942	118	19	126	3.8	4.2	1.5	0.8
84-1943	ND	ND	ND	ND	ND	ND	ND
84-1944	66	16	109	4.9	4.0	1.6	1.1
84-1945	101	23	144	3.8	4.1	2.3	1.3
84-1946	79	13	101	5.9	3.6	1.5	1.0
84-1947	155	16	158	5.3	3.5	2.9	0.9
84-1948	70	14	99	6.5	4.2	1.0	1.1

ND : NO DATA

APPENDIX C, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE CLINICAL CHEMISTRY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	NA mmol/L	K mmol/L	CL mmol/L	CA mmol/L	T PRO g/L	ALB g/L	GLOB g/L	A/G
CONTROL - 0 mg/kg								
84-1864	149	5.3	110	2.43	58	35	23	1.52
84-1866	147	5.0	112	2.33	55	32	23	1.39
84-1867	ND	ND	ND	ND	ND	ND	ND	ND
84-1868	149	5.1	107	2.47	59	33	26	1.27
84-1869	155	5.5	117	2.24	60	34	26	1.31
84-1871	147	4.9	108	2.44	57	32	25	1.28
84-1873	148	5.4	108	2.44	57	31	26	1.19
84-1874	149	5.3	117	2.55	59	35	24	1.46
84-1875	148	5.1	108	2.38	58	33	25	1.32
84-1878	149	5.2	111	2.46	57	35	22	1.59
LOW DOSE - 250 mg/kg								
84-1894	146	4.6	110	2.40	55	33	22	1.50
84-1895	153	5.5	113	2.27	59	33	26	1.27
84-1896	150	5.3	109	2.33	57	35	22	1.59
84-1897	147	4.8	109	2.33	64	34	30	1.13
84-1898	146	5.0	109	2.59	58	34	24	1.42
84-1899	143	5.0	109	2.52	58	32	26	1.23
84-1900	150	5.5	114	2.45	56	33	23	1.43
84-1901	151	4.2	104	2.43	60	33	27	1.22
84-1902	144	5.0	107	2.50	56	34	22	1.55
84-1903	145	4.7	110	2.44	55	33	22	1.50
MEDIUM DOSE - 500 mg/kg								
84-1914	149	5.2	111	2.35	54	33	21	1.57
84-1915	155	5.4	108	2.22	64	39	25	1.56
84-1916	148	4.8	113	2.47	55	34	21	1.62
84-1917	156	5.4	111	2.33	61	32	29	1.10
84-1918	148	4.9	106	2.57	55	34	21	1.62
84-1919	149	5.1	105	2.53	58	33	25	1.32
84-1920	149	4.8	115	2.52	52	33	19	1.74
84-1921	145	5.2	108	2.36	55	32	23	1.39
84-1922	147	5.3	106	2.46	54	34	20	1.70
84-1923	147	5.5	105	2.39	60	35	25	1.40
HIGH DOSE- 1000 mg/kg								
84-1936	147	5.6	109	2.34	54	34	20	1.70
84-1938	148	5.1	111	2.37	54	33	21	1.57
84-1940	147	5.1	111	2.45	52	33	19	1.74
84-1942	150	5.1	113	2.44	54	32	22	1.45
84-1943	ND	ND	ND	ND	ND	ND	ND	ND
84-1944	148	5.1	113	2.60	55	34	21	1.62
84-1945	155	6.3	107	2.26	61	33	28	1.18
84-1946	147	4.9	109	2.32	57	31	26	1.19
84-1947	147	5.6	105	2.46	56	31	25	1.24
84-1948	145	4.6	112	2.43	56	32	24	1.33

ND : NO DATA

S.A. 2448

APPENDIX C, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE CLINICAL CHEMISTRY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	AST U/L	ALT U/L	AP U/L	GLUCOSE mmol/L	UREA mmol/L	TOT BILI mmol/L	CHOL mmol/L
CONTROL - 0 mg/kg							
84-1879	105	12	86	6.0	6.8	2.4	1.6
84-1880	109	26	114	4.8	5.2	3.5	1.2
84-1881	82	17	104	5.0	4.5	0.7	1.5
84-1882	76	12	61	5.5	5.4	2.9	1.2
84-1886	54	13	84	8.6	4.7	2.2	1.6
84-1887	78	13	73	5.3	4.6	2.2	1.2
84-1888	75	14	68	7.1	5.2	1.4	1.1
84-1889	105	14	79	4.4	4.8	2.5	1.3
84-1890	95	19	85	4.8	5.0	3.7	1.3
84-1891	95	18	84	5.9	3.8	2.2	1.5
LOW DOSE - 250 mg/kg							
84-1904	85	37	69	5.8	4.9	2.6	1.4
84-1905	89	14	87	5.3	6.1	1.6	1.2
84-1906	94	19	89	4.1	6.6	2.7	1.2
84-1907	104	16	65	5.0	4.9	1.0	1.1
84-1908	96	19	84	4.3	3.9	1.9	1.7
84-1909	109	10	61	4.0	4.5	2.6	0.8
84-1910	67	14	56	6.3	4.9	1.6	0.9
84-1911	75	15	63	5.5	4.1	1.5	1.3
84-1912	134	42	126	5.1	5.5	2.5	0.5
84-1913	66	13	76	6.1	4.3	2.0	1.6
MEDIUM DOSE - 500 mg/kg							
84-1924	122	42	80	7.2	6.4	2.3	2.2
84-1925	117	15	82	5.6	4.6	1.5	1.3
84-1926	71	12	63	7.4	5.0	2.2	1.6
84-1927	64	12	84	5.2	4.1	1.3	1.1
84-1928	141	36	90	5.0	5.0	2.4	1.3
84-1929	108	14	87	3.9	4.4	3.0	1.4
84-1930	73	13	94	6.7	6.5	1.4	1.3
84-1931	85	8	63	5.8	5.5	1.0	1.0
84-1932	81	13	88	6.1	5.1	3.2	1.5
84-1933	85	13	96	4.5	4.3	0.9	0.7
HIGH DOSE - 1000 mg/kg							
84-1950	97	14	85	5.0	5.0	2.2	1.6
84-1951	155	18	94	6.9	4.9	2.0	1.3
84-1953	87	21	91	4.7	3.7	1.5	1.4
84-1954	71	15	73	4.6	4.7	3.4	1.1
84-1956	54	11	77	5.4	5.3	2.2	1.3
84-1957	53	16	71	5.3	4.8	0.9	0.7
84-1958	82	20	67	5.1	3.9	2.2	1.0
84-1959	88	11	109	6.0	3.7	1.6	0.7
84-1960	109	13	108	5.0	4.0	2.1	1.6
84-1962	66	12	66	5.4	5.0	0.7	1.4

ND : NO DATA

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APPENDIX C, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE CLINICAL CHEMISTRY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	NA mmol/L	K mmol/L	CL mmol/L	CA mmol/L	T PRO g/L	ALB g/L	GLOB g/L	A/G
CONTROL - 0 mg/kg								
84-1879	153	4.2	118	2.50	66	38	28	1.36
84-1880	146	4.5	110	2.41	58	37	21	1.76
84-1881	148	6.5	109	2.26	61	31	30	1.03
84-1882	143	4.7	112	2.35	59	35	24	1.46
84-1886	145	4.4	111	2.61	58	35	23	1.52
84-1887	158	4.7	117	2.38	65	36	29	1.24
84-1888	149	4.4	112	2.52	54	34	20	1.70
84-1889	149	5.2	111	2.30	60	34	26	1.31
84-1890	145	5.3	112	2.49	58	34	24	1.42
84-1891	149	4.4	105	2.45	60	35	25	1.40
LOW DOSE - 250 mg/kg								
84-1904	146	4.5	108	2.33	58	35	23	1.52
84-1905	149	4.6	115	2.35	60	33	27	1.22
84-1906	145	4.5	113	2.37	57	35	22	1.59
84-1907	146	4.9	108	2.36	64	35	29	1.21
84-1908	143	5.7	114	2.41	54	33	21	1.57
84-1909	143	4.9	108	2.34	56	33	23	1.43
84-1910	151	4.4	110	2.62	60	36	24	1.50
84-1911	148	4.5	109	2.48	60	36	24	1.50
84-1912	151	4.7	117	2.41	56	35	21	1.67
84-1913	145	5.7	111	2.35	56	32	24	1.33
MEDIUM DOSE - 500 mg/kg								
84-1924	148	4.8	111	2.33	56	35	21	1.67
84-1925	153	4.5	113	2.42	63	34	29	1.17
84-1926	147	4.2	109	2.33	58	37	21	1.76
84-1927	147	3.8	110	2.31	55	33	22	1.50
84-1928	145	5.3	114	2.42	57	35	22	1.59
84-1929	139	4.5	110	2.35	59	34	25	1.36
84-1930	148	4.9	117	2.50	53	33	20	1.65
84-1931	146	5.6	110	2.40	61	35	26	1.35
84-1932	147	5.7	114	2.55	58	34	24	1.42
84-1933	145	4.8	110	2.39	55	33	22	1.50
HIGH DOSE- 1000 mg/kg								
84-1950	147	4.9	111	2.31	57	37	20	1.85
84-1951	150	4.7	114	2.35	61	40	21	1.90
84-1953	142	4.7	108	2.34	63	34	29	1.17
84-1954	150	4.7	108	2.45	58	38	20	1.90
84-1956	146	4.7	110	2.54	58	35	23	1.52
84-1957	145	4.5	111	2.43	57	30	27	1.11
84-1958	147	5.2	114	2.54	56	34	22	1.55
84-1959	148	4.6	107	2.34	60	37	23	1.61
84-1960	146	5.5	110	2.49	58	36	22	1.64
84-1962	146	5.9	109	2.39	56	33	23	1.43

ND : NO DATA

S.A. 2448

APPENDIX D, TABLE 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE HEMATOLOGY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	HGB g/dL	HCT L/L	REC X10E12/L	MCV fL	MCH pg	MCHC g/dL	PT SECONDS	PLAT X10E9/L
CONTROL - 0 mg/kg								
84-1864	14.5	0.415	7.19	57.7	20.2	34.9	11.6	1435
84-1866	14.7	0.411	7.37	55.7	19.9	35.7	11.8	1710
84-1867	ND	ND	ND	ND	ND	ND	ND	ND
84-1868	14.5	0.427	7.33	58.2	19.8	34.0	12.4	1561
84-1869	14.4	0.415	7.37	56.3	19.6	34.7	11.9	1180
84-1871	14.2	0.409	6.83	59.9	20.8	34.7	11.5	1173
84-1873	15.4	0.438	7.17	61.1	21.5	35.1	11.3	1209
84-1874	15.5	0.448	7.75	57.7	20.0	34.7	12.0	1168
84-1875	14.5	0.423	7.40	57.1	19.6	34.4	ND	1095
84-1878	16.2	0.471	7.84	60.0	20.7	34.5	11.9	1305
LOW DOSE - 250 mg/kg								
84-1894	15.6	0.447	7.55	59.1	20.6	34.9	11.5	1170
84-1895	ND	ND	ND	ND	ND	ND	12.2	ND
84-1896	15.0	0.431	7.21	59.8	20.7	34.7	12.1	1188
84-1897	15.0	0.417	7.16	58.2	20.9	35.9	12.4	1231
84-1898	15.0	0.443	7.54	58.7	19.8	33.8	12.2	1349
84-1899	15.6	0.461	7.88	58.4	19.8	33.8	12.0	1351
84-1900	14.7	0.435	7.81	55.6	18.9	33.9	11.9	1348
84-1901	14.2	0.406	6.86	59.2	20.8	35.0	12.2	1305
84-1902	16.0	0.475	7.79	61.0	20.5	33.6	12.0	1110
84-1903	16.4	0.487	8.56	56.8	19.1	33.6	11.5	1223
MEDIUM DOSE - 500 mg/kg								
84-1914	15.0	0.422	7.02	60.1	21.4	35.5	ND	1367
84-1915	15.4	0.450	7.34	61.2	20.9	34.2	ND	1320
84-1916	15.3	0.452	7.88	57.3	19.4	33.9	10.9	1546
84-1917	14.7	0.420	7.09	59.2	20.7	34.9	11.9	1434
84-1918	15.8	0.463	8.00	57.8	19.7	34.0	12.1	1393
84-1919	15.0	0.454	7.60	59.7	19.7	32.9	11.8	1242
84-1920	15.9	0.448	7.54	59.3	21.1	35.6	11.3	1157
84-1921	16.1	0.472	7.73	61.0	20.8	34.1	11.8	1459
84-1922	15.5	0.461	8.18	56.3	18.9	33.6	12.3	1673
84-1923	15.4	0.441	7.73	56.9	20.0	35.1	12.4	1268
HIGH DOSE - 1000 mg/kg								
84-1936	14.6	0.417	7.37	56.5	19.8	34.9	11.2	1464
84-1938	14.7	0.423	7.22	58.5	20.4	34.9	12.0	1357
84-1940	14.7	0.423	7.35	57.5	20.1	34.8	11.5	1403
84-1942	14.5	0.424	7.52	56.4	19.3	34.2	12.6	1223
84-1943	13.9	0.390	6.75	57.8	20.7	35.8	ND	1351
84-1944	15.6	0.478	8.22	58.0	18.9	32.6	11.7	1441
84-1945	16.3	0.482	8.11	59.3	20.1	33.9	11.4	769
84-1946	15.2	0.441	7.64	57.7	19.9	34.5	11.7	1423
84-1947	15.5	0.435	7.36	58.9	21.1	35.7	12.1	1302
84-1948	15.6	0.450	7.84	57.4	19.9	34.6	11.3	1231

ND : NO DATA

APPENDIX D, TABLE 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
MALE HEMATOLOGY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	WBC X10E9/L	INEU %	MNEU %	LYM %	MON %	EOS %	BAS %
CONTROL - 0 mg/kg							
84-1864	5.0	0	5	91	4	0	0
84-1866	6.7	0	15	80	4	1	0
84-1867	ND	ND	ND	ND	ND	ND	ND
84-1868	5.9	0	11	87	2	0	0
84-1869	3.9	0	7	85	8	0	0
84-1871	2.1	0	7	90	3	0	0
84-1873	6.5	0	13	75	12	0	0
84-1874	10.2	0	5	91	3	1	0
84-1875	2.0	0	4	94	2	0	0
84-1878	16.9	0	5	91	3	1	0
LOW DOSE - 250 mg/kg							
84-1894	8.2	0	6	85	9	0	0
84-1895	ND	ND	ND	ND	ND	ND	ND
84-1896	6.1	0	8	89	2	1	0
84-1897	2.6	0	10	85	4	1	0
84-1898	9.4	0	9	89	2	0	0
84-1899	8.8	0	7	85	8	0	0
84-1900	9.0	0	12	88	0	0	0
84-1901	5.0	0	6	92	2	0	0
84-1902	11.2	0	3	95	2	0	0
84-1903	9.8	0	5	94	1	0	0
MEDIUM DOSE- 500 mg/kg							
84-1914	4.3	0	10	86	3	1	0
84-1915	3.6	0	13	83	4	0	0
84-1916	5.4	0	7	90	2	1	0
84-1917	2.9	0	23	75	2	0	0
84-1918	15.2	0	3	95	2	0	0
84-1919	5.9	0	11	82	7	0	0
84-1920	9.8	0	10	86	3	1	0
84-1921	15.2	0	7	90	3	0	0
84-1922	7.3	0	1	95	3	1	0
84-1923	6.3	0	5	91	4	0	0
HIGH DOSE - 1000 mg/kg							
84-1936	8.7	0	12	78	7	3	0
84-1938	7.4	0	13	86	1	0	0
84-1940	10.7	0	7	90	3	0	0
84-1942	9.2	0	8	89	2	1	0
84-1943	2.5	0	22	76	1	1	0
84-1944	9.2	0	3	92	3	2	0
84-1945	4.4	0	21	76	1	2	0
84-1946	6.1	0	14	81	5	0	0
84-1947	8.4	0	3	89	6	2	0
84-1948	8.4	0	11	84	4	1	0

ND : NO DATA

APPENDIX D, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE HEMATOLOGY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	HGB g/dL	HCT L/L	RBC X10E12/L	MCV fL	MCH pg	MCHC g/dL	PT SECONDS	PLAT X10E9/L
CONTROL - 0 mg/kg								
84-1879	14.8	0.419	7.38	56.7	20.0	35.3	12.0	1256
84-1880	15.3	0.441	7.43	59.2	20.6	34.8	12.8	1251
84-1881	14.7	0.410	7.28	56.2	20.2	36.0	12.5	1416
84-1882	14.5	0.399	7.07	56.4	20.5	36.4	11.7	1114
84-1886	14.5	0.418	7.04	59.3	20.6	34.7	12.0	1150
84-1887	ND	ND	ND	ND	ND	ND	ND	ND
84-1888	15.6	0.447	8.18	54.5	19.1	35.0	12.0	1209
84-1889	16.0	0.447	7.70	57.9	20.8	35.9	11.6	1203
84-1890	15.4	0.447	7.93	56.3	19.4	34.4	12.5	1434
84-1891	16.1	0.443	7.87	56.2	20.4	36.3	12.0	1280
LOW DOSE - 250 mg/kg								
84-1904	15.5	0.423	7.62	55.4	20.4	36.7	11.6	972
84-1905	14.4	0.399	7.19	55.5	20.0	36.0	12.1	1188
84-1906	15.3	0.431	7.64	56.3	20.1	35.6	11.9	1269
84-1907	14.8	0.411	7.36	55.8	20.2	36.1	ND	1176
84-1908	15.3	0.439	7.81	56.2	19.5	34.7	11.6	1228
84-1909	15.7	0.442	7.70	57.4	20.4	35.5	12.2	1243
84-1910	15.8	0.447	7.98	56.0	19.8	35.3	12.0	1140
84-1911	14.7	0.408	7.00	58.3	21.1	36.1	10.5	1229
84-1912	14.4	0.439	7.46	58.8	19.3	32.7	13.4	1213
84-1913	15.8	0.462	7.93	58.2	20.0	34.3	11.7	1287
MEDIUM DOSE - 500 mg/kg								
84-1924	14.7	0.405	7.13	56.7	20.5	36.2	11.9	1040
84-1925	14.3	0.400	7.10	56.3	20.1	35.8	13.1	1423
84-1926	ND	ND	ND	ND	ND	ND	11.2	ND
84-1927	15.2	0.438	7.50	58.4	20.3	34.7	11.5	1287
84-1928	14.6	0.409	7.18	57.0	20.3	35.6	12.3	1333
84-1929	14.2	0.400	6.65	60.1	21.3	35.4	12.1	1281
84-1930	15.8	0.457	7.98	57.3	19.8	34.5	12.4	1233
84-1931	16.0	0.443	8.03	55.1	19.9	36.2	11.6	1482
84-1932	15.3	0.433	7.33	59.0	20.9	35.4	12.5	1545
84-1933	14.8	0.431	7.01	61.5	21.1	34.3	ND	1296
HIGH DOSE - 1000 mg/kg								
84-1950	14.6	0.406	7.43	54.6	19.7	36.0	11.3	1342
84-1951	14.8	0.412	7.42	55.5	20.0	35.9	10.7	1048
84-1953	14.4	0.415	7.37	56.2	19.5	34.7	12.9	1288
84-1954	14.7	0.411	7.49	54.9	19.6	35.6	12.2	1200
84-1956	14.8	0.430	7.68	56.0	19.3	34.4	12.1	1443
84-1957	15.0	0.425	7.75	54.8	19.4	35.4	12.6	1512
84-1958	14.6	0.420	7.54	55.6	19.4	34.8	12.1	1340
84-1959	14.5	0.403	7.27	55.3	19.9	36.0	11.6	1134
84-1960	16.1	0.457	7.61	60.0	21.2	35.3	12.1	1348
84-1962	15.8	0.445	8.12	54.7	19.4	35.5	13.4	1323

