

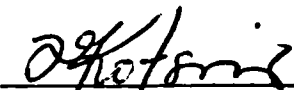
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129
IN THE DOG

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Safety Assessment Project Number 2449

Department of Product Safety Assessment


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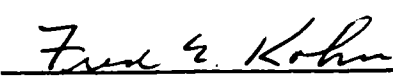
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DEPARTMENT OF PRODUCT SAFETY ASSESSMENT

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

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

Author(s): James L. Allen, Curtis D. Port, and Robin C. Guy

Study No.: S.A. 2449

Date: February 4, 1985

Type of Report: Final

Summary:

SC-19129 was administered by dietary admix for four weeks to Beagle dogs (3/sex/dosage group) at intended dosages of 0, 250, 500, and 1000 mg/kg. The actual dosages based on body weight and average weekly consumption were generally 70-95% of the intended low dosage, 61-91% of the intended medium dosage, and 84-99% of the intended high dosage.

None of the animals died. There were no meaningful treatment-related clinical signs or changes in body weights, feed consumption, water consumption, rectal temperatures, clinical laboratory determinations, electrocardiograms, or ophthalmic examinations.

There were no treatment related gross or microscopic findings. No significant differences were found in organ weights or organ to body weight ratios of treated versus control animals.

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

INTRODUCTION

SC-19129 was administered by dietary admix for four weeks to Beagle dogs (3/sex/dosage group) at intended dosages of 0, 250, 500, and 1000 mg/kg. Control animals received untreated diet. The purpose of this study was to determine toxic effects as evidenced by clinical signs and organ damage and to provide a basis for selecting dosages for longer studies.

MATERIALS AND METHODS

Materials

The chemical name of SC-19129 is N-L- β -aspartyl-L-phenylalanine, 1-methyl ester.

The test article was administered in the diet at concentrations of 0, 1.25, 2.5, and 5%. The identity, strength, purity, and composition of SC-19129 (lot number 84K-047-101 (840413)) were determined. Samples were taken to determine the stability of neat chemical and the stability, homogeneity, and concentration of test article in carrier. These samples were frozen and will be analyzed at a future date. The results of these analyses will be provided as a separate report by the Product Development Analytical Department. A summary of the analytical data is in Appendix J.

The test article was stored in well-closed, light-resistant containers at controlled room temperature. The test article diet admixtures were stored in plastic bags in plastic containers at controlled room temperature during the course of the study.

SC-19129 was mixed with Purina Certified Canine Meal 5007. Premix concentrates were first prepared using a Turbula mixer and the final concentrations prepared with a Patterson-Kelly cross-flow blender. Diet admixtures were used within 1 week of preparation.

The amount of diet provided to each animal was based on individual body weights determined on the day prior to the start of the respective dosing week. The appropriate amount of test article or control diet (20 g/kg body weight) was provided to each animal for two hours in the morning. The animals then received approximately 200-300g of untreated diet for one hour. The actual dosages based on body weight and average weekly feed consumption were generally 70-95% of the intended low dosage, 61-91% of the intended medium dosage, and 84-99% of the intended high dosage. The actual dosages are presented in Table 5 and Appendix D.

Animals, housing, and feed

Twenty-four (12/sex) Beagle dogs (Hazleton Research Laboratories, Inc., Cumberland, VA), approximately 7-8 months of age and weighing 7-14 kg, were used. To ensure that healthy animals were selected, animals were screened within the 3 weeks before chemical administration.

Pretreatment data (PT) included body weights, physical examination findings (including rectal temperatures), electrocardiograms, urinalysis, hematological, and serum clinicochemical determinations.