ND : NO DATA

APPENDIX D, TABLE 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE HEMATOLOGY, STUDY DAYS 29-30

INDIVIDUAL VALUES

	WBC X10E9/L	INEU %	MNEU %	LYM %	MON %	EOS %	BAS %
CONTROL - 0 mg/kg							
84-1879	1.8	0	27	68	3	2	0
84-1880	4.5	0	6	88	5	1	0
84-1881	4.1	0	7	93	0	0	0
84-1882	3.5	0	2	95	3	0	0
84-1886	7.3	0	4	93	3	0	0
84-1887	ND	ND	ND	ND	ND	ND	ND
84-1888	12.0	0	7	92	1	0	0
84-1889	7.6	0	6	92	1	1	0
84-1890	9.5	0	1	97	1	1	0
84-1891	1.1	0	13	81	5	1	0
LOW DOSE - 250 mg/kg							
84-1904	5.5	0	10	82	4	4	0
84-1905	5.1	0	2	96	1	1	0
84-1906	6.4	0	3	94	2	1	0
84-1907	2.8	0	16	79	5	0	0
84-1908	8.9	0	11	89	0	0	0
84-1909	8.7	0	7	84	8	1	0
84-1910	6.9	0	7	92	1	0	0
84-1911	4.5	0	1	93	6	0	0
84-1912	5.2	0	7	89	4	0	0
84-1913	7.3	0	6	92	1	1	0
MEDIUM DOSE- 500 mg/kg							
84-1924	8.6	0	8	88	2	2	0
84-1925	1.7	0	5	94	0	1	0
84-1926	ND	ND	ND	ND	ND	ND	ND
84-1927	6.7	0	8	84	8	0	0
84-1928	5.7	0	2	94	4	0	0
84-1929	1.8	0	17	83	0	0	0
84-1930	5.6	0	6	92	2	0	0
84-1931	6.9	0	4	89	6	1	0
84-1932	13.6	0	2	98	0	0	0
84-1933	3.6	0	20	72	6	2	0
HIGH DOSE - 1000 mg/kg							
84-1950	4.5	0	11	85	3	1	0
84-1951	2.4	0	16	80	4	0	0
84-1953	2.3	0	8	88	4	0	0
84-1954	2.9	0	1	96	2	1	0
84-1956	8.7	0	1	94	4	1	0
84-1957	9.5	0	8	87	5	0	0
84-1958	11.2	0	6	90	3	1	0
84-1959	1.8	0	6	88	6	0	0
84-1960	12.6	0	1	94	5	0	0
84-1962	3.9	0	9	79	7	5	0

ND : NO DATA

APPENDIX E, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES

	REFR INDEX a	pH b	PROTEIN c	GLUCOSE c	KETONES d	BILI d	OC BL d	UROB e
CONTROL - 0 mg/kg								
84-1864	1.345	7.5	1	0	0	0	0	0.1
84-1866	1.342	7.5	1	0	1	0	0	0.1
84-1867	1.344	8.0	1	0	0	0	0	1.0
84-1868	1.341	8.0	1	0	0	0	0	1.0
84-1869	1.356	8.0	1	0	0	0	0	0.1
84-1871	ND	ND	ND	ND	ND	ND	ND	ND
84-1873	1.349	7.5	2	0	1	0	0	0.1
84-1874	1.348	7.0	1	0	1	0	0	0.1
84-1875	1.346	8.5	1	0	0	0	0	1.0
84-1878	ND	ND	ND	ND	ND	ND	ND	ND
LOW DOSE - 250 mg/kg								
84-1894	1.351	7.0	1	0	1	0	0	1.0
84-1895	1.347	7.0	1	0	0	0	0	0.1
84-1896	1.361	6.5	2	0	0	0	0	1.0
84-1897	ND	ND	ND	ND	ND	ND	ND	ND
84-1898	1.349	7.5	1	0	1	0	0	0.1
84-1899	1.349	7.0	2	0	1	0	0	0.1
84-1900	1.341	8.0	1	0	0	0	0	1.0
84-1901	1.344	7.5	1	0	0	0	0	1.0
84-1902	1.354	7.0	1	0	0	0	0	1.0
84-1903	1.347	7.5	1	0	1	0	0	1.0
MEDIUM DOSE - 500 mg/kg								
84-1914	1.348	7.0	1	0	0	0	0	1.0
84-1915	1.349	8.0	1	0	0	0	0	1.0
84-1916	1.355	7.0	2	0	0	0	0	1.0
84-1917	1.352	7.5	1	0	0	0	0	0.1
84-1918	1.358	6.5	2	0	0	0	1	1.0
84-1919	1.348	8.5	1	0	1	0	0	1.0
84-1920	ND	ND	ND	ND	ND	ND	ND	ND
84-1921	1.351	7.0	1	0	0	0	0	1.0
84-1922	1.356	6.5	1	0	1	0	0	1.0
84-1923	1.351	7.5	1	0	0	0	0	1.0

a : REFRACTIVITY X10E-4 + 1.333

b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)

c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1

d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)

e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)

ND : NO DATA

APPENDIX E, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES

	REFR INDEX a	pH b	PROTEIN c	GLUCOSE c	KETONES d	BILI d	OC BL d	UROB e
HIGH DOSE - 1000 mg/kg								
84-1936	1.347	8.0	1	0	1	0	1	1.0
84-1938	ND	ND	ND	ND	ND	ND	ND	ND
84-1940	1.360	6.5	1	0	0	0	0	1.0
84-1942	ND	ND	ND	ND	ND	ND	ND	ND
84-1943	1.346	8.0	1	0	1	0	0	0.1
84-1944	ND	ND	ND	ND	ND	ND	ND	ND
84-1945	1.349	7.5	1	0	1	0	0	1.0
84-1946	1.348	7.0	1	0	0	0	0	0.1
84-1947	1.344	7.5	1	0	1	0	0	1.0
84-1948	1.342	8.0	1	0	0	0	0	0.1

a : REFRACTIVITY X10E-4 + 1.333

b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)

c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1

d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)

e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)

ND : NO DATA

APPENDIX E, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES

	CASTS f	CRYS g	RBC h	WBC h	BACT g	VOLUME mL
CONTROL - 0 mg/kg						
84-1864	0	1	0	0	1	59
84-1866	0	1	0	1	1	65 *
84-1867	0	2	0	0	1	40
84-1868	0	0	0	0	1	52
84-1869	0	1	0	0	1	1
84-1871	ND	ND	ND	ND	ND	15
84-1873	0	1	0	0	1	3
84-1874	0	1	0	0	1	18
84-1875	0	1	0	0	1	5
84-1878	ND	ND	ND	ND	ND	22
LOW DOSE - 250 mg/kg						
84-1894	0	1	0	0	1	5
84-1895	0	1	0	0	1	30
84-1896	0	0	0	0	1	13
84-1897	ND	ND	ND	ND	ND	8
84-1898	0	1	0	0	1	26
84-1899	0	1	0	0	1	8
84-1900	0	1	0	0	1	35
84-1901	0	1	0	1	1	14
84-1902	0	1	0	1	1	4
84-1903	0	1	0	0	1	49
MEDIUM DOSE - 500 mg/kg						
84-1914	0	1	0	0	1	33
84-1915	0	2	0	0	1	23
84-1916	0	1	0	0	1	65 *
84-1917	0	1	0	0	1	8
84-1918	0	0	0	0	1	65 *
84-1919	0	2	0	0	1	14
84-1920	ND	ND	ND	ND	ND	35
84-1921	0	0	0	0	1	25
84-1922	0	1	0	0	2	35
84-1923	0	1	0	0	1	16
HIGH DOSE- 1000 mg/kg						
84-1936	0	1	0	0	1	31
84-1938	ND	ND	ND	ND	ND	40
84-1940	0	1	0	0	1	3
84-1942	ND	ND	ND	ND	ND	53
84-1943	0	1	0	0	1	28
84-1944	ND	ND	ND	ND	ND	6
84-1945	0	0	0	0	1	28
84-1946	0	1	0	0	1	8
84-1947	0	1	0	0	1	29
84-1948	0	1	0	0	1	18

f : CASTS PER LOW POWER FIELD

g : VALUE REPRESENTS A GRADING SYSTEM BASED ON A SUBJECTIVE MICROSCOPIC DETERMINATION OF THE NUMBER PRESENT (FEW TO MANY) IN A SAMPLE

h : CELLS PER HIGH POWER FIELD

ND : NO DATA

* : TRUNCATED VALUE

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APPENDIX E, TABLE 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES

	REFR INDEX a	pH b	PROTEIN c	GLUCOSE c	KETONES d	BILI d	OC BL d	UROB e
CONTROL - 0 mg/kg								
84-1879	1.343	8.5	1	0	0	0	0	1.0
84-1880	1.342	8.0	1	0	0	0	0	1.0
84-1881	ND	ND	ND	ND	ND	ND	ND	ND
84-1882	1.351	7.0	1	0	0	0	0	1.0
84-1886	1.344	8.0	1	0	0	0	0	1.0
84-1887	ND	ND	ND	ND	ND	ND	ND	ND
84-1888	1.349	6.0	1	0	0	0	0	1.0
84-1889	1.347	8.0	1	0	0	0	0	1.0
84-1890	1.351	7.0	1	0	0	0	0	1.0
84-1891	1.344	8.0	1	0	0	0	0	1.0
LOW DOSE - 250 mg/kg								
84-1904	1.344	7.0	1	0	0	0	0	1.0
84-1905	1.344	8.0	1	0	0	0	0	0.1
84-1906	1.348	7.0	1	0	0	0	0	1.0
84-1907	1.345	8.5	1	0	0	0	0	1.0
84-1908	1.342	7.0	1	0	0	0	0	0.1
84-1909	ND	ND	ND	ND	ND	ND	ND	ND
84-1910	1.343	8.0	1	0	0	0	0	0.1
84-1911	1.349	6.5	1	0	0	0	0	1.0
84-1912	ND	ND	ND	ND	ND	ND	ND	ND
84-1913	1.355	7.0	1	0	0	0	0	1.0
MEDIUM DOSE - 500 mg/kg								
84-1924	1.352	6.5	1	0	0	0	0	1.0
84-1925	1.353	7.5	1	0	0	0	0	1.0
84-1926	1.350	7.0	1	0	0	0	0	1.0
84-1927	1.354	5.0	1	0	0	0	0	0.1
84-1928	1.354	6.5	1	0	0	0	0	1.0
84-1929	ND	ND	ND	ND	ND	ND	ND	ND
84-1930	1.341	7.0	0	0	0	0	0	0.1
84-1931	1.352	7.0	1	0	0	0	0	1.0
84-1932	ND	ND	ND	ND	ND	ND	ND	ND
84-1933	1.353	8.5	1	0	0	0	0	1.0

a : REFRACTIVITY X10E-4 + 1.333
b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)
c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1
d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)
e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)
ND : NO DATA

APPENDIX E, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES

	REFR INDEX a	pH b	PROTEIN c	GLUCOSE c	KETONES d	BILI d	OC BL d	UROB e
HIGH DOSE - 1000 mg/kg								
84-1950	1.341	8.0	1	0	0	0	0	0.1
84-1951	1.345	7.0	1	0	0	0	0	0.1
84-1953	ND	ND	ND	ND	ND	ND	ND	ND
84-1954	ND	ND	ND	ND	ND	ND	ND	ND
84-1956	ND	ND	ND	ND	ND	ND	ND	ND
84-1957	1.344	7.0	1	0	0	0	0	0.1
84-1958	1.351	6.5	1	0	0	0	0	1.0
84-1959	1.344	8.5	1	0	0	0	0	1.0
84-1960	1.343	7.0	1	0	0	0	0	0.1
84-1962	1.346	8.0	1	0	0	0	0	0.1

a : REFRACTIVITY X10E-4 + 1.333

b : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0-8.5)

c : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 4) - TRACE AMOUNTS INDICATED BY 1

d : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)

e : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)

ND : NO DATA

APPENDIX E, TABLE 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT
FEMALE URINALYSIS, STUDY DAYS 28-29

INDIVIDUAL VALUES						
	CASTS f	CRYS g	RBC h	WBC h	BACT g	VOLUME mL
CONTROL - 0 mg/kg						
84-1879	0	0	0	0	1	2
84-1880	0	0	0	0	1	ND
84-1881	ND	ND	ND	ND	ND	10
84-1882	0	1	0	0	1	ND
84-1886	0	0	0	0	1	2
84-1887	ND	ND	ND	ND	ND	3
84-1888	0	0	0	0	1	5
84-1889	0	0	0	0	1	4
84-1890	0	1	0	0	1	15
84-1891	0	1	0	0	1	10
LOW DOSE - 250 mg/kg						
84-1904	0	1	0	0	1	ND
84-1905	0	1	0	0	1	14
84-1906	0	1	0	0	0	65 *
84-1907	0	0	0	0	1	4
84-1908	0	1	0	0	1	5
84-1909	ND	ND	ND	ND	ND	3
84-1910	0	1	0	0	1	31
84-1911	0	1	0	1	2	15
84-1912	ND	ND	ND	ND	ND	2
84-1913	0	0	0	0	1	5
MEDIUM DOSE - 500 mg/kg						
84-1924	0	0	0	0	1	4
84-1925	0	1	0	0	1	8
84-1926	0	0	0	0	1	65 *
84-1927	0	1	0	0	1	3
84-1928	0	0	0	0	1	40
84-1929	ND	ND	ND	ND	ND	5
84-1930	0	0	0	0	1	15
84-1931	0	1	0	0	1	3
84-1932	ND	ND	ND	ND	ND	5
84-1933	0	1	0	0	1	4
HIGH DOSE- 1000 mg/kg						
84-1950	0	1	0	0	1	10
84-1951	0	0	0	0	1	27
84-1953	ND	ND	ND	ND	ND	12
84-1954	ND	ND	ND	ND	ND	12
84-1956	ND	ND	ND	ND	ND	12
84-1957	0	0	0	0	1	10
84-1958	0	1	0	0	1	10
84-1959	0	0	0	0	1	5
84-1960	0	1	0	0	2	12
84-1962	0	0	0	0	1	12

f : CASTS PER LOW POWER FIELD
g : VALUE REPRESENTS A GRADING SYSTEM BASED ON A SUBJECTIVE MICROSCOPIC
DETERMINATION OF THE NUMBER PRESENT (FEW TO MANY) IN A SAMPLE
h : CELLS PER HIGH POWER FIELD
ND : NO DATA
* : TRUNCATED VALUE

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APPENDIX F

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

OPHTHALMIC EXAMINATION REPORT

Methods

The examinations were performed October 29, 1984.

One to two drops of 1% tropicamide (Mydrilac^R) (Alcon Laboratories) were placed in each eye.

Approximately 10-60 minutes after the application of tropicamide the eyes were examined under reduced illumination to increase the contrast between the different ocular structures. The adnexa, cornea, anterior chamber, iris and lens were evaluated by biomicroscopy with the Kowa SL-2 Zoom Slit Lamp. Magnification was varied from 5 to 20X.

The fundus of each eye was then evaluated by binocular indirect ophthalmoscopy using the Fison Binocular Ophthalmoscope^R (Keeler Optical, Inc.) and a Nikon 20⁺ or 28⁺ Diopter examining lens. The fundus was also evaluated using the American Optical Monocular Indirect Ophthalmoscope^R in some animals.

Results

Control Dose Group: The following 24 animals were normal: 84-1864, 84-1866, 84-1869, 84-1870, 84-1871, 84-1872, 84-1874, 84-1876, 84-1877, 84-1878, 84-1879, 84-1880, 84-1881, 84-1882, 84-1884, 84-1885, 84-1886, 84-1887, 84-1888, 84-1889, 84-1890, 84-1891, 84-1892, and 84-1893.

Animals 84-1865, 84-1875 and 84-1883 each had mild central subepithelial corneal dystrophy of both eyes as the only abnormality noted.

Animal 84-1867 had mild central subepithelial corneal dystrophy of both eyes and an anterior subcapsular suture line cataract of the right eye as the only abnormalities noted.

Animal 84-1868 had mild red tinged periocular exudate and diffuse corneal epithelial disruption of both eyes as the only abnormalities noted.

Animal 84-1873 had a central leukoma due to anterior synechia in the left eye. The rest of the examination was normal.

Low Dose Group: The following 19 animals were normal: 84-1894, 84-1895, 84-1897, 84-1898, 84-1899, 84-1900, 84-1901, 84-1902, 84-1903, 84-1904, 84-1905, 84-1906, 84-1907, 84-1908, 84-1909, 84-1910, 84-1911, 84-1912, and 84-1913.

Animal 84-1896 had resorbing vitreal hemorrhage associated with a persistent hyaloid system of the left eye. The rest of the examination was normal.

Medium Dose Group: The following 18 animals were normal: 84-1914, 84-1915, 84-1916, 84-1917, 84-1918, 84-1919, 84-1920, 84-1921, 84-1922, 84-1923, 84-1924, 84-1925, 84-1926, 84-1927, 84-1928, 84-1929, 84-1930, and 84-1931.

Animal 84-1932 had mild central subepithelial corneal dystrophy of each eye as the only abnormality noted.

Animal 84-1933 had vitreal hemorrhage due to persistent hyaloid system in the right eye. The rest of the examination was normal.

High Dose Group: The following 29 animals were normal:
84-1934, 84-1935, 84-1936, 84-1937, 84-1938, 84-1940,
84-1941, 84-1942, 84-1943, 84-1944, 84-1945, 84-1946,
84-1947, 84-1948, 84-1949, 84-1950, 84-1951, 84-1952,
84-1953, 84-1954, 84-1955, 84-1956, 84-1957, 84-1958,
84-1959, 84-1960, 84-1961, 84-1962, and 84-1963.

Animal 84-1939 had mild central subepithelial corneal dystrophy of the right eye as the only abnormality noted.

Discussion

The corneal dystrophy noted in a total of 6 animals is an epithelial to subepithelial disruption of the tissue or deposition of material not uncommon in the laboratory rat. The nature of this disruption or deposition may or may not be evident histopathologically. Due to the low incidence and occurrence in different groups this is not considered significant. Similarly the cataract in animal 84-1867 is an incidental random occurrence not uncommon in laboratory rats. Due to the low incidence this is not significant.

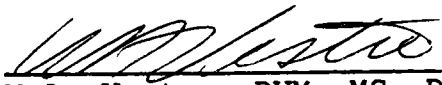
The red tinged exudate and corneal epithelial disruption in animal 84-1868 may be due to infection or inflammation of the lacrimal and Harder gland (chromodacryorrhea) or due to corneal infection or trauma. The

exact etiology was not determined but due to the low incidence this is not considered significant.

The central leukoma and synechia in animal 84-1873 is most probably due to corneal trauma which is relatively common in the laboratory rat. This is not significant.

The vitreal hemorrhage in animals 84-1896 and 84-1933 is due to delayed resorption of normal embryonic structures and is common in low numbers in the laboratory rat. This is not significant in the low number and random occurrence noted here.

Based on this terminal ophthalmic examination there do not appear to be any compound related ocular effects.

 12/26/84
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APPENDIX G, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN WEIGHTS (g)

	BODY WT	BRAIN	HEART	LIVER	KIDNEY	ADRENAL	THYROID
CONTROL - 0 mg/kg							
84-1864	289.	2.06	1.04	8.86	2.52	0.060	0.020
84-1866	258.	1.92	0.99	7.23	2.14	0.051	0.015
84-1867	284.	1.92	1.41	8.66	2.26	0.058	0.019
84-1868	281.	1.97	1.14	8.19	2.42	0.066	0.018
84-1869	198.	1.82	0.76	5.39	1.71	0.050	0.017
84-1871	280.	2.10	1.13	8.39	2.46	0.058	0.023
84-1873	281.	1.88	0.96	7.90	2.46	0.047	0.016
84-1874	253.	1.93	0.94	7.73	2.28	0.050	0.021
84-1875	279.	1.98	1.22	7.75	2.31	0.054	0.019
84-1878	263.	1.93	1.01	7.35	2.08	0.058	0.019
LOW DOSE - 250 mg/kg							
84-1894	286.	2.04	0.98	8.14	2.34	0.056	0.013
84-1895	270.	2.11	0.91	7.86	2.27	0.047	0.020 *
84-1896	238.	1.82	0.89	6.01	1.93	0.054	0.015
84-1897	275.	2.01	1.08	8.36	2.32	0.049	0.022
84-1898	283.	1.95	1.15	8.76	2.23	0.050	0.015
84-1899	270.	1.95	0.95	8.75	2.27	0.047	0.020
84-1900	230.	2.00	0.90	6.78	1.82	0.054	0.017
84-1901	277.	1.93	1.06	9.11	2.44	0.055	0.023
84-1902	303.	2.03	1.13	9.36	2.48	0.060	0.015
84-1903	249.	1.97	0.99	7.51	2.26	0.053	0.016
MEDIUM DOSE - 500 mg/kg							
84-1914	290.	2.13	0.93	8.93	2.27	0.054	0.024
84-1915	298.	2.00	1.16	9.59	2.79	0.056	0.023
84-1916	265.	1.95	0.88	7.90	2.19	0.047	0.017
84-1917	243.	1.81	0.87	7.10	2.03	0.037	0.019
84-1918	280.	2.06	1.12	8.14	2.41	0.061	0.021
84-1919	309.	2.01	1.18	9.22	2.49	0.055	0.015
84-1920	279.	1.99	0.95	7.61	2.39	0.050	0.017
84-1921	276.	2.06	0.99	8.27	2.37	0.057	0.017
84-1922	270.	2.02	1.11	7.72	2.31	0.058	0.024
84-1923	281.	2.10	0.97	8.19	2.26	0.058	0.020
HIGH DOSE - 1000 mg/kg							
84-1936	315.	1.96	1.25	10.21	2.63	0.068	0.016
84-1938	291.	2.06	1.15	9.06	2.15	0.070	0.023
84-1940	241.	1.93	0.86	7.46	1.81	0.045	0.012
84-1942	257.	2.03	0.97	6.73	2.27	0.054	0.027
84-1943	307.	1.96	1.20	9.99	2.41	0.046	0.021
84-1944	265.	1.98	1.02	7.43	2.19	0.042	0.017
84-1945	281.	1.90	1.23	11.03	2.80	0.059	0.025
84-1946	248.	1.90	0.94	7.28	2.27	0.048	0.014
84-1947	270.	1.94	1.07	8.29	2.32	0.061	0.018
84-1948	306.	1.99	1.21	9.85	2.62	0.049	0.020

* : THYROID WEIGHED AFTER FIXATION, DATA NOT INCLUDED IN STATISTICAL CALCULATIONS.

APPENDIX G, TABLE 1

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN WEIGHTS (g)

	THYMUS	PITUITARY	SPLEEN	SAL GL	TESTIS	PROSTATE	EPIDIDYMIS
CONTROL - 0 mg/kg							
84-1864	0.56	0.014	0.51	0.62	2.86	0.44	1.01
84-1866	0.48	0.010	0.49	0.50	2.76	0.33	0.83
84-1867	0.49	0.008	0.55	0.86	2.83	0.53	1.03
84-1868	0.61	0.010	0.58	0.73	3.12	0.41	0.89
84-1869	0.33	0.008	0.43	0.45	2.77	0.23	0.95
84-1871	0.57	0.010	0.55	0.79	2.80	0.39	1.09
84-1873	0.67	0.010	0.52	0.51	2.77	0.38	0.79
84-1874	0.49	0.008	0.44	0.50	3.13	0.20	0.91
84-1875	0.47	0.011	0.48	0.73	2.81	0.55	0.98
84-1878	0.71	0.008	0.51	0.63	2.52	0.49	0.85
LOW DOSE - 250 mg/kg							
84-1894	0.55	0.010	0.52	0.63	2.93	0.39	0.93
84-1895	0.45	0.011	0.56	0.55	3.34	0.23	0.83
84-1896	0.49	0.008	0.49	0.53	2.86	0.47	0.91
84-1897	0.60	0.010	0.52	0.68	2.85	0.52	1.12
84-1898	0.55	0.011	0.45	0.60	3.04	0.30	0.93
84-1899	0.51	0.010	0.51	0.51	2.70	0.42	0.72
84-1900	0.38	0.007	0.50	0.61	2.57	0.34	0.75
84-1901	0.59	0.010	0.61	0.84	2.73	0.46	1.22
84-1902	0.68	0.010	0.58	0.59	3.04	0.30	0.95
84-1903	0.55	0.007	0.50	0.55	2.70	0.34	0.80
MEDIUM DOSE - 500 mg/kg							
84-1914	0.49	0.009	0.48	0.62	2.75	0.41	1.03
84-1915	0.72	0.011	0.62	0.66	3.05	0.50	1.08
84-1916	0.79	0.010	0.54	0.53	2.41	0.34	0.78
84-1917	0.54	0.010	0.52	0.64	2.68	0.26	0.81
84-1918	0.60	0.011	0.58	0.74	2.68	0.51	1.13
84-1919	0.56	0.012	0.50	0.69	2.92	0.50	0.96
84-1920	0.36	0.010	0.57	0.52	2.91	0.28	0.83
84-1921	0.46	0.012	0.58	0.61	3.04	0.29	0.87
84-1922	0.55	0.012	0.53	0.65	3.26	0.42	0.98
84-1923	0.50	0.010	0.55	0.72	2.90	0.52	0.86
HIGH DOSE - 1000 mg/kg							
84-1936	0.58	0.012	0.47	0.61	3.19	0.33	0.92
84-1938	0.45	0.011	0.56	0.69	2.96	0.43	1.03
84-1940	0.44	0.009	0.51	0.52	2.82	0.30	0.81
84-1942	0.45	0.010	0.49	0.75	2.53	0.34	0.82
84-1943	0.55	0.009	0.44	0.54	2.82	0.29	0.76
84-1944	0.47	0.008	0.47	0.48	2.53	0.17	0.81
84-1945	0.66	0.011	0.51	0.70	2.88	0.44	0.87
84-1946	0.50	0.010	0.48	0.53	2.69	0.31	0.89
84-1947	0.68	0.009	0.56	0.72	3.09	0.40	1.08
84-1948	0.44	0.011	0.55	0.68	2.64	0.31	0.78

APPENDIX G, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN WEIGHTS (g)

	BODY WT	BRAIN	HEART	LIVER	KIDNEY	ADRENAL	THYROID
CONTROL - 0 mg/kg							
84-1879	159.	1.73	0.73	5.33	1.53	0.068	0.014
84-1880	176.	1.96	0.82	5.29	1.55	0.073	0.012
84-1881	168.	1.81	0.64	5.27	1.44	0.048	0.013
84-1882	202.	1.89	0.83	6.58	1.85	0.080	0.012
84-1886	179.	1.69	0.74	5.98	1.54	0.083	0.020
84-1887	174.	1.95	0.80	5.23	1.63	0.069	0.019
84-1888	151.	1.87	0.60	4.82	1.68	0.053	0.014
84-1889	164.	1.83	0.72	5.00	1.57	0.063	0.017
84-1890	179.	1.91	0.81	5.38	1.77	0.083	0.019
84-1891	160.	1.78	0.86	5.28	1.42	0.056	0.011
LOW DOSE - 250 mg/kg							
84-1904	156.	1.95	0.72	4.97	1.61	0.058	0.010
84-1905	160.	1.80	0.59	4.16	1.30	0.041	0.011
84-1906	184.	1.85	0.75	5.00	1.63	0.062	0.019
84-1907	163.	1.85	0.74	5.25	1.54	0.058	0.016
84-1908	158.	1.80	0.61	4.79	1.40	0.040	0.012
84-1909	158.	1.64	0.60	4.36	1.37	0.053	0.018
84-1910	191.	1.80	0.82	5.45	1.49	0.081	0.020
84-1911	180.	1.79	0.73	5.84	1.56	0.064	0.017
84-1912	139.	1.85	0.61	4.77	1.55	0.068	0.012
84-1913	215.	1.91	0.82	6.54	1.87	0.078	0.014
MEDIUM DOSE - 500 mg/kg							
84-1924	185.	1.81	0.74	6.50	1.62	0.070	0.021
84-1925	189.	1.76	0.87	5.65	1.72	0.079	0.014
84-1926	163.	1.74	0.63	5.06	1.38	0.054	0.015
84-1927	163.	1.70	0.67	4.59	1.41	0.050	0.014
84-1928	183.	1.76	0.82	5.97	1.57	0.073	0.017
84-1929	192.	2.00	0.78	5.90	1.62	0.065	0.017
84-1930	171.	1.88	0.71	5.30	1.56	0.060	0.016
84-1931	166.	1.82	0.73	6.09	1.59	0.061	0.012
84-1932	158.	1.76	0.73	4.63	1.55	0.061	0.016
84-1933	183.	1.93	0.69	5.22	1.56	0.065	0.022
HIGH DOSE - 1000 mg/kg							
84-1950	163.	1.91	0.65	5.55	1.70	0.052	0.012
84-1951	161.	1.86	0.64	4.81	1.44	0.057	0.013
84-1953	172.	1.89	0.65	5.51	1.66	0.063	0.022
84-1954	139.	1.79	0.72	4.29	1.42	0.066	0.010
84-1956	177.	1.75	0.68	5.39	1.72	0.057	0.011
84-1957	177.	1.78	0.73	5.46	1.49	0.067	0.015
84-1958	187.	1.85	0.79	5.71	1.58	0.064	0.018
84-1959	133.	1.83	0.65	4.15	1.42	0.071	0.022
84-1960	181.	1.83	0.62	5.31	1.54	0.050	0.015
84-1962	187.	1.85	0.76	5.54	1.67	0.064	0.013

APPENDIX G, TABLE 2

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN WEIGHTS (g)

	THYMUS	PITUITARY	SPLEEN	SAL GL	OVARY	UTERUS
CONTROL - 0 mg/kg						
84-1879	0.38	0.009	0.33	0.52	0.13	0.37
84-1880	0.38	0.009	0.36	0.47	0.11	0.33
84-1881	0.44	0.011	0.36	0.46	0.07	0.46
84-1882	0.49	0.015	0.45	0.44	0.07	0.61
84-1886	0.34	0.011	0.34	0.51	0.15	0.47
84-1887	0.42	0.009	0.33	0.59	0.12	0.37
84-1888	0.33	0.010	0.30	0.42	0.01	0.37
84-1889	0.34	0.010	0.42	0.39	0.07	0.37
84-1890	0.44	0.011	0.40	0.54	0.12	0.35
84-1891	0.43	0.009	0.29	0.48	0.13	0.41
LOW DOSE - 250 mg/kg						
84-1904	0.36	0.010	0.40	0.44	0.08	0.60
84-1905	0.47	0.008	0.31	0.32	0.06	0.39
84-1906	0.57	0.011	0.45	0.50	0.12	0.46
84-1907	0.31	0.007	0.30	0.58	0.11	0.55
84-1908	0.38	0.010	0.32	0.35	0.06	0.34
84-1909	0.50	0.009	0.32	0.36	0.06	0.33
84-1910	0.53	0.008	0.39	0.43	0.13	0.68
84-1911	0.52	0.014	0.45	0.51	0.12	0.48
84-1912	0.33	0.009	0.23	0.38	0.08	0.40
84-1913	0.34	0.011	0.33	0.36	0.09	0.39
MEDIUM DOSE - 500 mg/kg						
84-1924	0.61	0.014	0.50	0.50	0.13	0.53
84-1925	0.55	0.011	0.43	0.54	0.13	0.44
84-1926	0.38	0.010	0.36	0.42	0.06	0.48
84-1927	0.30	0.007	0.31	0.38	0.07	0.34
84-1928	0.48	0.010	0.35	0.51	0.14	0.59
84-1929	0.37	0.007	0.34	0.51	0.12	0.50
84-1930	0.29	0.009	0.31	0.40	0.07	0.41
84-1931	0.42	0.006	0.38	0.37	0.08	0.33
84-1932	0.40	0.008	0.39	0.38	0.11	0.39
84-1933	0.31	0.011	0.37	0.45	0.10	0.47
HIGH DOSE - 1000 mg/kg						
84-1950	0.40	0.011	0.38	0.27	0.08	0.47
84-1951	0.33	0.009	0.31	0.32	0.07	0.53
84-1953	0.43	0.009	0.37	0.51	0.12	0.58
84-1954	0.27	0.012	0.29	0.42	0.19	0.39
84-1956	0.44	0.010	0.36	0.38	0.08	0.34
84-1957	0.47	0.011	0.39	0.44	0.09	0.32
84-1958	0.54	0.010	0.42	0.48	0.13	0.70
84-1959	0.32	0.004	0.27	0.42	0.12	0.51
84-1960	0.40	0.010	0.36	0.46	0.08	0.39
84-1962	0.37	0.014	0.34	0.39	0.07	0.29

APPENDIX G, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	BRAIN X10E-3	HEART X10E-3	LIVER X10E-2	KIDNEY X10E-3	ADRENAL X10E-4	THYROID X10E-5
CONTROL - 0 mg/kg						
84-1864	7.1	3.6	3.1	8.7	2.1	6.9
84-1866	7.4	3.8	2.8	8.3	2.0	5.8
84-1867	6.8	5.0	3.0	8.0	2.0	6.7
84-1868	7.0	4.1	2.9	8.6	2.3	6.4
84-1869	9.2	3.8	2.7	8.6	2.5	8.6
84-1871	7.5	4.0	3.0	8.8	2.1	8.2
84-1873	6.7	3.4	2.8	8.8	1.7	5.7
84-1874	7.6	3.7	3.1	9.0	2.0	8.3
84-1875	7.1	4.4	2.8	8.3	1.9	6.8
84-1878	7.3	3.8	2.8	7.9	2.2	7.2
LOW DOSE - 250 mg/kg						
84-1894	7.1	3.4	2.8	8.2	2.0	4.5
84-1895	7.8	3.4	2.9	8.4	1.7	7.4 *
84-1896	7.6	3.7	2.5	8.1	2.3	6.3
84-1897	7.3	3.9	3.0	8.4	1.8	8.0
84-1898	6.9	4.1	3.1	7.9	1.8	5.3
84-1899	7.2	3.5	3.2	8.4	1.7	7.4
84-1900	8.7	3.9	2.9	7.9	2.3	7.4
84-1901	7.0	3.8	3.3	8.8	2.0	8.3
84-1902	6.7	3.7	3.1	8.2	2.0	5.0
84-1903	7.9	4.0	3.0	9.1	2.1	6.4
MEDIUM DOSE - 500 mg/kg						
84-1914	7.3	3.2	3.1	7.8	1.9	8.3
84-1915	6.7	3.9	3.2	9.4	1.9	7.7
84-1916	7.4	3.3	3.0	8.3	1.8	6.4
84-1917	7.4	3.6	2.9	8.4	1.5	7.8
84-1918	7.4	4.0	2.9	8.6	2.2	7.5
84-1919	6.5	3.8	3.0	8.1	1.8	4.9
84-1920	7.1	3.4	2.7	8.6	1.8	6.1
84-1921	7.5	3.6	3.0	8.6	2.1	6.2
84-1922	7.5	4.1	2.9	8.6	2.1	8.9
84-1923	7.5	3.5	2.9	8.0	2.1	7.1
HIGH DOSE - 1000 mg/kg						
84-1936	6.2	4.0	3.2	8.3	2.2	5.1
84-1938	7.1	4.0	3.1	7.4	2.4	7.9
84-1940	8.0	3.6	3.1	7.5	1.9	5.0
84-1942	7.9	3.8	2.6	8.8	2.1	10.5
84-1943	6.4	3.9	3.3	7.9	1.5	6.8
84-1944	7.5	3.8	2.8	8.3	1.6	6.4
84-1945	6.8	4.4	3.9	10.0	2.1	8.9
84-1946	7.7	3.8	2.9	9.2	1.9	5.6
84-1947	7.2	4.0	3.1	8.6	2.3	6.7
84-1948	6.5	4.0	3.2	8.6	1.6	6.5

* : THYROID WEIGHED AFTER FIXATION, DATA NOT INCLUDED IN STATISTICAL CALCULATIONS.