During the dosing period, the animals were housed individually in stainless steel cages in a temperature ($72^{\circ}\text{F} \pm 5^{\circ}\text{F}$) and humidity (25% or greater) controlled room maintained on a 12-hour light, 12-hour dark cycle. Each animal was identified by an ear tattoo applied by the supplier and a tag with a unique identification number attached to a collar. Purina Certified Canine Meal 5007 (Purina Lab Chows, St. Louis, MO) was provided to all animals. The feeding period was approximately 3 hours each day. Tap water from the municipal water supply was available ad libitum. Special analyses of food and water were not performed since no contaminants known to be capable of interfering with this study were reasonably expected to be present.

Experimental design

<u>Group</u>	<u>Intended Dosage (mg/kg)</u>	<u>Animals/Sex</u>	<u>Sacrifice Animals/Day</u>
1	0	3	3
2	250	3	3
3	500	3	3
4	1000	3	3

To distribute animals of each sex to dosage groups, the 12 animals were ranked by body weight. The ranked list was divided into 3 blocks of 4 animals and one animal

was randomly selected from each block and assigned to the first group. The same procedure was followed for the remaining 3 groups. The randomization achieved was evaluated by testing the significance of intergroup differences for each quantitative clinicochemical and hematological variable (except immature neutrophil, basophil, eosinophil, and monocyte percentages) and for urinary refractivity. Balance among the groups was achieved in 22 iterations for males and four iterations for females. The 4 groups were then assigned to dosage groups using a random number table. Permanent identification numbers were assigned to animals within each group according to the order which appeared on the randomization print out. During week 4, animals were randomly assigned to either the day 29 or 30 sacrifice.

Dosing began on October 18, 1984 and concluded on November 15, 1984. The sacrifices were on November 15 and 16, 1984. A copy of the protocol and amendments is Appendix L.

Clinical observations and physical, electrocardio-graphic, ophthalmic examinations, water consumption, and urine volume

Each animal was observed before and after feeding on weekdays and before feeding on weekends.

Physical examinations were performed before feeding on day 1 and after feeding on days 12 and 28. The physical examination consisted of the measurement of rectal temperature, observation of gait and general demeanor, palpation of the head, thorax, and abdomen, examination of

eyes, ears, and body orifices, and testing of the following reflexes: pupillary, patellar, front and rear hopping, and righting.

Body weights were determined on days 7, 14, 21, 29 and 30.

Food consumption was determined daily beginning within 3 weeks before initiation of dosing.

Electrocardiographic examinations (Leads II, aVL, V₁₀) on restrained prone animals were recorded before feeding on day 1, and after feeding on days 12 and 28.

Ophthalmic examinations were performed on day 26. The direct and consensual pupillary light response was evaluated. The eyelids, membrana nictitans, conjunctiva, cornea, and iris were examined with the focal light source and 2.5X magnification. The pupils were then dilated with Mydriacyl (Alcon Laboratories, Inc., Fort Worth, TX). The adnexa, cornea, anterior chamber, and lens were examined under reduced illumination by biomicroscopy. The fundus was also evaluated.

Water consumption and urine volume were determined for approximate 24 hour periods during week 4.

Clinical laboratory determinations

Venous blood was collected before feeding on day 1 and after feeding on days 12, 15, and 28. All animals had slightly elevated urea and bilirubin concentrations on

day 12. To confirm this finding, the day 12 serum was reanalyzed and samples were collected on day 15 to analyze for urea and bilirubin concentrations. Samples were collected in evacuated tubes containing EDTA and evacuated tubes containing citrate for hematological determinations and in plain evacuated tubes for clinicochemical determinations. The following hematological parameters were determined: white blood cell count, red blood cell count, hemoglobin concentration, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count, activated partial thromboplastin time, and prothrombin time. A differential smear evaluation also was done.

The following serum clinicochemical parameters were determined: alanine aminotransferase activity, aspartate aminotransferase activity, urea concentration, creatinine concentration, glucose concentration, alkaline phosphatase activity, cholesterol concentration, total bilirubin concentration, sodium concentration, potassium concentration, chloride concentration, calcium concentration, total protein concentration, albumin (A) concentration, globulin (G) concentration (calculated), and A/G ratio (calculated).