APPENDIX G, TABLE 3

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	THYMUS X10E-4	PITUITARY X10E-5	SPLEEN X10E-4	SAL GL X10E-3	TESTIS X10E-3	PROSTATE X10E-4	EPIDIDYMIS X10E-3
CONTROL - 0 mg/kg							
84-1864	19.4	4.8	1.8	2.1	9.9	15.2	3.5
84-1866	18.6	3.9	1.9	1.9	10.7	12.8	3.2
84-1867	17.3	2.8	1.9	3.0	10.0	18.7	3.6
84-1868	21.7	3.6	2.1	2.6	11.1	14.6	3.2
84-1869	16.7	4.0	2.2	2.3	14.0	11.6	4.8
84-1871	20.4	3.6	2.0	2.8	10.0	13.9	3.9
84-1873	23.8	3.6	1.9	1.8	9.9	13.5	2.8
84-1874	19.4	3.2	1.7	2.0	12.4	7.9	3.6
84-1875	16.8	3.9	1.7	2.6	10.1	19.7	3.5
84-1878	27.0	3.0	1.9	2.4	9.6	18.6	3.2
LOW DOSE - 250 mg/kg							
84-1894	19.2	3.5	1.8	2.2	10.2	13.6	3.3
84-1895	16.7	4.1	2.1	2.0	12.4	8.5	3.1
84-1896	20.6	3.4	2.1	2.2	12.0	19.7	3.8
84-1897	21.8	3.6	1.9	2.5	10.4	18.9	4.1
84-1898	19.4	3.9	1.6	2.1	10.7	10.6	3.3
84-1899	18.9	3.7	1.9	1.9	10.0	15.6	2.7
84-1900	16.5	3.0	2.2	2.7	11.2	14.8	3.3
84-1901	21.3	3.6	2.2	3.0	9.9	16.6	4.4
84-1902	22.4	3.3	1.9	1.9	10.0	9.9	3.1
84-1903	22.1	2.8	2.0	2.2	10.8	13.7	3.2
MEDIUM DOSE - 500 mg/kg							
84-1914	16.9	3.1	1.7	2.1	9.5	14.1	3.6
84-1915	24.2	3.7	2.1	2.2	10.2	16.8	3.6
84-1916	29.8	3.8	2.0	2.0	9.1	12.8	2.9
84-1917	22.2	4.1	2.1	2.6	11.0	10.7	3.3
84-1918	21.4	3.9	2.1	2.6	9.6	18.2	4.0
84-1919	18.1	3.9	1.6	2.2	9.4	16.2	3.1
84-1920	12.9	3.6	2.0	1.9	10.4	10.0	3.0
84-1921	16.7	4.3	2.1	2.2	11.0	10.5	3.2
84-1922	20.4	4.4	2.0	2.4	12.1	15.6	3.6
84-1923	17.8	3.6	2.0	2.6	10.3	18.5	3.1
HIGH DOSE - 1000 mg/kg							
84-1936	18.4	3.8	1.5	1.9	10.1	10.5	2.9
84-1938	15.5	3.8	1.9	2.4	10.2	14.8	3.5
84-1940	18.3	3.7	2.1	2.2	11.7	12.4	3.4
84-1942	17.5	3.9	1.9	2.9	9.8	13.2	3.2
84-1943	17.9	2.9	1.4	1.8	9.2	9.4	2.5
84-1944	17.7	3.0	1.8	1.8	9.5	6.4	3.1
84-1945	23.5	3.9	1.8	2.5	10.2	15.7	3.1
84-1946	20.2	4.0	1.9	2.1	10.8	12.5	3.6
84-1947	25.2	3.3	2.1	2.7	11.4	14.8	4.0
84-1948	14.4	3.6	1.8	2.2	8.6	10.1	2.5

APPENDIX G, TABLE 4

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	BRAIN X10E-3	HEART X10E-3	LIVER X10E-2	KIDNEY X10E-3	ADRENAL X10E-4	THYROID X10E-5
CONTROL - 0 mg/kg						
84-1879	10.9	4.6	3.4	9.6	4.3	8.8
84-1880	11.1	4.7	3.0	8.8	4.1	6.8
84-1881	10.8	3.8	3.1	8.6	2.9	7.7
84-1882	9.4	4.1	3.3	9.2	4.0	5.9
84-1886	9.4	4.1	3.3	8.6	4.6	11.2
84-1887	11.2	4.6	3.0	9.4	4.0	10.9
84-1888	12.4	4.0	3.2	11.1	3.5	9.3
84-1889	11.2	4.4	3.0	9.6	3.8	10.4
84-1890	10.7	4.5	3.0	9.9	4.6	10.6
84-1891	11.1	5.4	3.3	8.9	3.5	6.9
LOW DOSE - 250 mg/kg						
84-1904	12.5	4.6	3.2	10.3	3.7	6.4
84-1905	11.3	3.7	2.6	8.1	2.6	6.9
84-1906	10.1	4.1	2.7	8.9	3.4	10.3
84-1907	11.3	4.5	3.2	9.4	3.6	9.8
84-1908	11.4	3.9	3.0	8.9	2.5	7.6
84-1909	10.4	3.8	2.8	8.7	3.4	11.4
84-1910	9.4	4.3	2.9	7.8	4.2	10.5
84-1911	9.9	4.1	3.2	8.7	3.6	9.4
84-1912	13.3	4.4	3.4	11.2	4.9	8.6
84-1913	8.9	3.8	3.0	8.7	3.6	6.5
MEDIUM DOSE - 500 mg/kg						
84-1924	9.8	4.0	3.5	8.8	3.8	11.4
84-1925	9.3	4.6	3.0	9.1	4.2	7.4
84-1926	10.7	3.9	3.1	8.5	3.3	9.2
84-1927	10.4	4.1	2.8	8.7	3.1	8.6
84-1928	9.6	4.5	3.3	8.6	4.0	9.3
84-1929	10.4	4.1	3.1	8.4	3.4	8.9
84-1930	11.0	4.2	3.1	9.1	3.5	9.4
84-1931	11.0	4.4	3.7	9.6	3.7	7.2
84-1932	11.1	4.6	2.9	9.8	3.9	10.1
84-1933	10.5	3.8	2.9	8.5	3.6	12.0
HIGH DOSE - 1000 mg/kg						
84-1950	11.7	4.0	3.4	10.4	3.2	7.4
84-1951	11.6	4.0	3.0	8.9	3.5	8.1
84-1953	11.0	3.8	3.2	9.7	3.7	12.8
84-1954	12.9	5.2	3.1	10.2	4.7	7.2
84-1956	9.9	3.8	3.0	9.7	3.2	6.2
84-1957	10.1	4.1	3.1	8.4	3.8	8.5
84-1958	9.9	4.2	3.1	8.4	3.4	9.6
84-1959	13.8	4.9	3.1	10.7	5.3	16.5
84-1960	10.1	3.4	2.9	8.5	2.8	8.3
84-1962	9.9	4.1	3.0	8.9	3.4	7.0

APPENDIX G, TABLE 4

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	THYMUS X10E-4	PITUITARY X10E-5	SPLEEN X10E-4	SAL GL X10E-3	OVARY X10E-4	UTERUS X10E-3
CONTROL - 0 mg/kg						
84-1879	23.9	5.7	2.1	3.3	8.2	2.3
84-1880	21.6	5.1	2.0	2.7	6.3	1.9
84-1881	26.2	6.5	2.1	2.7	4.2	2.7
84-1882	24.3	7.4	2.2	2.2	3.5	3.0
84-1886	19.0	6.1	1.9	2.8	8.4	2.6
84-1887	24.1	5.2	1.9	3.4	6.9	2.1
84-1888	21.9	6.6	2.0	2.8	0.5	2.5
84-1889	20.7	6.1	2.6	2.4	4.3	2.3
84-1890	24.6	6.1	2.2	3.0	6.7	2.0
84-1891	26.9	5.6	1.8	3.0	8.1	2.6
LOW DOSE - 250 mg/kg						
84-1904	23.1	6.4	2.6	2.8	5.1	3.8
84-1905	29.4	5.0	1.9	2.0	3.8	2.4
84-1906	31.0	6.0	2.4	2.7	6.5	2.5
84-1907	19.0	4.3	1.8	3.6	6.7	3.4
84-1908	24.1	6.3	2.0	2.2	3.8	2.2
84-1909	31.6	5.7	2.0	2.3	3.8	2.1
84-1910	27.7	4.2	2.0	2.3	6.8	3.6
84-1911	28.9	7.8	2.5	2.8	6.7	2.7
84-1912	23.7	6.5	1.7	2.7	5.8	2.9
84-1913	15.8	5.1	1.5	1.7	4.2	1.8
MEDIUM DOSE - 500 mg/kg						
84-1924	33.0	7.6	2.7	2.7	7.0	2.9
84-1925	29.1	5.8	2.3	2.9	6.9	2.3
84-1926	23.3	6.1	2.2	2.6	3.7	2.9
84-1927	18.4	4.3	1.9	2.3	4.3	2.1
84-1928	26.2	5.5	1.9	2.8	7.7	3.2
84-1929	19.3	3.6	1.8	2.7	6.3	2.6
84-1930	17.0	5.3	1.8	2.3	4.1	2.4
84-1931	25.3	3.6	2.3	2.2	4.8	2.0
84-1932	25.3	5.1	2.5	2.4	7.0	2.5
84-1933	16.9	6.0	2.0	2.5	5.5	2.6
HIGH DOSE - 1000 mg/kg						
84-1950	24.5	6.7	2.3	1.7	4.9	2.9
84-1951	20.5	5.6	1.9	2.0	4.3	3.3
84-1953	25.0	5.2	2.2	3.0	7.0	3.4
84-1954	19.4	8.6	2.1	3.0	13.7	2.8
84-1956	24.9	5.6	2.0	2.1	4.5	1.9
84-1957	26.6	6.2	2.2	2.5	5.1	1.8
84-1958	28.9	5.3	2.2	2.6	7.0	3.7
84-1959	24.1	3.0	2.0	3.2	9.0	3.8
84-1960	22.1	5.5	2.0	2.5	4.4	2.2
84-1962	19.8	7.5	1.8	2.1	3.7	1.6

APPENDIX G, TABLE 5

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	HEART X10E-1	LIVER	KIDNEY X10E-1	ADRENAL X10E-2	THYROID X10E-3	THYMUS X10E-1
CONTROL - 0 mg/kg						
84-1864	5.0	4.3	12.2	2.9	9.7	2.7
84-1866	5.2	3.8	11.1	2.7	7.8	2.5
84-1867	7.3	4.5	11.8	3.0	9.9	2.6
84-1868	5.8	4.2	12.3	3.4	9.1	3.1
84-1869	4.2	3.0	9.4	2.7	9.3	1.8
84-1871	5.4	4.0	11.7	2.8	11.0	2.7
84-1873	5.1	4.2	13.1	2.5	8.5	3.6
84-1874	4.9	4.0	11.8	2.6	10.9	2.5
84-1875	6.2	3.9	11.7	2.7	9.6	2.4
84-1878	5.2	3.8	10.8	3.0	9.8	3.7
LOW DOSE - 250 mg/kg						
84-1894	4.8	4.0	11.5	2.7	6.4	2.7
84-1895	4.3	3.7	10.8	2.2	9.5*	2.1
84-1896	4.9	3.3	10.6	3.0	8.2	2.7
84-1897	5.4	4.2	11.5	2.4	10.9	3.0
84-1898	5.9	4.5	11.4	2.6	7.7	2.8
84-1899	4.9	4.5	11.6	2.4	10.3	2.6
84-1900	4.5	3.4	9.1	2.7	8.5	1.9
84-1901	5.5	4.7	12.6	2.8	11.9	3.1
84-1902	5.6	4.6	12.2	3.0	7.4	3.3
84-1903	5.0	3.8	11.5	2.7	8.1	2.8
MEDIUM DOSE - 500 mg/kg						
84-1914	4.4	4.2	10.7	2.5	11.3	2.3
84-1915	5.8	4.8	13.9	2.8	11.5	3.6
84-1916	4.5	4.1	11.2	2.4	8.7	4.1
84-1917	4.8	3.9	11.2	2.0	10.5	3.0
84-1918	5.4	4.0	11.7	3.0	10.2	2.9
84-1919	5.9	4.6	12.4	2.7	7.5	2.8
84-1920	4.8	3.8	12.0	2.5	8.5	1.8
84-1921	4.8	4.0	11.5	2.8	8.3	2.2
84-1922	5.5	3.8	11.4	2.9	11.9	2.7
84-1923	4.6	3.9	10.8	2.8	9.5	2.4
HIGH DOSE - 1000 mg/kg						
84-1936	6.4	5.2	13.4	3.5	8.2	3.0
84-1938	5.6	4.4	10.4	3.4	11.2	2.2
84-1940	4.5	3.9	9.4	2.3	6.2	2.3
84-1942	4.8	3.3	11.2	2.7	13.3	2.2
84-1943	6.1	5.1	12.3	2.3	10.7	2.8
84-1944	5.2	3.8	11.1	2.1	8.6	2.4
84-1945	6.5	5.8	14.7	3.1	13.2	3.5
84-1946	4.9	3.8	11.9	2.5	7.4	2.6
84-1947	5.5	4.3	12.0	3.1	9.3	3.5
84-1948	6.1	4.9	13.2	2.5	10.1	2.2

* : THYROID WEIGHED AFTER FIXATION, DATA NOT INCLUDED IN STATISTICAL CALCULATIONS.

APPENDIX G, TABLE 5

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

MALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	PITUITARY X10E-3	SPLEEN X10E-1	SAL GL X10E-1	TESTIS	PROSTATE X10E-2	EPIDIDYMIS X10E-1
CONTROL - 0 mg/kg						
84-1864	6.8	2.5	3.0	1.4	21.4	4.9
84-1866	5.2	2.6	2.6	1.4	17.2	4.3
84-1867	4.2	2.9	4.5	1.5	27.6	5.4
84-1868	5.1	2.9	3.7	1.6	20.8	4.5
84-1869	4.4	2.4	2.5	1.5	12.6	5.2
84-1871	4.8	2.6	3.8	1.3	18.6	5.2
84-1873	5.3	2.8	2.7	1.5	20.2	4.2
84-1874	4.1	2.3	2.6	1.6	10.4	4.7
84-1875	5.6	2.4	3.7	1.4	27.8	4.9
84-1878	4.1	2.6	3.3	1.3	25.4	4.4
LOW DOSE - 250 mg/kg						
84-1894	4.9	2.5	3.1	1.4	19.1	4.6
84-1895	5.2	2.7	2.6	1.6	10.9	3.9
84-1896	4.4	2.7	2.9	1.6	25.8	5.0
84-1897	5.0	2.6	3.4	1.4	25.9	5.6
84-1898	5.6	2.3	3.1	1.6	15.4	4.8
84-1899	5.1	2.6	2.6	1.4	21.5	3.7
84-1900	3.5	2.5	3.1	1.3	17.0	3.8
84-1901	5.2	3.2	4.4	1.4	23.8	6.3
84-1902	4.9	2.9	2.9	1.5	14.8	4.7
84-1903	3.6	2.5	2.8	1.4	17.3	4.1
MEDIUM DOSE - 500 mg/kg						
84-1914	4.2	2.3	2.9	1.3	19.2	4.8
84-1915	5.5	3.1	3.3	1.5	25.0	5.4
84-1916	5.1	2.8	2.7	1.2	17.4	4.0
84-1917	5.5	2.9	3.5	1.5	14.4	4.5
84-1918	5.3	2.8	3.6	1.3	24.8	5.5
84-1919	6.0	2.5	3.4	1.5	24.9	4.8
84-1920	5.0	2.9	2.6	1.5	14.1	4.2
84-1921	5.8	2.8	3.0	1.5	14.1	4.2
84-1922	5.9	2.6	3.2	1.6	20.8	4.9
84-1923	4.8	2.6	3.4	1.4	24.8	4.1
HIGH DOSE - 1000 mg/kg						
84-1936	6.1	2.4	3.1	1.6	16.8	4.7
84-1938	5.3	2.7	3.3	1.4	20.9	5.0
84-1940	4.7	2.6	2.7	1.5	15.5	4.2
84-1942	4.9	2.4	3.7	1.2	16.7	4.0
84-1943	4.6	2.2	2.8	1.4	14.8	3.9
84-1944	4.0	2.4	2.4	1.3	8.6	4.1
84-1945	5.8	2.7	3.7	1.5	23.2	4.6
84-1946	5.3	2.5	2.8	1.4	16.3	4.7
84-1947	4.6	2.9	3.7	1.6	20.6	5.6
84-1948	5.5	2.8	3.4	1.3	15.6	3.9

APPENDIX G, TABLE 6

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	HEART X10E-1	LIVER	KIDNEY X10E-1	ADRENAL X10E-2	THYROID X10E-3	THYMUS X10E-1
CONTROL - 0 mg/kg						
84-1879	4.2	3.1	8.8	3.9	8.1	2.2
84-1880	4.2	2.7	7.9	3.7	6.1	1.9
84-1881	3.5	2.9	8.0	2.7	7.2	2.4
84-1882	4.4	3.5	9.8	4.2	6.3	2.6
84-1886	4.4	3.5	9.1	4.9	11.8	2.0
84-1887	4.1	2.7	8.4	3.5	9.7	2.2
84-1888	3.2	2.6	9.0	2.8	7.5	1.8
84-1889	3.9	2.7	8.6	3.4	9.3	1.9
84-1890	4.2	2.8	9.3	4.3	9.9	2.3
84-1891	4.8	3.0	8.0	3.1	6.2	2.4
LOW DOSE - 250 mg/kg						
84-1904	3.7	2.5	8.3	3.0	5.1	1.8
84-1905	3.3	2.3	7.2	2.3	6.1	2.6
84-1906	4.1	2.7	8.8	3.4	10.3	3.1
84-1907	4.0	2.8	8.3	3.1	8.6	1.7
84-1908	3.4	2.7	7.8	2.2	6.7	2.1
84-1909	3.7	2.7	8.4	3.2	11.0	3.0
84-1910	4.6	3.0	8.3	4.5	11.1	2.9
84-1911	4.1	3.3	8.7	3.6	9.5	2.9
84-1912	3.3	2.6	8.4	3.7	6.5	1.8
84-1913	4.3	3.4	9.8	4.1	7.3	1.8
MEDIUM DOSE - 500 mg/kg						
84-1924	4.1	3.6	9.0	3.9	11.6	3.4
84-1925	4.9	3.2	9.8	4.5	8.0	3.1
84-1926	3.6	2.9	7.9	3.1	8.6	2.2
84-1927	3.9	2.7	8.3	2.9	8.2	1.8
84-1928	4.7	3.4	8.9	4.1	9.7	2.7
84-1929	3.9	3.0	8.1	3.3	8.5	1.9
84-1930	3.8	2.8	8.3	3.2	8.5	1.5
84-1931	4.0	3.3	8.7	3.4	6.6	2.3
84-1932	4.1	2.6	8.8	3.5	9.1	2.3
84-1933	3.6	2.7	8.1	3.4	11.4	1.6
HIGH DOSE - 1000 mg/kg						
84-1950	3.4	2.9	8.9	2.7	6.3	2.1
84-1951	3.4	2.6	7.7	3.1	7.0	1.8
84-1953	3.4	2.9	8.8	3.3	11.6	2.3
84-1954	4.0	2.4	7.9	3.7	5.6	1.5
84-1956	3.9	3.1	9.8	3.3	6.3	2.5
84-1957	4.1	3.1	8.4	3.8	8.4	2.6
84-1958	4.3	3.1	8.5	3.5	9.7	2.9
84-1959	3.6	2.3	7.8	3.9	12.0	1.7
84-1960	3.4	2.9	8.4	2.7	8.2	2.2
84-1962	4.1	3.0	9.0	3.5	7.0	2.0

APPENDIX G, TABLE 6

FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE RAT

FEMALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	PITUITARY X10E-3	SPLEEN X10E-1	SAL GL X10E-1	OVARY X10E-2	UTERUS X10E-1
CONTROL - 0 mg/kg					
84-1879	5.2	1.9	3.0	7.5	2.1
84-1880	4.6	1.8	2.4	5.6	1.7
84-1881	6.1	2.0	2.5	3.9	2.5
84-1882	7.9	2.4	2.3	3.7	3.2
84-1886	6.5	2.0	3.0	8.9	2.8
84-1887	4.6	1.7	3.0	6.2	1.9
84-1888	5.3	1.6	2.2	0.4	2.0
84-1889	5.5	2.3	2.1	3.8	2.0
84-1890	5.8	2.1	2.8	6.3	1.8
84-1891	5.1	1.6	2.7	7.3	2.3
LOW DOSE - 250 mg/kg					
84-1904	5.1	2.1	2.3	4.1	3.1
84-1905	4.4	1.7	1.8	3.3	2.2
84-1906	5.9	2.4	2.7	6.5	2.5
84-1907	3.8	1.6	3.1	5.9	3.0
84-1908	5.6	1.8	1.9	3.3	1.9
84-1909	5.5	2.0	2.2	3.7	2.0
84-1910	4.4	2.2	2.4	7.2	3.8
84-1911	7.8	2.5	2.8	6.7	2.7
84-1912	4.9	1.2	2.1	4.3	2.2
84-1913	5.8	1.7	1.9	4.7	2.0
MEDIUM DOSE - 500 mg/kg					
84-1924	7.7	2.8	2.8	7.2	2.9
84-1925	6.3	2.4	3.1	7.4	2.5
84-1926	5.7	2.1	2.4	3.4	2.8
84-1927	4.1	1.8	2.2	4.1	2.0
84-1928	5.7	2.0	2.9	8.0	3.4
84-1929	3.5	1.7	2.5	6.0	2.5
84-1930	4.8	1.6	2.1	3.7	2.2
84-1931	3.3	2.1	2.0	4.4	1.8
84-1932	4.5	2.2	2.2	6.3	2.2
84-1933	5.7	1.9	2.3	5.2	2.4
HIGH DOSE - 1000 mg/kg					
84-1950	5.8	2.0	1.4	4.2	2.5
84-1951	4.8	1.7	1.7	3.8	2.8
84-1953	4.8	2.0	2.7	6.3	3.1
84-1954	6.7	1.6	2.3	10.6	2.2
84-1956	5.7	2.1	2.2	4.6	1.9
84-1957	6.2	2.2	2.5	5.1	1.8
84-1958	5.4	2.3	2.6	7.0	3.8
84-1959	2.2	1.5	2.3	6.6	2.8
84-1960	5.5	2.0	2.5	4.4	2.1
84-1962	7.6	1.8	2.1	3.8	1.6

Appendix H

Explanatory Note to Pathology Tables

1. Terminal body weights can be found in Appendix G. The notation "terminal body weight: not taken" in the following tables refers to the fact that the weights were not entered into the computer system used to generate these tables.
2. No pretest animal number was entered into the computer system used to generate these tables, therefore the system automatically inserted a number into the pretest animal number space. These numbers are not applicable to this study.
3. The term "no microscopic observations for this animal" appearing in the microscopic tissue observation section of Group 2 and 3 sheets and Group 1 and 4 sheets with the sacrifice status of "Final Sacrifice" means the animal was not examined microscopically (with the exceptions noted on page 6 of the report text). This term in Group 1 and 4 animals means the tissues were examined and were unremarkable.

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84

PRINTED: 5-JAN-85
PAGE: 1
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1864/PRETEST=
DATE OF DEATH: 1-NOV-84

1 SEX: MALE
STUDY DAY OF DEATH: 30

DOSE GROUP: 1
STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
-HYALIN DROPLETS IN TUBULAR CELLS
PARATHYROID

TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 2

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1865/PRETEST= DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 28-NOV-84 STUDY DAY OF DEATH: 57 STUDY WEEK OF DEATH: 9 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
 TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

1

1

SEARLE RESEARCH & DEVELOPMENT				INDIVIDUAL ANIMAL DATA REPORT				PRINTED: 5-JAN-85	
PRODUCT SAFETY ASSESSMENT				STUDY NUMBER: SA2448				PAGE: 3	
SKOKIE, ILLINOIS 60077				STUDY START DATE: 3-OCT-84				STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
SPECIES: RAT/CHARLES RIVER CD									
ANIMAL NUMBER: 84-1866/PRETEST=		3 SEX: MALE		DOSE GROUP: 1		SACRIFICE STATUS: INTERIM SACRIFICE 1			
DATE OF DEATH: 1-NOV-84		STUDY DAY OF DEATH: 30		STUDY WEEK OF DEATH: 5		TERMINAL BODY WEIGHT: NOT TAKEN			
ORGAN NAME		<< GROSS ORGAN OBSERVATIONS >>		SEVERITY GROSS FREE-TEXT COMMENTS					
SKIN(SK)		KEYWORDS / PHRASES		CRUST		OVER SHOULDERS, 5 MM DIAMETER, NOT SAVED			
TISSUE / HISTOPATHOLOGIC FINDINGS				MICROSCOPIC TISSUE OBSERVATIONS >>				DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS	
KIDNEY									
-INFLAMMATION, CHRONIC									
PARATHYROID								TISSUE IS MISSING	

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 4

ANIMAL NUMBER: 84-1867/PRETEST=
DATE OF DEATH: 31-OCT-84
SEX: MALE
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS
NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
ANIMAL NUMBER: 84-1868/PRETEST=
DATE OF DEATH: 1-NOV-84
STUDY DAY OF DEATH: 30
STUDY START DATE: 3-OCT-84
STUDY NUMBER: SA2448
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 5

DOSE GROUP: 1
SEX: MALE
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN
ORGAN NAME
KIDNEY(KD)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
HYDRONEPHROSIS
SEVERITY GROSS FREE-TEXT COMMENTS
UNILATERAL

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS
<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
-HYDRONEPHROSIS
-MICROCALCULI

SEARLE RESEARCH & DEVELOPMENT		INDIVIDUAL ANIMAL DATA REPORT		PRINTED: 5-JAN-85						
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 6						
SKOKIE, ILLINOIS 60077										
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84	STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX							
ANIMAL NUMBER: 84-1869/PRETEST=		6 SEX: MALE	DOSE GROUP: 1	SACRIFICE STATUS: INTERIM SACRIFICE 1						
DATE OF DEATH: 31-OCT-84		STUDY DAY OF DEATH: 29	STUDY WEEK OF DEATH: 5	TERMINAL BODY WEIGHT: NOT TAKEN						
<< GROSS ORGAN OBSERVATIONS >>										
KEYWORDS / PHRASES		SEVERITY GROSS FREE-TEXT COMMENTS								
WHOLE BODY(WB)		NORMAL								
<hr/>										
<table border="0"> <tr> <td><< MICROSCOPIC FINDINGS</td> <td>TISSUE</td> <td>OBSERVATIONS >></td> </tr> <tr> <td colspan="2"></td> <td>DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS</td> </tr> </table>					<< MICROSCOPIC FINDINGS	TISSUE	OBSERVATIONS >>			DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
<< MICROSCOPIC FINDINGS	TISSUE	OBSERVATIONS >>								
		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS								
<hr/>										
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL										

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 7

ANIMAL NUMBER: 84-1870/PRETEST=
DATE OF DEATH: 28-NOV-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

7 SEX: MALE
DOSE GROUP: 1
SACRIFICE STATUS: FINAL SACRIFICE
STUDY DAY OF DEATH: 57
STUDY WEEK OF DEATH: 9
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 8

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1871/PRETEST= 8 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB) NORMAL

S.A. 2448

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

LIVER
-MICROGRANULOMA(S)
ADRENAL GLAND
-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS MULTI-FOCAL
PERIPHERAL NERVE TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 9

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1872/PRETEST= DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 28-NOV-84 STUDY DAY OF DEATH: 57 STUDY WEEK OF DEATH: 9 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
 TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 10

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1873/PRETEST= DOSE GROUP: 1 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

S.A. 2448

T 11

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY FOCAL
 -INFLAMMATION, CHRONIC

LIVER
 -MICROGRANULOMA(S)

PARATHYROID TISSUE IS MISSING

1

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
ANIMAL NUMBER: 84-1874/PRETEST=
DATE OF DEATH: 1-NOV-84
STUDY DAY OF DEATH: 30
SEX: MALE
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1874/PRETEST=
DATE OF DEATH: 1-NOV-84
STUDY DAY OF DEATH: 30
SEX: MALE
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS
NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

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PAGE: 12

ANIMAL NUMBER: 84-1875/PRETEST=

DOSE GROUP: 1

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1876/PRETEST=

13 SEX: MALE

DOSE GROUP: 1

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

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PAGE: 14

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1877/PRETEST=

14 SEX: MALE

DOSE GROUP: 1

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

SEVERITY GROSS FREE-TEXT COMMENTS

KIDNEY(KD)

HYDRONEPHROSIS

LEFT

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

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ANIMAL NUMBER: 84-1878/PRETEST=
DATE OF DEATH: 1-NOV-84
15 SEX: MALE
STUDY DAY OF DEATH: 30
DOSE GROUP: 1
STUDY WEEK OF DEATH: 5
SACRIFICE STATUS: INTERIM SACRIFICE 1
TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME
WHOLE BODY(WB) NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

HEART -INFLAMMATION FOCAL
KIDNEY -INFLAMMATION, CHRONIC MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

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STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1894/PRETEST=

16 SEX: MALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
ANIMAL NUMBER: 84-1895/PRETEST=
DATE OF DEATH: 31-OCT-84
STUDY DAY OF DEATH: 29
17 SEX: MALE
DOSE GROUP: 2
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
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ORGAN NAME
TESTIS(TE)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SMALL
SEVERITY GROSS FREE-TEXT COMMENTS
UNILATERAL

TISSUE / HISTOPATHOLOGIC FINDINGS
<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1896/PRETEST=

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

<< GROSS ORGAN OBSERVATIONS >>

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

KEYWORDS / PHRASES

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

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SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1897/PRETEST=

19 SEX: MALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
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ANIMAL NUMBER: 84-1898/PRETEST=
DATE OF DEATH: 1-NOV-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

20 SEX: MALE
STUDY DAY OF DEATH: 30

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

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PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 21
SKOKIE, ILLINOIS 60077		STUDY START DATE: 3-OCT-84		
SPECIES: RAT/CHARLES RIVER CD		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX		
ANIMAL NUMBER: 84-1899/PRETEST=		DOSE GROUP: 2	SACRIFICE STATUS: INTERIM SACRIFICE 1	
DATE OF DEATH: 31-OCT-84		STUDY DAY OF DEATH: 29	STUDY WEEK OF DEATH: 5	
		TERMINAL BODY WEIGHT: NOT TAKEN		
<< GROSS ORGAN OBSERVATIONS >>				
KEYWORDS / PHRASES		SEVERITY GROSS FREE-TEXT COMMENTS		
WHOLE BODY(WB)		NORMAL		
<< MICROSCOPIC TISSUE OBSERVATIONS >>				
TISSUE / HISTOPATHOLOGIC FINDINGS		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS		
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL				

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1900/PRETEST= 22 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

S.A. 2448

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APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT		INDIVIDUAL ANIMAL DATA REPORT		PRINTED: 5-JAN-85
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 23
SKOKIE, ILLINOIS 60077				
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84	STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
ANIMAL NUMBER: 84-1901/PRETEST=	23 SEX: MALE	DOSE GROUP: 2	SACRIFICE STATUS: INTERIM SACRIFICE 1	
DATE OF DEATH: 31-OCT-84	STUDY DAY OF DEATH: 29	STUDY WEEK OF DEATH: 5	TERMINAL BODY WEIGHT: NOT TAKEN	
<< GROSS ORGAN OBSERVATIONS >>				
ORGAN NAME	KEYWORDS / PHRASES	SEVERITY	GROSS FREE-TEXT COMMENTS	
WHOLE BODY(WB)	NORMAL			
<< MICROSCOPIC TISSUE OBSERVATIONS >>				
TISSUE / HISTOPATHOLOGIC FINDINGS				
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL				

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1902/PRETEST#

24 SEX: MALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN
KEYWORDS / PHRASES

OBSERVATIONS >>

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

TISSUE << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1903/PRETEST=

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

SEX: MALE

DOSE GROUP: 2

STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

HYDRONEPHROSIS

BILATERAL

TISSUE

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY

-HYDRONEPHROSIS

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1914/PRETEST= 26 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN
 STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY (WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1915/PRETEST= 27 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1916/PRETEST-
 DATE OF DEATH: 1-NOV-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

28 SEX: MALE
 STUDY DAY OF DEATH: 30

DOSE GROUP: 3
 STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1
 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
 WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
 TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

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ANIMAL NUMBER: 84-1917/PRETEST=

29 SEX: MALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME

WHOLE BODY(WB)

<< GROSS

KEYWORDS / PHRASES

ORGAN

SEVERITY

OBSERVATIONS >>

GROSS FREE-TEXT COMMENTS

TISSUE

MICROSCOPIC FINDINGS

OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1918/PRETEST= 30 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT		INDIVIDUAL ANIMAL DATA REPORT		PRINTED: 5-JAN-85
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 32
SKOKIE, ILLINOIS 60077		STUDY START DATE: 3-OCT-84		
SPECIES: RAT/CHARLES RIVER CD		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX		
ANIMAL NUMBER: 84-1920/PRETEST=	32 SEX: MALE	DOSE GROUP: 3	SACRIFICE STATUS: INTERIM SACRIFICE 1	
DATE OF DEATH: 1-NOV-84	STUDY DAY OF DEATH: 30	STUDY WEEK OF DEATH: 5	TERMINAL BODY WEIGHT: NOT TAKEN	
<< GROSS ORGAN OBSERVATIONS >>				
ORGAN NAME	KEYWORDS / PHRASES	SEVERITY	GROSS FREE-TEXT COMMENTS	
WHOLE BODY (WB)	NORMAL			
<< MICROSCOPIC TISSUE OBSERVATIONS >>				
TISSUE / HISTOPATHOLOGIC FINDINGS		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS		
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL				

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**KIDNEY
-HYDRONEPHROSIS**

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE	OBSERVATIONS >>	DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

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ANIMAL NUMBER: 84-1922/PRETEST-
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
 STUDY START DATE: 3-OCT-84 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
 KIDNEY(KD) HYDRONEPHROSIS UNILATERAL

S.A. 2448

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APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
 -HYDRONEPHROSIS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1923/PRETEST=

35 SEX: MALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

S.A. 2448

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APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

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SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1935/PRETEST=

37 SEX: MALE

DOSE GROUP: 4

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

S.A. 2448

APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 38

STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1936/PRETEST= 38 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
KIDNEY(KD) HYDRONEPHROSIS UNILATERAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
-HYALIN DROPLETS IN TUBULAR CELLS
-HYDRONEPHROSIS
-MICROCALCULI

PARATHYROID TISSUE IS MISSING
EYE FOCAL
-CONGENITAL RETINAL FOLD

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 39

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1937/PRETEST= 39 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 28-NOV-84 STUDY DAY OF DEATH: 57 STUDY WEEK OF DEATH: 9 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

PRINTED: 5-JAN-85

PAGE: 41

ANIMAL NUMBER: 84-1939/PRETEST=

DATE OF DEATH: 28-NOV-84

41 SEX: MALE

STUDY DAY OF DEATH: 57

DOSE GROUP: 4

STUDY WEEK OF DEATH: 9

SACRIFICE STATUS: FINAL SACRIFICE

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

SEVERITY GROSS FREE-TEXT COMMENTS

KEYWORDS / PHRASES

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT		INDIVIDUAL ANIMAL DATA REPORT		PRINTED: 5-JAN-85
PRODUCT SAFETY ASSESSMENT		STUDY NUMBER: SA2448		PAGE: 42
SKOKIE, ILLINOIS 60077				
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84	STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
ANIMAL NUMBER: 84-1940/PRETEST=		42 SEX: MALE	DOSE GROUP: 4	SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 1-NOV-84		STUDY DAY OF DEATH: 30	STUDY WEEK OF DEATH: 5	TERMINAL BODY WEIGHT: NOT TAKEN
ORGAN NAME	<< GROSS ORGAN OBSERVATIONS >>	SEVERITY GROSS FREE-TEXT COMMENTS		
WHOLE BODY(WB)	KEYWORDS / PHRASES			
	NORMAL			
TISSUE / HISTOPATHOLOGIC FINDINGS				
<< MICROSCOPIC TISSUE OBSERVATIONS >>				
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS				
PARATHYROID TISSUE IS MISSING				

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 43

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1941/PRETEST= 43 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 28-NOV-84 STUDY DAY OF DEATH: 57 STUDY WEEK OF DEATH: 9 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME	<< GROSS ORGANS	OBSERVATIONS >>
WHOLE BODY(WB)	KEYWORDS / PHRASES	SEVERITY GROSS FREE-TEXT COMMENTS
	NORMAL	

TISSUE / HISTOPATHOLOGIC FINDINGS	TISSUE	OBSERVATIONS >>
		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 44

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1942/PRETEST= 44 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

PROSTATE
 -INFLAMMATION, CHRONIC

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 45
ANIMAL NUMBER: 84-1943/PRETEST=
DATE OF DEATH: 31-OCT-84
45 SEX: MALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 29
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS
NORMAL

TISSUE
MICROSCOPIC FINDINGS
KIDNEY
-HYALIN DROPLETS IN TUBULAR CELLS
-INFLAMMATION, CHRONIC
OBSERVATIONS
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 46

STUDY START DATE: 3-OCT-84
 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1944/PRETEST= 46 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

EYE FOCAL
 -CONGENITAL RETINAL FOLD

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 47

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1945/PRETEST= DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

KIDNEY(KD) HYDRONEPHROSIS BILATERAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
 TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
 -HYALIN DROPLETS IN TUBULAR CELLS
 -HYDRONEPHROSIS
 -INFLAMMATION, CHRONIC

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 48

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1946/PRETEST= 48 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

LIVER
 -MICROGRANULOMA(S)

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 49

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1947/PRETEST= 49 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY (WB) NORMAL

S.A. 2448

F 50

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

HEART FOCAL
 -AMYLOIDOSIS

KIDNEY
 -HYALIN DROPLETS IN TUBULAR CELLS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 50

ANIMAL NUMBER: 84-1948/PRETEST= 50 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB) NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

PARATHYROID TISSUE IS MISSING
PROSTATE
-INFLAMMATION, CHRONIC

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 51

ANIMAL NUMBER: 84-1879/PRETEST=
DATE OF DEATH: 31-OCT-84
51 SEX: FEMALE
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 29
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS
NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
MICROSCOPIC TISSUE OBSERVATIONS
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
INT LG-RECTUM
MAMMARY GLAND
TISSUE IS MISSING
TISSUE IS MISSING

PRINTED: 5-JAN-85
PAGE: 52

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

<< GROSS ORGAN OBSERVATIONS >>

NORMAL

H- 53

OBSERVATIONS >>

KIDNEY
--HYDRONEPHROSIS

TISSUE IS MISSING

TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 53

ANIMAL NUMBER: 84-1881/PRETEST=
DATE OF DEATH: 31-OCT-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

53 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY (WB) NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

LIVER
-MICROGRANULOMA(S)

ADRENAL GLAND
-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS FOCAL

PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

SPECIES: RAT/CHARLES RIVER CD

PRINTED: 5-JAN-85

PAGE: 54

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1882/PRETEST=

54 SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

KIDNEY(KD)

HYDRONEPHROSIS

UNILATERAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY

-HYDRONEPHROSIS

PITUITARY GLAND

-CYST(S)

ADRENAL GLAND

-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS

MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 55

STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1883/PRETEST=
DATE OF DEATH: 28-NOV-84
55 SEX: FEMALE
DOSE GROUP: 1
SACRIFICE STATUS: FINAL SACRIFICE
STUDY DAY OF DEATH: 57
STUDY WEEK OF DEATH: 9
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5--JAN-85

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ANIMAL NUMBER: 84-1884/PRETEST=

56 SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY (WB)

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1885/PRETEST=

DATE OF DEATH: 28-NOV-84

57 SEX: FEMALE

STUDY DAY OF DEATH: 57

DOSE GROUP: 1

SACRIFICE STATUS: FINAL SACRIFICE

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

PRINTED: 5-JAN-85

PAGE: 57

ORGAN NAME

KIDNEY(KD)