Urine was collected during weeks 2 and 4. The following urinary parameters were determined: pH, refractive index, glucose, bilirubin, protein, ketones, occult blood, and urobilinogen. Microscopic examination of the centrifuged sediment was also done.

Smears of bone marrow collected at necropsy were prepared but not examined.

Test article bioavailability

Venous blood samples (approximately 7 ml) were collected in evacuated tubes containing heparin from each animal before feeding on day 1, and 2, 4, 6, and 24 hours after the initiation of the feeding period on days 1, 15, and 28. Blood samples were centrifuged and plasma samples were frozen for future determination of SC-19129 concentrations. The results of these analyses will be provided as a separate report by the Department of Drug Metabolism.

Postmortem procedures

The dogs were killed by an overdose of sodium pentobarbital and examined immediately. The following organs were weighed in their fresh state: adrenal, brain, epididymis, heart, kidney, liver, ovary, pituitary gland, prostate, salivary gland, stomach (although not specified in the protocol), testis, thymus, thyroid, and uterus. Representative samples of the following organs and tissues were taken for microscopic examination: adrenal, aorta, bone, sternum, brain, epididymis, esophagus, eye, gallbladder, heart, duodenum, jejunum, ileum, cecum, colon, rectum, kidney, larynx, liver, lung, lymph node, mammary gland (females only), ovary, pancreas, peripheral nerve, pituitary gland, prostate, salivary gland, skeletal muscle, skin, spinal cord, spleen, stomach, testis, thymus, thyroid gland, parathyroid (only if included in the section of thyroid), tongue, trachea, urinary bladder, uterus, and vagina. Costal bone marrow was taken from each dog and submitted to hematology for preparation of a smear and

microscopic examination, if necessary. The testes were fixed in Bouin's solution and the eyes in Zenker's solution. All other tissues were fixed in Carson's solution (buffered 10% formalin). Any gross lesion that required microscopic examination was also placed in fixative.

After fixation, the tissues were embedded in paraffin, sectioned and stained with hematoxylin and eosin. Tissues of all dogs from all dosage groups were examined microscopically.

Statistical procedures

Means and standard deviations were calculated for all quantitative variables for each sex and for pooled sexes except those involving body weights, feed consumption, and organ weights. Analyses of these variables were done separately for each sex. Body weight, body weight change, water consumption, urine volume, clinicochemical, hematological (except immature neutrophil, monocyte, basophil, and eosinophil percentages), urinary refractivity, rectal temperature, organ weight, organ/body weight ratio, and organ/brain weight ratio data were analyzed by one-way analysis of variance (Winer, 1971) at each observation period. If the F-test among all groups was significant ($p < 0.05$), two-tailed t-tests of each SC-19129-treated group versus the control group were done using the pooled error term from the one-way analysis of variance. If the F-test among all groups was not significant at the 5% level, the t-tests were not done. A homogeneity-of-variance test using the Bartlett-Box method (Box, 1949) was done on all variables mentioned above. Significances of the various tests are indicated in the tables.

Data storage

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

Quality assurance

The Quality Assurance Statement is in Appendix M.

Professionals

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

Study Director/ Study Toxicologist	J. Allen
Study Pathologist	C. Port
Study Supervisor	R. Guy
Analytical Coordinator	K. Pilipauskas
Clinical Chemistry	J. North
Clinical Hematology	R. Leonard
Data Assessment	G. Kirby
Department of Drug Metabolism	E. Burton
Histology	P. Hemmer
Laboratory Animal Resources	J. Erickson
Ophthalmic Examinations	D. Vestre
Product Development Analytical Department	J. Jiu
Study Statistician	P. Sanders

RESULTS AND DISCUSSION

Quality and integrity of the data

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

Mortality and clinical observations

None of the animals died during the study.