<< GROSS

ORGAN

OBSERVATIONS >>

KEYWORDS / PHRASES

HYDRONEPHROSIS

SEVERITY

GROSS FREE-TEXT COMMENTS

BILATERAL

TISSUE

MICROSCOPIC

HISTOPATHOLOGIC FINDINGS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 58

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1886/PRETEST= 58 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

S.A. 2448

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TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

ADRENAL GLAND
 -HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS MULTI-FOCAL

PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 59

ANIMAL NUMBER: 84-1887/PRETEST=
DATE OF DEATH: 31-OCT-84
SEX: FEMALE
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 29
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY (WB)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS
<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

INT LG-RECTUM
TISSUE IS MISSING

LIVER
-MICROGRANULOMA(S)

ADRENAL GLAND
-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS
MULTI-FOCAL

MAMMARY GLAND
TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 60

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1888/PRETEST=

60 SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY

-INFLAMMATION, CHRONIC

ADRENAL GLAND

-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS

MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 61

ANIMAL NUMBER: 84-1889/PRETEST= 61 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

MAMMARY GLAND TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 62

SPECIES: RAT/CHARLES RIVER CD
 STUDY START DATE: 3-OCT-84
 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1890/PRETEST=
 DATE OF DEATH: 1-NOV-84
 62 SEX: FEMALE
 STUDY DAY OF DEATH: 30
 DOSE GROUP: 1
 STUDY WEEK OF DEATH: 5
 SACRIFICE STATUS: INTERIM SACRIFICE 1
 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
 WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
 KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

LIVER
 -MITROGRANULOMA(S)

1

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
PRINTED: 5-JAN-85
PAGE: 63
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1891/PRETEST=
DATE OF DEATH: 31-OCT-84
63 SEX: FEMALE
STUDY DAY OF DEATH: 29
DOSE GROUP: 1
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME	<< GROSS ORGAN OBSERVATIONS >> KEYWORDS / PHRASES	SEVERITY	GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB)	NORMAL		

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >> DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
INT LG-RECTUM	TISSUE IS MISSING
ADRENAL GLAND -HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS	FOCAL
MAMMARY GLAND	TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 64

ANIMAL NUMBER: 84-1892/PRETEST=

DATE OF DEATH: 28-NOV-84

64 SEX: FEMALE

STUDY DAY OF DEATH: 57

DOSE GROUP: 1

STUDY WEEK OF DEATH: 9

SACRIFICE STATUS: FINAL SACRIFICE

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

PRINTED: 5-JAN-85

PAGE: 65

ANIMAL NUMBER: 84-1893/PRETEST=

DATE OF DEATH: 28-NOV-84

65 SEX: FEMALE

STUDY DAY OF DEATH: 57

DOSE GROUP: 1

STUDY WEEK OF DEATH: 9

SACRIFICE STATUS: FINAL SACRIFICE

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

I

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 66

ANIMAL NUMBER: 84-1904/PRETEST=
DATE OF DEATH: 1-NOV-84
SEX: FEMALE
STUDY DAY OF DEATH: 30
DOSE GROUP: 2
STUDY WEEK OF DEATH: 5
SACRIFICE STATUS: INTERIM SACRIFICE 1
TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY (WB) NORMAL

S.A. 2448

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APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

INDIVIDUAL ANIMAL DATA REPORT		PRINTED: 5-JAN-85	
STUDY NUMBER: SA2448		PAGE: 67	
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84	
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX			
ANIMAL NUMBER: 84-1905/PRETEST=	67 SEX: FEMALE	DOSE GROUP: 2	SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84	STUDY DAY OF DEATH: 29	STUDY WEEK OF DEATH: 5	TERMINAL BODY WEIGHT: NOT TAKEN
ORGAN NAME	<< G R O S S O R G A N O B S E R V A T I O N S >>		
WHOLE BODY(WB)	KEYWORDS / PHRASES	SEVERITY GROSS FREE-TEXT COMMENTS	
	NORMAL		
<< M I C R O S C O P I C T I S S U E O B S E R V A T I O N S >>		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS	
TISSUE / HISTOPATHOLOGIC FINDINGS			
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL			

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 68

ANIMAL NUMBER: 84-1906/PRETEST=

DATE OF DEATH: 1-NOV-84

68 SEX: FEMALE

STUDY DAY OF DEATH: 30

DOSE GROUP: 2

STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGANS OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT PRODUCT SAFETY ASSESSMENT SKOKIE, ILLINOIS 60077		INDIVIDUAL ANIMAL DATA REPORT STUDY NUMBER: SA2448		PRINTED: 5-JAN-85 PAGE: 69	
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
ANIMAL NUMBER: 84-1907/PRETEST=		DOSE GROUP: 2		SACRIFICE STATUS: INTERIM SACRIFICE 1	
DATE OF DEATH: 31-OCT-84		STUDY DAY OF DEATH: 29		STUDY WEEK OF DEATH: 5	
				TERMINAL BODY WEIGHT: NOT TAKEN	
ORGAN NAME		<< GROSS ORGAN OBSERVATIONS >>			
KEYWORDS / PHRASES		SEVERITY GROSS FREE-TEXT COMMENTS			
WHOLE BODY(WB)		NORMAL			
TISSUE / HISTOPATHOLOGIC FINDINGS		TISSUE		OBSERVATIONS >>	
				DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS	
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL					

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

PRINTED: 5-JAN-85

PAGE: 70

ANIMAL NUMBER: 84-1908/PRETEST=

DATE OF DEATH: 1-NOV-84

70 SEX: FEMALE

STUDY DAY OF DEATH: 30

DOSE GROUP: 2

STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

PRINTED: 5-JAN-85

PAGE: 71

ANIMAL NUMBER: 84-1909/PRETEST=

71 SEX: FEMALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGANS OBSERVATIONS >>

KEYWORDS / PHRASES

NORMAL

SEVERITY

GROSS FREE-TEXT COMMENTS

TISSUE

OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 72

ANIMAL NUMBER: 84-1910/PRETEST= 72 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: INTERIM SACRIFICE 1
 DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ORGAN NAME	<< GROSS ORGAN KEYWORDS / PHRASES	OBSERVATIONS >> SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB)	NORMAL	

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >> DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL	

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SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 73

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1911/PRETEST= 73 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB) NORMAL

S.A. 2448

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APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 74

ANIMAL NUMBER: 84-1912/PRETEST=

74 SEX: FEMALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

LIVER(LI)

DISCOLORATION, PALE

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

PRINTED: 5-JAN-85

PAGE: 75

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1913/PRETEST=

75 SEX: FEMALE

DOSE GROUP: 2

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC FINDINGS

TISSUE

OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 76

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1924/PRETEST-76 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 1-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

I

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 77

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1925/PRETEST=

77 SEX: FEMALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN
KEYWORDS / PHRASES

OBSERVATIONS >>

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

S.A. 2448

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APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 78

ANIMAL NUMBER: 84-1926/PRETEST=

DATE OF DEATH: 1-NOV-84

78 SEX: FEMALE

STUDY DAY OF DEATH: 30

DOSE GROUP: 3

STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

S.A. 2448

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APPENDIX H

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 79

ANIMAL NUMBER: 84-1927/PRETEST=

DATE OF DEATH: 31-OCT-84

79 SEX: FEMALE

STUDY DAY OF DEATH: 29

DOSE GROUP: 3

STUDY WEEK OF DEATH: 5

SACRIFICE STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 80

ANIMAL NUMBER: 84-1928/PRETEST=

80 SEX: FEMALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT PRODUCT SAFETY ASSESSMENT SKOKIE, ILLINOIS 60077				INDIVIDUAL ANIMAL DATA REPORT STUDY NUMBER: SA2448		PRINTED: 5-JAN-85 PAGE: 81	
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX			
ANIMAL NUMBER: 84-1929/PRETEST=		81 SEX: FEMALE		DOSE GROUP: 3		SACRIFICE STATUS: INTERIM SACRIFICE 1	
DATE OF DEATH: 31-OCT-84		STUDY DAY OF DEATH: 29		STUDY WEEK OF DEATH: 5		TERMINAL BODY WEIGHT: NOT TAKEN	
ORGAN NAME		<< GROSS ORGAN OBSERVATIONS >>		SEVERITY GROSS FREE-TEXT COMMENTS			
WHOLE BODY(WB)		KEYWORDS / PHRASES		NORMAL			
TISSUE / HISTOPATHOLOGIC FINDINGS		<< MICROSCOPIC TISSUE OBSERVATIONS >>		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS			
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL							

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1930/PRETEST=

82 SEX: FEMALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

PRINTED: 5-JAN-85

PAGE: 82

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

NORMAL

SEVERITY

GROSS FREE-TEXT COMMENTS

TISSUE

MICROSCOPIC FINDINGS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 83

STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1931/PRETEST= 83 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

S.A. 2448

T 84

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

PRINTED: 5-JAN-85

PAGE: 84

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1932/PRETEST=

84 SEX: FEMALE

DOSE GROUP: 3

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

I

SEARLE RESEARCH & DEVELOPMENT PRODUCT SAFETY ASSESSMENT SKOKIE, ILLINOIS 60077		INDIVIDUAL ANIMAL DATA REPORT STUDY NUMBER: SA2448		PRINTED: 5-JAN-85 PAGE: 85	
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
ANIMAL NUMBER: 84-1933/PRETEST=		85 SEX: FEMALE		DOSE GROUP: 3	
DATE OF DEATH: 31-OCT-84		STUDY DAY OF DEATH: 29		SACRIFICE STATUS: INTERIM SACRIFICE 1	
				STUDY WEEK OF DEATH: 5	
				TERMINAL BODY WEIGHT: NOT TAKEN	
ORGAN NAME		<< GROSS ORGAN OBSERVATIONS >>		SEVERITY GROSS FREE-TEXT COMMENTS	
LYMPH NODE(LN)		DISCOLORED		SUBMAXILLARY, RED, RIGHT SIDE	
TISSUE / HISTOPATHOLOGIC FINDINGS		<< MICROSCOPIC TISSUE		OBSERVATIONS >>	
LYMPH N-SUBMAX				DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS	
-INFLAMMATION					

1

SEARLE RESEARCH & DEVELOPMENT PRODUCT SAFETY ASSESSMENT SKOKIE, ILLINOIS 60077		INDIVIDUAL ANIMAL DATA REPORT STUDY NUMBER: SA2448		PRINTED: 5-JAN-85 PAGE: 86			
SPECIES: RAT/CHARLES RIVER CD		STUDY START DATE: 3-OCT-84		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX			
ANIMAL NUMBER: 84-1949/PRETEST=		86 SEX: FEMALE		DOSE GROUP: 4		SACRIFICE STATUS: FINAL SACRIFICE	
DATE OF DEATH: 28-NOV-84		STUDY DAY OF DEATH: 57		STUDY WEEK OF DEATH: 9		TERMINAL BODY WEIGHT: NOT TAKEN	
ORGAN NAME		<< GROSS ORGAN OBSERVATIONS >>		SEVERITY		GROSS FREE-TEXT COMMENTS	
WHOLE BODY(WB)		NORMAL					
TISSUE / HISTOPATHOLOGIC FINDINGS		<< MICROSCOPIC TISSUE		OBSERVATIONS >>		DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS	
NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL							

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1950/PRETEST=

DATE OF DEATH: 1-NOV-84

STUDY DAY OF DEATH: 30

SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: INTERIM SACRIFICE 1

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

PRINTED: 5-JAN-85

PAGE: 87

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

NORMAL

SEVERITY

GROSS FREE-TEXT COMMENTS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 88

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1951/PRETEST=

88 SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB)

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

INT SM-ILEUM TISSUE IS MISSING

ADRENAL GLAND MULTI-FOCAL

-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 89

ANIMAL NUMBER: 84-1952/PRETEST=

89 SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
ANIMAL NUMBER: 84-1953/PRETEST= 90 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: INTERIM SACRIFICE 1
DATE OF DEATH: 31-OCT-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN
STUDY START DATE: 3-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
PRINTED: 5-JAN-85
PAGE: 90

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB) NORMAL

APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
INT LG-RECTUM TISSUE IS MISSING
LIVER
-MICROGRANULOMA(S)
BONE-FEMUR SECTION IS AT EDGE OF JOINT CAPSULE, GIVING FALSE IMPRESSION OF
CARTILAGENOUS DEGENERATION

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
PRINTED: 5-JAN-85
PAGE: 91
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1954/PRETEST=
DATE OF DEATH: 1-NOV-84
91 SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 30
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
MICROSCOPIC TISSUE OBSERVATIONS
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

KIDNEY
-INFLAMMATION, CHRONIC
MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 92

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1955/PRETEST=
DATE OF DEATH: 28-NOV-84

92 SEX: FEMALE
STUDY DAY OF DEATH: 57

DOSE GROUP: 4
STUDY WEEK OF DEATH: 9

SACRIFICE STATUS: FINAL SACRIFICE
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY (WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS

<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

PRINTED: 5-JAN-85

PAGE: 93

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1956/PRETEST=

DATE OF DEATH: 1-NOV-84

93 SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: INTERIM SACRIFICE 1

STUDY DAY OF DEATH: 30

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME

WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >>	DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
LIVER -MICROGRANULOMA(S)		
PARATHYROID		TISSUE IS MISSING
MAMMARY GLAND		TISSUE IS MISSING
PERIPHERAL NERVE		TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 94

ANIMAL NUMBER: 84-1957/PRETEST-
DATE OF DEATH: 31-OCT-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

94 SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 29
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS
ADRENAL GLAND

<< MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS
MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 95

STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1958/PRETEST=
DATE OF DEATH: 1-NOV-84
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 30
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

APPENDIX H

<< MICROSCOPIC TISSUE OBSERVATIONS >>
TISSUE / HISTOPATHOLOGIC FINDINGS DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

LIVER
-MICROGRANULOMA(S)

ADRENAL GLAND
-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS FOCAL

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
 PAGE: 96

SPECIES: RAT/CHARLES RIVER CD

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1959/PRETEST=

96 SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: INTERIM SACRIFICE 1

DATE OF DEATH: 31-OCT-84

STUDY DAY OF DEATH: 29

STUDY WEEK OF DEATH: 5

TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME	<< GROSS ORGAN OBSERVATIONS >> KEYWORDS / PHRASES	SEVERITY	GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB)	NORMAL		

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >> DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
ADRENAL GLAND -HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS	MULTI-FOCAL
MAMMARY GLAND	TISSUE IS MISSING
BONE-FEMUR	SECTION IS AT EDGE OF JOINT CAPSULE, GIVING FALSE IMPRESSION OF CARTILAGENOUS DEGENERATION

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
PRINTED: 5-JAN-85
PAGE: 97

ANIMAL NUMBER: 84-1960/PRETEST=
DATE OF DEATH: 1-NOV-84
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY DAY OF DEATH: 30
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME	<< GROSS ORGAN OBSERVATIONS >> KEYWORDS / PHRASES	SEVERITY GROSS FREE-TEXT COMMENTS
WHOLE BODY(WB)	NORMAL	

APPENDIX H

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >> DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
KIDNEY -MICROCALCULI	
LIVER -MICROGRANULOMA(S)	
MAMMARY GLAND	TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 98

ANIMAL NUMBER: 84-1961/PRETEST=
DATE OF DEATH: 28-NOV-84

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

98 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
STUDY DAY OF DEATH: 57 STUDY WEEK OF DEATH: 9 TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME << GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES SEVERITY GROSS FREE-TEXT COMMENTS

WHOLE BODY(WB) NORMAL

TISSUE << MICROSCOPIC TISSUE OBSERVATIONS >>
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: RAT/CHARLES RIVER CD
ANIMAL NUMBER: 84-1962/PRETEST=
DATE OF DEATH: 31-OCT-84
STUDY DAY OF DEATH: 29
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN
STUDY START DATE: 3-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2448

PRINTED: 5-JAN-85
PAGE: 99

ANIMAL NUMBER: 84-1962/PRETEST=
DATE OF DEATH: 31-OCT-84
STUDY DAY OF DEATH: 29
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: INTERIM SACRIFICE 1
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
WHOLE BODY(WB)
GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SEVERITY GROSS FREE-TEXT COMMENTS

NORMAL

APPENDIX H

S.A. 2448

T100

TISSUE
MICROSCOPIC TISSUE OBSERVATIONS >>
HISTOPATHOLOGIC FINDINGS
DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

ADRENAL GLAND
-HYPERTROPHIED CELLS, ZONA FASCICULATA/RETICULARIS
MULTI-FOCAL

SEARLE RESEARCH & DEVELOPMENT

PRODUCT SAFETY ASSESSMENT

SKOKIE, ILLINOIS 60077

SPECIES: RAT/CHARLES RIVER CD

INDIVIDUAL ANIMAL DATA REPORT

STUDY NUMBER: SA2448

STUDY START DATE: 3-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 5-JAN-85

PAGE: 100

ANIMAL NUMBER: 84-1963/PRETEST=

100 SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: FINAL SACRIFICE

DATE OF DEATH: 28-NOV-84

STUDY DAY OF DEATH: 57

STUDY WEEK OF DEATH: 9

TERMINAL BODY WEIGHT: NOT TAKEN

<< GROSS ORGAN OBSERVATIONS >>

KEYWORDS / PHRASES

SEVERITY GROSS FREE-TEXT COMMENTS

ORGAN NAME

WHOLE BODY(WB)

NORMAL

<< MICROSCOPIC TISSUE OBSERVATIONS >>

TISSUE / HISTOPATHOLOGIC FINDINGS

DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

NO MICROSCOPIC OBSERVATIONS FOR THIS ANIMAL

R&D PRODUCT DEVELOPMENT FUNCTION
REPORT REVIEW AND RELEASE

Page 1 of 3

DEPARTMENT: Product Development Analytical

DOCUMENT NUMBER: F-305-034-01

TITLE OF REPORT: SC-19129

TYPE OF REPORT: Analytical Summary in Support of Product Safety
Assessment Study Number 2448

AUTHOR(S):	DATE	REVIEWER(S):	DATE
<u>James Jiu</u>	<u>12/06/84</u>	<u>Daniel L. Sweeney</u>	<u>12-6-84</u>
_____	_____	_____	_____
_____	_____	_____	_____

APPROVAL:	DATE
James Jiu <u>James Jiu</u>	<u>12/06/84</u>
_____	_____

TECHNICAL WRITER:
Michele Newcomb Michele Newcomb

APPROVAL FOR RELEASE:

<u>R. Baum</u>	<u>12/10/84</u>	<u>R. Baum for L. Hansen</u>	<u>12/10/84</u>
R. Baum, Director	Date	L. Hansen,	Date
Analytical Development		Senior Director	
		Product Development	

NORTH AMERICAN PRECLINICAL RESEARCH AND DEVELOPMENT
SEARLE PHARMACEUTICALS AND CONSUMER PRODUCTS
SKOKIE, ILLINOISS.A. 2448
I-1

Subject: SC-19129

Summary Number: F-305-034-01

Applicable to SA Study Number: 2448

Test Article Characterization and Stability

Lot 84K-047-101 (formerly 840413) was analyzed using the release methods of testing, released against the current specifications (NS-S84-015-A), and given a re-evaluation period of one year prior to use in this study.

Table 1

	Prior to Hydration(1)		After Hydration(1)
Lot Designation	840413	840413	84K-047-101
Analysis Report #	84N1007	84N1009	84N1058
Completion Date	10/03/84	10/01/84	10/16/84
Identity (HPLC)	Conforms to Standard	Conforms to Standard	Conforms to Standard
Assay (on dried basis)	(Titration) 99.9% n = 3 s = 0.1	(HPLC) 99.0% n = 3 s = 0.3	(HPLC) 100.0% n = 3 s = 0.2
Loss on Drying	0.6%		
Water		0.6%(1)	9.8%(1)

(1) Lot 840413 was hygroscopic. To circumvent percent water variability, this lot was allowed to equilibrate to a more stable water content, and was designated as Lot 84K-047-101.

These results and all other results, coupled with the use of lot 84K-047-101 within its re-evaluation period indicate that lot 84K-047-101 of SC-19129 was suitable for use in this study.

Subject: SC-19129

Summary Number: F-305-034-01

Applicable to SA Study Number: 2448

GLP Compliance Statement

-

To the best of our knowledge, the support activities provided by the Product Development Analytical Department for this study were conducted in compliance with the Good Laboratory Practices Regulations, as set forth in part 58, 21 CFR.

PROTOCOL

1. Study Title: Two Week Range-Finding Dietary Admix
Toxicity Study of Beta Aspartame in the Rat

*THIS STUDY IS NOT INTENDED TO SUPPORT APPLICATIONS
*FOR RESEARCH OR MARKETING PERMITS FOR PRODUCTS
*REGULATED BY GOVERNMENTAL AGENCIES. THIS IS AN
*EXPLORATORY/RANGE-FINDING STUDY AND IS NOT WITHIN
*THE SCOPE OF GOOD LABORATORY PRACTICE REGULATIONS.

2. Study Sponsor: G. D. Searle & Co.
3. Facility: G. D. Searle & Co., 4901 Searle Parkway,
Skokie, Illinois 60077.
4. Proposed Dates:
 - 4.1. First Dosing: October 3, 1984
 - 4.2. Sacrifice: October 17 and 18, 1984
5. Purpose: To determine toxic effects as evidenced by
clinical signs and specific organ damage and to
provide a basis for selecting dosages for
longer studies.
6. Overview of Study Design:

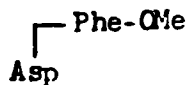
Group	Intended*	Animals/Sex	Week 3 Sacrifice Animals/Sex
	Dosage (mg/kg)		
Control	0	10	10
Low	250	10	10
Medium	500	10	10
High	1000	10	10
Very High	1500	10	10

*See Section 9.3.

7. Laboratory Procedures: This is an exploratory/range-
finding study and is not within the scope of the Good
Laboratory Practice Regulations.
8. Proposed Clinical Use: Beta aspartame is found in small
amounts in aspartame.

9. Test Article:

9.1. Chemical Structure:



9.2. Chemical Name: N-L- β -aspartyl-L-phenylalanine, 1-methyl ester.

9.3. Formulation: Appropriate amounts of test article will be mixed with diet. In order to give the intended dose the diet concentration will be adjusted each time food consumption and body weights are measured. The concentration will be based on the average projected body weight and food consumption of the animals for the next feeding interval.

9.4. Administration:

9.4.1. Route: The test article will be given in the diet. The oral route will be used because that is the intended route in humans.

9.4.2. Dosage: The very high dosage (1500 mg/kg) is the highest that can be given without markedly altering the nutrient composition of the diet. The low, medium, and high dosages (250, 500, and 1000 mg/kg, respectively) are 17%, 33%, and 67% of the very high dosage.

9.4.3. Frequency: Test article mixed with diet will be available ad libitum from the first day of dosing until the start of fasting at approximately 4:00 P.M. on day 14 or 15.

9.4.4. Duration: 14 to 15 days.

9.5. Analyses:

9.5.1. Test Article:

9.5.1.1. Identity and relative purity:
Will be determined before use.

9.5.1.2. Stability: Will be determined before use.

9.5.2. Test article in carrier: The stability of Beta Aspartame in diet will be determined.

9.5.3. Additional samples will be obtained to develop methods with the test article in carrier but will not be reported.

9.6. Storage:

9.6.1. Test article: Will be stored in a well-closed, light resistant container at controlled room temperature.

9.6.2. Test article in carrier: Will be stored in a plastic container at controlled room temperature.

9.7. Estimated Requirements: 400g

10. Test System, Housing and Diet:

10.1. Test System:

10.1.1. Species, age and weight range: Charles River CD rats (Portage, Michigan) of both sexes, approximately 3 weeks old on arrival, will be used. The body weight range of these animals is usually 40-60 grams for both males and females on arrival. The animals will be acclimated for approximately 2 weeks. The Charles River CD rat has been used extensively in safety studies and a large amount of biological data is available.

10.1.2. Selection: Animals to be used during the study will be selected on the basis of acceptable findings from the weight gain, feed consumption, and physical examination results. Healthy animals in excess of the number needed will be deleted by a procedure similar to that described in 10.1.3. (below).

10.1.3. Randomization: Assignment to dosage group: For each sex, a list of animals to be used will be ranked by the last pretreatment body weight. Dosage groups

will be selected from this list as follows: 1) The ranked list will be divided into blocks--the number of blocks will be equal to the number of animals in the group to be selected. 2) One animal will be randomly selected from each block and assigned to the first group. 3) The same procedure will be followed for the remaining groups. 4) The groups will be assigned to dosage groups by a random permutation.

- 10.1.4. Identification: Permanent identification numbers will be assigned to animals within each group using a computer generated random permutation. Each animal will be uniquely identified with an ear tag.

10.2. Housing:

- 10.2.1. Caging: Animals will be housed individually in suspended, stainless steel, wire-mesh cages in room J-329.
- 10.2.2. General environment:
 - 10.2.2.1. Temperature: Will be $72^{\circ} \pm 5^{\circ}\text{F}$ ($22^{\circ} \pm 3^{\circ}\text{C}$) and monitored.
 - 10.2.2.2. Humidity: Will be 25% or greater and monitored.
 - 10.2.2.3. Lighting: 12 hour light, 12 hour dark cycles.

10.3. Diet:

- 10.3.1. Feed: Purina Certified Rodent Chow 5002 (meal) will be available ad libitum.
- 10.3.2. Water: Tap water from a municipal water supply will be available ad libitum.
- 10.3.3. Analyses:
 - 10.3.3.1. General: Release of each lot of feed by the manufacturer is based on analysis of composite samples of each lot which has met specifications set by the manufacturer. In addition,

water is routinely analyzed for chemical and microbial impurities.

- 10.3.3.2. Special: Special analyses of feed and water will not be performed since no contaminants known to be capable of interfering with the study are reasonably expected to be present.

11. Clinical Observations:

- 11.1. Daily Observations: An observation of physical appearance and behavior will be performed each weekday morning. On weekends, company holidays, and days when physical examinations are done no daily observations will be performed. In addition, animals will be checked daily for survival and moribundity.
- 11.2. Physical Examinations: Will be performed pre-treatment and in the afternoon once per week during weeks 1 and 2.
- 11.3. Body Weight and Feed Consumption:
- 11.3.1. Body weight: Will be measured on -7, -1, 1, 3, 6, 8, 10 and 14. Final body weights will be taken prior to sacrifice.
- 11.3.2. Feeder weight: Will be measured on days -7, -1, 1, 3, 6, 8, 10 and 14.
- 11.4. Clinical Laboratory Determinations:
- 11.4.1. Collection: Blood will be collected the day of sacrifice from the abdominal aorta of animals which are fasted overnight and anesthetized with ether.
- 11.4.2. Parameters to be determined:
- 11.4.2.1. Clinical chemistry:
- glucose concentration
aspartate aminotransferase
activity
alanine aminotransferase
activity

urea concentration
alkaline phosphatase activity
cholesterol concentration
total bilirubin concentration
total protein concentration
albumin (A) concentration
globulin (G) concentration
A/G ratio
sodium concentration
potassium concentration
chloride concentration
calcium concentration

11.4.2.2. Hematology:

white blood cell count
red blood cell count
hemoglobin concentration
hematocrit
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin
concentration
differential smear evaluation
platelet count
prothrombin time

11.4.3. Urine:

11.4.3.1. Collection: Urine will be collected from all animals one day prior to sacrifice.

11.4.3.2. Parameters to be determined:

pH
refractive index
glucose
bilirubin
protein
ketones
occult blood
urobilinogen
microscopic examination of
centrifuged sediment

11.5. Additional clinical observations and examinations may be done by the study toxicologist to elucidate any observed clinical signs.

12. Postmortem Procedures:

12.1. Animal Disposition:

12.1.1. Animals found dead: Will be refrigerated and necropsied at the earliest possible time.

12.1.2. Animals found moribund or to be killed by design: Will be sacrificed by exsanguination from the abdominal aorta while anesthetized with ether and then necropsied.

12.2. Sacrifice Schedule: Animals are to be sacrificed on days 15 and 16.

12.3. Necropsy:

12.3.1. Organ Weights: The organs underlined below will be weighed for all animals killed by design. Organs of animals found dead, killed in extremis, or killed accidentally will not be weighed.

12.3.2. Tissue Collection:

12.3.2.1. Standard:

adrenal gland
bone, sternum
brain
heart
kidney
liver
lung
testis
thyroid gland*

*The parathyroid will be weighed with the thyroid and will be examined microscopically if it is included in the section of thyroid.

12.3.2.2. Additional specimens may be collected as designated by the study pathologist.

12.3.2.3. Fixative: Carson's fixative (buffered 10% formalin) except

for the testes, which will be fixed in Bouin's solution. The testes of animals found dead will be fixed in Carson's fixative.

12.4. Histology Examination:

12.4.1. Standard: Histological sections will be prepared from the preserved specimens and stained with hematoxylin and eosin. All tissues of the control and high dose animals and gross lesions that require microscopic confirmation will be examined histologically. Target organs will be examined in all groups.

12.4.2. Additional sectioning, staining, and examining may be done at the request of the study pathologist to elucidate the nature of any tissue changes.

13. Statistical Procedures:

13.1. Variables:

body weights
body weight changes
feed consumption
clinical chemistry data
hematology data
urinalysis data
organ weights
organ/body weight ratios
organ/brain weight ratios

13.2. Analyses: Statistical analyses will be done separately for each sex. For each variable, mean values and standard deviations will be determined. A one-way analysis of variance will be performed for each variable at each time period. If the F-ratio from the analysis of variance is significant at the 5% level, two-tailed t-tests comparing the control group to each of the treated groups will be performed (using the pooled error variance from the analysis of variance). The Bartlett-Box test for homogeneity of variance will also be done. Significance levels achieved will be reported for 5%, 1%, and 0.1% for t-tests, and for 5% for the Bartlett-Box test. The one-way analysis of variance, t-tests, and Bartlett-Box test will not

be done for immature neutrophil, monocyte, eosinophil, and basophil percentages and absolute counts and urinalysis parameters except refractivity.

- 13.3. Additional analyses will be performed when necessary to augment the standard analyses described above.
14. Archiving of Materials: All raw data, supporting documents, protocol, specimens and the final report will be transferred to the R&D Central File.

15. Protocol Approval:

15.1. D. E. Semler, M.S.
Diplomate, A.B.T.
Study Director

Product Safety Assessment: *DES* 9/27/84
Date

15.2. F. N. Kotsonis, Ph.D.
Diplomate, A.B.T.
Director, Toxicology

Product Safety Assessment: *FN Kotsonis* 9/27/84
Date

15.3. D. C. Dodd, B.V.Sc., M.A.
Diplomate, A.C.V.P.
Director, Pathology

Product Safety Assessment: *DC Dodd* 9-27-84
Date

15.4. F. E. Kohn, Ph.D.
Senior Director,

Product Safety Assessment: *FE Kohn* 9/27/84
Date

PROTOCOL AMENDMENT

Effective Date: October 3, 1984

Protocol Amendment #1

S.A. 2448

Four Week Dietary Admix Toxicity Study of Beta Aspartame in the Rat

The indicated protocol sections are changed to read as follows:

1. Section 1. (Study Title) Four Week Dietary Admix Toxicity Study of Beta Aspartame in the Rat
2. Section 4.2. Sacrifice
 - 4.2.1. Week 5 October 31 to November 1, 1984
 - 4.2.2. Week 9 November 28, 1984
3. Section 5. (Purpose) To determine toxic effects as evidenced by clinical signs and specific organ damage and to assess reversal of these effects.
4. Section 6. (Overview of Study Design)

Group	Intended Dosage (mg/kg)	Animals/ Sex	Sacrifice Animals/Sex	
			Week 5	Week 9
Control	0	15	10	5
Low	250	10	10	
Medium	500	10	10	
High	1000	15	10	5

* Dosing of these animals will be discontinued after 4 weeks at which time the animals will enter a 4 week reversal period.

5. Section 7. (Laboratory Procedures) This study will be conducted in compliance with the Good Laboratory Practice Regulations set forth in Part 58 of Title 21 of the Code of Federal Regulations.
6. Section 9.4.3. (Frequency) Test article mixed with diet will be available ad libitum from the first day of dosing until the start of fasting at approximately 4:00 P.M. on day 29 or 30.
7. Section 9.4.4. (Duration) 29 to 30 days.

S.A. 2448

8. Section 9.5 (Analyses)

9.5.1. Test article:

9.5.1.1. Identity, strength, purity, and composition: Will be determined.

9.5.1.2. Stability: Will be determined.

9.5.2. Test article in carrier: Appropriate samples will be taken to determine the stability, homogeneity, and concentration of test article in carrier. These samples will be frozen and analyzed at a later time.

9.5.3. Report: The results of these analyses will appear in a separate report provided to the study director by the Product Development Analytical Department.

9. Section 11.2. (Physical Examinations) Will be performed pretreatment and in the morning once weekly during the treatment and reversal periods.

10. Section 11.3.1. (Body Weight) Will be measured on days -7, -1, 1, 3, 6, 8, 10, 15, 22, 28, 36, 43, 50, and 56. Final body weights will be taken prior to sacrifice.

11. Section 11.3.2. (Feeder Weight) Will be measured on days -7, -1, 1, 3, 6, 8, 10, 15, 22, 28, 36, 43, 50, and 56.

12. Section 12.2. (Sacrifice Schedule) 10 animals/sex/dosage during week 5 and 5 animals/sex in the control and high dosage groups during week 9.

13. Section 12.3.2.1. (Standard tissues to be collected)

adrenal gland

aorta

bone, femur (including marrow and articular surface)

bone, sternum

bone marrow smear (except for animals found dead or killed in extremis)

brain

epididymis

esophagus

eye
heart
intestine, small-duodenum
intestine, small-jejunum
intestine, small-ileum
intestine, large-cecum
intestine, large-colon
intestine, large-rectum
kidney
lacrimal gland, Harderian
liver
lung
lymph node, submaxillary
lymph node, mesenteric
mammary gland (females only)
ovary
pancreas
peripheral nerve, sciatic
pituitary gland
prostate
salivary gland, submaxillary
skeletal muscle
seminal vesicle
skin
spinal cord
spleen
stomach
testis
thymus
thyroid gland*
tongue
trachea
urinary bladder
uterus
vagina

- * The parathyroid will be weighed with the thyroid and will be examined microscopically if it is included in the section of thyroid.

Reason for changes: A decision was made to expand the duration and scope of this study.

APPROVAL:

D-28 10/3/84
D. Semler Date
Study Director

PROTOCOL AMENDMENT

Effective Date: October 8, 1984

Protocol Amendment #2

S.A. 2448

Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat

The indicated protocol sections are changed to read as follows:

Section 1. (Study Title) Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat.

Reason for change: Analytical results have allowed a more precise test article designation.

Section 9.4.2 (Dosage) Deleted.

Reason for change: This section is not required.

 10/8/84
D. Semler

S.A. 2448

PROTOCOL AMENDMENT

Effective Date: October 29, 1984

Protocol Amendment #3

S.A. 2448

- Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat

The subject protocol has been amended as follows:

1. Section 11 (Clinical Observations): Ophthalmic Examinations will be done on all animals during weeks 4 and, if required, on all reversal animals during week 8.
2. Section 11.4.3.2. (Urine parameters to be determined): Urine volume is added to the list of parameters to be determined.

Reason for changes: Ophthalmic examinations and urine volumes are being added to determine any test article related changes.

3. Section 9.4.3. (Dosing Frequency): Fasting will begin earlier than 4:00 P.M. on days 29 or 30.

Reason for change: Urine collection will start in the morning of the designated days and feed will be removed at the start of collection.

 10/29/84
D. Semler

S.A. 2448

PROTOCOL AMENDMENT

Effective Date: November 1, 1984

Protocol Amendment #4

S.A. 2448

Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat

The subject protocol has been amended as follows:

Section 11.1. (Daily Observations): Daily observations for physical appearance and behavior will not be done during the reversal period. The daily check for survival and moribundity will still be performed.

Reason for change: The weekly physical examinations will provide an adequate assessment the animal's physical appearance and behavior during the reversal period.

 11/1/84
D. Semler

S.A. 2448

PROTOCOL AMENDMENT

Effective Date: November 13, 1984

Protocol Amendment #5

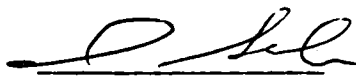
S.A. 2448

Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat

The subject protocol has been amended as follows:

1. Section 11. (Clinical Observations): No ophthalmic examinations will be performed at week 8.
2. Section 11.4. (Clinical Laboratory Determinations): No clinical laboratory determinations will be performed on reversal animals at the week 9 sacrifice.
3. Section 12.3.1 (Organ Weights): No organs will be weighed at the week 9 sacrifice.

Reason for change: A review of the results through week 5 shows no test article related changes in the above parameters, therefore no reversal need be demonstrated.

 11/13/84
D. Semler

S.A. 2448

PROTOCOL AMENDMENT

Effective date: November 21, 1984

Protocol Amendment #6

S.A. 2448

Four Week Dietary Admix Toxicity Study of SC-19129 in the Rat

The subject protocol has been amended as follows:

Section 12.3.2.1. (Tissues to be collected): Bone marrow smears will not be collected for animals at the reversal sacrifice.

Reason for change: A review of bone marrow collected at the week 5 sacrifice shows no test article related changes.

 11/21/84

D. Semler

S.A. 2448

APPENDIX K

QUALITY ASSURANCE STATEMENT - SA-2448 SC-19129

The conduct of this type of short-term study has been subjected to periodic inspections and this report has been audited by R&D Quality -Quality Assurance Monitoring Department. The dates of inspection/audit are given below.

<u>Date of Inspec./Audit</u>	<u>Monitor</u>	<u>Date of Report to Mgmt.</u>
10/05/84 Observations, Diet	L. Derrick	10/8/84
10/10/84 Diet Admix, Physical Exams	L. Derrick	10/12/84
10/29/84 Ophthalmic Exams, Urine Colelction	L. Derrick	11/06/84
11/01/84 Necropsy Phase	H. Schniepp	11/07/84
12/10/84-1/07/85 Comparing Raw Data Against the Draft Final Report	L. Derrick	01/14/85

This report accurately describes the methods used in the study and the reported results accurately reflect the raw data.

Ronald D. Howard
Quality Assurance

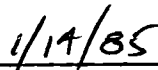
Jan. 14, 1985
Date

GLP COMPLIANCE STATEMENT

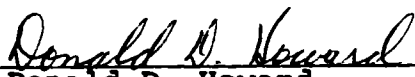
To our knowledge this study (SA-2448) (SC-19129) was conducted in compliance with the Good Laboratory Practices Regulations as set forth in part 58, 21 CFR.