Soft/watery stool was observed in all groups however, the incidence appeared to be slightly higher in the high dose group during weeks 3 and 4. The incidence of soft/watery stool at the high dosage is not unusual for laboratory Beagles. Other observations seen during the study were convulsions in a control animal on day 1, swollen vulva with a red discharge, emesis, and injected sclerae. These signs were of the type commonly seen in laboratory Beagles or occurred in a few instances with no particular pattern.

Body weights and feed and water consumption

Mean values for body weights, body weight changes, food consumption, and water consumption are in Tables 1, 2, 3, and 4, respectively. Individual values are in Appendix A, B, and C.

There were no meaningful changes in body weights or feed and water consumption.

Rectal temperatures

Mean values for rectal temperatures are in Table 6 and individual values are in Appendix E.

There were no meaningful changes in rectal temperatures.

Clinical laboratory determinations

Mean values for clinical chemistry, hematology and urinalysis are in Tables 7, 8, and 9, respectively. Individual values are in Appendices F, G, and H.

There were increases in urea, total bilirubin concentrations, and globulin compared to pretreatment values in all groups. These changes may have been the result of the time of blood collection relative to feeding. That is, during pretreatment and on day 1 prior to SC-19129 administration, blood was collected from overnight fasted animals, while on days 12, 15 and 28 blood was collected after feeding. Other changes in clinical laboratory values were incidental and generally within the range of normal physiologic variation.

Electrocardiographic examinations

There were no meaningful electrocardiographic changes.

Ophthalmic examinations

The ophthalmic examination report is in Appendix I.

There were no compound related changes seen during the ophthalmic examination.

Pathology

The incidence of microscopic findings is in Table 11. Individual animal findings are presented in Appendix K.

The only findings at necropsy were an abscess of the epididymis (84-2002) and petechial hemorrhage of the colon (84-2013). Dilated ventricles, annotated as hydrocephalus, were present when the brain of one dog was trimmed (84-2017). These were considered incidental and unimportant.

Microscopically the main findings were congenital tubular hypoplasia in two high dosage males and testicular germinal epithelial degeneration, considered to be due to immaturity, in one control dog. Various degrees of testicular immaturity were present in all the males. Because of the changes that are commonly seen in the testes of immature animals, identification and evaluation for possible chemical effects becomes difficult. The abscess of the epididymis was diagnosed as a sperm granuloma. The petechial hemorrhage in the colon was not confirmed microscopically, but this is not unexpected. Other microscopic findings, including valvular endocardiosis, cysts in the pituitary, thymus, thyroid, and parathyroid, as well as mineralization of the kidney medulla are known spontaneous conditions in dogs and are considered incidental and unimportant. Thus, there were no treatment related findings.

Organ weight and organ to body weight ratios

Mean organ weights and ratios are in Table 12. Individual organ weights and ratios are in Appendix K, Tables 1 and 2.

No significant differences were found in organ weights or ratios between control and compound treated animals.

REFERENCES

Box, G.E.P. (1949). A general distribution theory for a class of likelihood criteria, Biometrika, 36, pp. 317-346.

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

TABLE 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE BODY WEIGHTS (kg)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	PT	-1	7	14	21	29-30
CONTROL	11.3	11.1	11.0	11.0	11.3	11.3	11.3
0 mg/kg	2.15	2.05	2.12	2.13	2.11	2.10	2.00
	3	3	3	3	3	3	3
LOW DOSE	11.7	11.6	11.2	11.2	11.4	11.4	11.3
250 mg/kg	1.27	1.36	1.25	1.30	1.18	1.24	1.23
	3	3	3	3	3	3	3
MEDIUM DOSE	11.6	11.5	11.3	11.3	11.3	11.5	11.5
500 mg/kg	1.31	1.32	1.25	1.33	1.27	1.51	1.26
	3	3	3	3	3	3	3
HIGH DOSE	10.6	10.5	10.5	10.4	10.6	10.8	10.8
1000 mg/kg	2.10	2.05	2.00	2.01	2.10	2.31	2.20
	3	3	3	3	3	3	3