Study Director

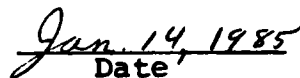


Date



Donald D. Howard

Dir., R&D Quality Assurance



Date

Revision or Amendment Notice

Searle Research and Development

SEARLE

Notice of change to report stored in R&D Central File

Departmental Document or PSA Study Number	R&D Central File Holding Number
S.A. 2448	R-19129-19809-00
Originating Department	
Product Safety Assessment	
Report Title	
Four Week Dietary Admix Toxicity Study of SC-19129 in the	
Rat; S.A. 2448	

Affected
Portion of
Report

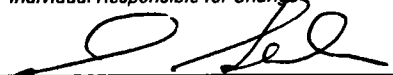
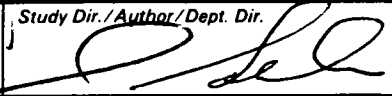

Indicate page numbers or text sections and describe how revised version differs from original.

Revised Analytical Report to Replace Appendix I
in the Above Document

Reason for Change

In revised report, PDAD has (1) included stability, homogeneity, and in-study data not previously available, (2) revised terminology, (3) provided a chart of the Dosing Concentrations and (4) revised a water loss on drying value for one test article lot.

Approval
Signatures


Individual Responsible for Change	Date	Study Dir./Author/Dept. Dir.	Date
	4/25/85		4/25/85
Authorized Submitter	Date	R&D CF Information Scientist	Date
	5/3/85	Eden M. Mante	5/3/85

REPORT AMENDMENT NUMBER 1

Four Week Dietary Admix Toxicity Study of SC-19129
in the Rat

S.A. 2448

The attached analytical report should replace Appendix I in the above document. In their revised report, the Product Development Analytical Department has (1) included stability, homogeneity, and in-study data not previously available, (2) provided a chart of the Dosing Concentrations, (3) revised terminology, and (4) revised a water loss on drying value for one test article lot. This amendment does not alter the conclusions drawn in this study.

 4/25/85

David Semler Date
Study Director
Product Safety Assessment

R&D PRODUCT DEVELOPMENT FUNCTION
REPORT REVIEW AND RELEASE

Page 1 of 18

DEPARTMENT: Product Development Analytical

DOCUMENT NUMBER: F-305-034-01B

TITLE OF REPORT: SC-19129

TYPE OF REPORT: Analytical Summary in Support of Product Safety
Assessment Study Number 2448

AUTHOR(S):	DATE	REVIEWER(S):	DATE
<u>Mary E. Napier</u>	<u>3/13/85</u>	<u>Daniel J. Sweney</u>	<u>4-4-85</u>
<u>James Jiu</u>	<u>13 March 85</u>	<u>Robert W. Dinnick</u>	<u>4-5-85</u>

APPROVAL:	DATE
James Jiu <u>James Jiu</u>	<u>13 March 85</u>

TECHNICAL WRITER:

Michele Newcomb Michele Newcomb

APPROVAL FOR RELEASE:

<u>R. Baum</u>	<u>4/16/85</u>	<u>Larry Hansen</u>	<u>4/24/85</u>
R. Baum, Director	Date	L. Hansen,	Date
Analytical Development		Senior Director	
		Product Development	

NORTH AMERICAN PRECLINICAL RESEARCH AND DEVELOPMENT
SEARLE PHARMACEUTICALS AND CONSUMER PRODUCTS
SKOKIE, ILLINOIS

Justification for Revision: B

1. Chart of Dosing Concentration added, page 11.
2. Terminology revised throughout for clarity.

Justification for Revision: A

1. Include stability, homogeneity and in-study data.
2. LOD value for Lot 84N1007 was changed to 0.5%.

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Test Article Characterization and Stability

Lot 84K-047-101 (formerly 840413) was analyzed using the release methods of testing, released against the current specifications (NS-S84-015-A), and given a re-evaluation period of one year prior to use in this study.

Table 1

Prior to Hydration⁽¹⁾

Lot Designation	840413	840413	840413
Analysis Report #	84N1007	84N1009	84N1046
Completion Date	10/03/84	10/01/84	10/17/84
Identity (HPLC)	Conforms to Standard	Conforms to Standard	---
Assay (on dried basis)	(Titration) 99.9% n = 3 s = 0.1	(HPLC) 99.0% n = 3 s = 0.3	---
Loss on Drying	0.5%	---	---
Water	---	0.6% ⁽¹⁾	1.08% ^{(1), (2)}

(1) Lot 840413 was hygroscopic. To circumvent percent water variability, this lot was allowed to equilibrate to a more stable water content, and was designated as Lot 84K-047-101.

(2) The diet admixture samples for Study Week 2 were prepared using the SC-19129 from Lot 840413. The water content was assayed at the time of sample preparation.

These results and all other results, coupled with the use of lot 84K-047-101 within its re-evaluation period indicate that lot 84K-047-101 of SC-19129 was suitable for use in this study.

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Test Article Characterization and Stability

Lot 84K-047-101 (formerly 840413) was analyzed using the release methods of testing, released against the current specifications (NS-S84-015-A), and given a re-evaluation period of one year prior to use in this study.

Table 2
After Hydration⁽¹⁾

		Post-Study
Lot Designation	84K-047-101	84K-047-101
Analysis Report #	84N1058	85N0013
Completion Date	10/16/84	01/24/85
Identity (HPLC)	Conforms to Standard	Conforms to Standard
Assay (on dried basis)	(HPLC) 100.0% n = 3 s = 0.2	(HPLC) 98.5% n = 3 s = 1.3
Water	9.8% ⁽¹⁾	9.8% ⁽¹⁾

(1) Lot 840413 was hygroscopic. To circumvent percent water variability, this lot was allowed to equilibrate to a more stable water content, and was designated as Lot 84K-047-101.

These results and all other results, coupled with the use of lot 84K-047-101 within its re-evaluation period indicate that lot 84K-047-101 of SC-19129 was suitable for use in this study.

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Stability of Test Article in Carrier

The stability of SC-19129 in rodent diet admixture was determined by using a stability indicating HPLC method (M84-045-A). Diet admixture samples prepared at dosing concentrations of 1 g and 50 g of SC-19129/kg of rodent diet chow were stored at ambient conditions. Samples were prepared over a thirteen day period for days 0, 1, 2, 5, 9, 12, and 13. The results of the analysis are given in Tables 3 and 4. The statistics are based on the percent relative recovery values.

For the low dosing concentration, 1 g/kg, Table 3, the results of the linear regression analysis (MINITAB, Reference 1) for the relative percent recovery of SC-19129 versus time gave a t-ratio value less than the table value (Reference 2, Table A-4), indicating no significant downward trend. The correlation between the observed recovery values and the predicted values exhibited a normal probability plot (Reference 1 and 3). The results indicate that SC-19129 in rodent diet admixture at 1 g/kg, stored at ambient conditions does not undergo significant degradation for at least thirteen days.

For the high dosing concentration, 50 g/kg, Table 4, the results of the linear regression analysis (MINITAB, Reference 1) for the relative percent recovery of SC-19129 versus time gave a t-ratio value less than the table value (Reference 2, Table A-4) indicating no significant downward trend. The correlation between the observed recovery values and the predicted values exhibited a normal probability plot (References 1 and 3). The results indicate that SC-19129 in rodent diet admixture at 50 g/kg, stored at ambient conditions does not undergo significant degradation for at least thirteen days.

Since SC-19129 is stable on-shelf at low and high dosing concentrations at ambient conditions, all dosing concentrations between 1 g and 50 g of SC-19129/kg of rodent diet chow are considered to be stable for at least thirteen days when stored under equivalent conditions.

Notebook Reference: M. Napier, PDAD-0028, pp. 225-235

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Table 3

On-Shelf Stability of Test Article in Carrier

1 g of SC-19129/kg of Rodent Diet Admixture

Time (Days)	Sample	% SC-19129 Recovered	% Relative Recovery
0	3	96.0	Reference
	4	98.6	
	5	96.6	$\bar{X} = 97.0$
	6	97.0	
1	1	100.0	103.1
	2	96.9	99.9
2	1	97.1	100.1
	2	95.2	98.1
5	1	97.3	100.3
	2	97.5	100.5
9	1	95.1	98.0
	2	96.8	99.8
12	1	98.7	101.8
	2	99.8	102.9
13	1	98.9	102.0
	2	97.2	100.2
Intercept			100.0
Slope			0.083
t-Ratio			0.81
t (0.95, df)			1.812
Degrees of Freedom (df)			10
Correlation: Predicted vs Observed			0.986

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Table 4

On-Shelf Stability of the Test Article in Carrier

50 g of SC-19129/kg of Rodent Diet Admixture

Time (Days)	Sample	% SC-19129 Recovered	% Relative Recovery
0	3	100.3	Reference $\bar{X} = 100.2$
	4	100.2	
	5	99.4	
	6	100.7	
1	1	99.3	99.1
	2	98.4	98.2
2	1	97.5	97.3
	2	98.9	98.7
5	1	98.3	98.1
	2	98.3	98.1
9	1	99.5	99.3
	2	97.1	96.9
12	1	100.2	100.0
	2	99.8	99.6
13	1	99.2	99.0
	2	99.1	98.9
Intercept			98.0
Slope			0.0831
t-Ratio			1.56
t (0.95, df)			1.812
Degrees of Freedom (df)			10
Correlation: Predicted vs Observed			0.961

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Homogeneity of Test Article in Carrier

The content uniformity of SC-19129 (Lot 84K-047-101) in diet admixture (Ralston Purina Lot 5002) was determined for the female rat group, low dosing concentration and the male rat group, high dosing concentration during Study Week 2 and Study Week 4. The analysis was conducted by using a stability indicating HPLC method (M84-045-A).

Product Safety Assessment personnel prepared and sampled the diet admixture during Study Week 2 and Study Week 4. The diet admixtures were prepared using a Turbula mixer for Study Week 2 and both the Turbula mixer and a Cross-flow mixer for Study Week 4. Nine 1 gram samples were randomly taken from the storage container using a bag trier.

The results of the analyses are presented in Tables 5 and 6.

The content uniformity for the Study Week 2, female group, low dosing concentration (Table 5, column 2) were shown to be normally distributed ($\alpha = 0.05$), having a normality correlation coefficient above the table value, $t = 0.912$ (References 1 and 3). The calculated tolerance interval (Reference 2, Table A-6) indicates that with 95% confidence, at least 95% of future samples should be between 1.87 and 2.37 g/kg diet admixture for the female group, low dosing concentration. This is equivalent to $\pm 11.8\%$. The SC-19129 is considered uniformly distributed in the diet admixture used.

The results for content uniformity for Study Week 2, male group, high dosing concentration (Table 5, column 4) were shown to be normally distributed ($\alpha = 0.05$), having a normality correlation coefficient above the table value, $t = 0.912$. The calculated tolerance interval indicates that with 95% confidence, at least 95% of future samples should be between 7.27 and 9.61 g/kg diet admixture for the male group, high dosing concentration. This is equivalent to $\pm 13.9\%$. The SC-19129 is considered uniformly distributed in the diet admixture used.

Since the Study Week 2, female group, low dosing concentration and the male group, high dosing concentration are shown to be homogeneous, all the Study Week 2 diet admixture dosing concentrations are considered homogeneous.

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

The results for the content uniformity for Study Week 4, female group, low dosing concentration (Table 6, column 2) were shown to be not normally distributed ($\alpha = 0.05$), having a normality correlation coefficient below the table value, $t = 0.912$. However, this non-normality was due to the high precision of eight out of the nine values. The percent RSD for the eight high precision values is 1.6%, while the percent RSD for the nine values is 4.3%. This latter assay variance for the nine values is considered acceptable. The calculated tolerance interval indicates that with 95% confidence, at least 95% of the future samples should be between 2.15 and 2.93 g/kg diet admixture for the female group, low dosing concentration. This is equivalent to + 15.4%. The SC-19129 is considered uniformly distributed in the diet admixture used.

The results for content uniformity for the Study Week 4, male group, high dosing concentration (Table 6, column 4) were shown to be normally distributed ($\alpha = 0.05$), having a normality correlation coefficient above the table value, $t = 0.912$. The calculated tolerance interval indicates that with 95% confidence, at least 95% of the future samples should be between 10.1 and 14.3 g/kg diet admixture for the male group, high dosing concentration. This is equivalent to +17.2%. The SC-19129 is considered uniformly distributed in the diet admixture used.

Since the Study Week 4, female group, low dosing concentration and male group, high dosing concentration are shown to be homogeneous, all the Study Week 4 diet admixture dosing concentrations are considered homogeneous.

Additionally, since the Study Week 2 diet admixtures, prepared using the Turbula mixer, and the Study Week 4 diet admixtures, prepared using both the Turbula and the Cross-flow mixers, are shown to be homogeneous, all the diet admixtures prepared for this study are considered homogeneous.

Notebook Reference: M. Napier, PDAD-0028, pp. 160-178, 207-224

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Table 5

Study Week 2

SC-19129, g/kg

Analysis Report #	84-1965		84-1970
Dose	Low Female		High Male
Sample #		Sample #	
G00204	2.03	G00225	8.14
G00205	2.03	G00226	7.93
G00206	2.17	G00227	8.74
G00207	2.03	G00228	9.06
G00208	2.18	G00229	8.45
G00209	2.14	G00230	8.47
G00210	2.17	G00231	8.53
G00211	2.18	G00232	8.40
G00212	2.11	G00233	8.22
\bar{X}	2.12		8.44
s	0.07		0.33
Normality Correlation Coefficient	0.949		0.982
Tolerance Interval	± 0.25		± 1.17

Subject: SC-19129

Summary Number: F-305-034-01B

Applicable to SA Study Number: 2448

Table 6

Study Week 4

SC-19129, g/kg

Analysis Report #		84-2076	84-2081
Dose	Low Female		High Male
Sample #		Sample #	
G00404	2.46	G00425	12.4
G00405	2.83	G00426	12.7
G00406	2.53	G00427	11.5
G00407	2.53	G00428	13.4
G00408	2.58	G00429	12.1
G00409	2.47	G00430	12.1
G00410	2.48	G00431	12.4
G00411	2.48	G00432	11.5
G00412	2.53	G00433	11.9
\bar{X}	2.54		12.2
s	0.11		0.6
Normality Correlation Coefficient	0.829		0.985
Tolerance Interval	\pm 0.39		\pm 2.1

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Concentration of Test Article in Carrier

The concentration of SC-19129 (Lot 84K-047-101) in diet admixtures (Ralston Purina Lot 5002) was determined during Study Week 2 and Study Week 4. The analyses were conducted using a stability indicating HPLC method (M84-045-A).

Product Safety Assessment personnel prepared and sampled the diet admixtures. The Study Week 2 diet admixtures were prepared using a Turbula mixer and the Study Week 4 diet admixtures were prepared using the Turbula mixer and the Cross-flow mixer. Three or nine 1 gram samples for each dosing concentration were randomly taken from the storage container using a bag trier.

The control samples were prepared by sham (no test article) mixing, using the appropriate mixer depending on the study week.

See Chart 1 below for dosing concentrations.

The results of the analyses are reported in Tables 7 through 12.

Notebook Reference: M. Napier, PDAD-0028, pp. 160-178, 194-224

Chart 1

Designated Dosing Concentrations

SC-19129, g/kg

Study Week		Low	Medium	High
2	Female	2.326	4.489	9.244
	Male	2.407	4.658	9.363
4	Female	2.717	5.428	10.932
	Male	3.123	6.329	12.492

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Table 7

Dosing Control Sample

SC-19129, g/kg

Study Week 2

Analysis Report #	84-1964
Dose	Dosing Control Sample
Sample #	
G00201	Less than 0.1
G00202	Less than 0.1
G00203	Less than 0.1

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Table 8
Study Week 2⁽³⁾
Female Dose Group
SC-19129, g/kg

Analysis Report #	84-1965		84-1967		84-1969
Dose	Low		Medium		High
Sample #		Sample #		Sample #	
G00204	2.03	G00216	4.03	G00222	9.30
G00205	2.03	G00217	4.21	G00223	9.30
G00206	2.17	G00218	4.19	G00224	8.63
G00207	2.03				
G00208	2.18				
G00209	2.14				
G00210	2.17				
G00211	2.18				
G00212	2.11				
\bar{X}	2.12		4.14		9.08
s	0.07		0.10		0.39

(3) The diet admixtures for Study Week 2 were prepared using SC-19129 from Lot 840413. See Report of Analysis 84N1046 for the water content results.

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Table 9
Study Week 2⁽³⁾
Male Dose Group
SC-19129, g/kg

Analysis Report #	84-1966		84-1968		84-1970
Dose	Low		Medium		High
Sample #		Sample #		Sample #	
G00213	2.22	G00219	4.19	G00225	8.14
G00214	2.23	G00220	4.20	G00226	7.93
G00215	2.22	G00221	4.41	G00227	8.74
				G00228	9.06
				G00229	8.45
				G00230	8.47
				G00231	8.53
				G00232	8.40
				G00233	8.22
\bar{X}	2.22		4.27		8.44
s	0.01		0.12		0.33

(3) The diet admixtures for Study Week 2 were prepared using SC-19129 from Lot 840413. See Report of Analysis 84N1046 for the water content results.

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Table 10

Dosing Control Sample

SC-19129, g/kg

Study Week 4

Analysis Report #	84-2075
Dose	Dosing Control Sample
Sample #	
G00401	Less than 0.1
G00402	Less than 0.1
G00403	Less than 0.1

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Table 11

Study Week 4

Female Dose Group

SC-19129, g/kg

Analysis Report #	84-2076		84-2078		84-2080
Dose	Low		Medium		High
Sample #		Sample #		Sample #	
G00404	2.46	G00416	4.99	G00422	10.1
G00405	2.83	G00417	4.94	G00423	11.5
G00406	2.53	G00418	5.30	G00424	10.2
G00407	2.53				
G00408	2.58				
G00409	2.47				
G00410	2.48				
G00411	2.48				
G00412	2.53				
\bar{X}	2.54		5.08		10.6
s	0.11		0.20		0.8

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Table 12

Study Week 4

Male Dose Group

SC-19129, g/kg

Analysis Report #	84-2077		84-2079		84-2081
Dose	Low		Medium		High
Sample #		Sample #		Sample #	
G00413	2.86	G00419	6.75	G00425	12.4
G00414	3.02	G00420	5.72	G00426	12.7
G00415	3.05	G00421	5.69	G00427	11.5
				G00428	13.4
				G00429	12.1
				G00430	12.1
				G00431	12.4
				G00432	11.5
				G00433	11.9
\bar{X}	2.98		6.05		12.2
s	0.10		0.60		0.6

References:

1. Ryan, Jr., T. A., Joiner, B. L., and Ryan, B. F., "MINITAB Student Handbook", 1976, Wadsworth Publishing Co., Inc.
2. Natrella, M. G., "Experimental Statistics, National Bureau of Standards Handbook 91", 1963, US Government Printing Office
3. Filliben, J., Technometrics, 17 (1), 111 (1975)

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GLP Compliance Statement

To the best of our knowledge, the support activities provided by the Product Development Analytical Department for this study were conducted in compliance with the Good Laboratory Practices Regulations, as set forth in part 58, 21 CFR.