PT : PRETREATMENT

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 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

FEMALE BODY WEIGHTS (kg)							
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES							
STUDY DAY	PT	PT	-1	7	14	21	29-30
CONTROL	9.4	9.4	9.4	9.4	9.7	9.7	9.7
0 mg/kg	0.67	0.79	0.70	0.76	0.64	0.72	0.83
	3	3	3	3	3	3	3
LOW DOSE	10.0	9.7	9.6	9.4	9.7	9.7	9.7
250 mg/kg	0.91	0.95	1.04	1.04	0.99	1.42	1.14
	3	3	3	3	3	3	3
MEDIUM DOSE	9.4	9.2	9.0	8.9	9.0	8.9	8.7
500 mg/kg	1.23	1.17	1.26	1.26	1.31	1.15	1.06
	3	3	3	3	3	3	3
HIGH DOSE	9.8	9.6	9.5	9.4	9.4	9.5	9.4
1000 mg/kg	0.67	0.61	0.51	0.47	0.40	0.31	0.21
	3	3	3	3	3	3	3

PT : PRETREATMENT

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 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE BODY WEIGHT CHANGE (kg) FROM PRECEDING PERIOD
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-1	7	14	21	29-30
CONTROL	-0.1	0.0	0.3	0.0	-0.1
0 mg/kg	0.21	0.06	0.17	0.06	0.12
	3	3	3	3	3
LOW DOSE	-0.3	0.0	0.2	0.1	-0.2
250 mg/kg	0.15	0.12	0.12	0.06	0.31
	3	3	3	3	3
MEDIUM DOSE	-0.2	-0.1	0.1	0.2	0.0
500 mg/kg	0.12	0.25	0.15	0.38	0.25
	3	3	3	3	3
HIGH DOSE	0.0	-0.1	0.2	0.2	0.0
1000 mg/kg	0.10	0.06	0.15	0.23	0.12
	3	3	3	3	3

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 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE BODY WEIGHT CHANGE (kg) FROM PRECEDING PERIOD
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-1	7	14	21	29-30
CONTROL	0.0	0.0 Y	0.3 F	0.0	0.0
0 mg/kg	0.10	0.15	0.17	0.12	0.12
	3	3	3	3	3
LOW DOSE	-0.1	-0.2	0.3	0.0	0.0
250 mg/kg	0.15	0.10	0.12	0.46	0.35
	3	3	3	3	3
MEDIUM DOSE	-0.2	-0.1	0.0 *	-0.1	-0.2
500 mg/kg	0.30	0.00	0.06	0.17	0.20
	3	3	3	3	3
HIGH DOSE	-0.2	0.0	0.0 *	0.1	-0.1
1000 mg/kg	0.25	0.06	0.10	0.26	0.10
	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-16	-15	-14	-13	-12	-11	-10	-9
CONTROL	156.	192.	233.	258.	258.	259.	295.	326.
0 mg/kg	59.2 3	54.7 3	61.2 3	20.0 3	78.9 3	53.9 3	45.0 3	40.2 3
LOW DOSE	207.	204.	238.	269.	206.	257.	292.	267.
250 mg/kg	70.1 3	69.0 3	24.1 3	31.8 3	33.5 3	74.5 3	26.9 3	35.3 3
MEDIUM DOSE	208.	207.	303.	235.	228.	279.	301.	277.
500 mg/kg	71.8 3	51.3 3	71.0 3	38.6 3	25.4 3	114.4 3	7.2 3	28.7 3
HIGH DOSE	244.	260.	239.	316.	221.	281.	314.	295.
1000 mg/kg	84.1 3	81.4 3	46.0 3	103.2 3	33.2 3	110.3 3	22.3 3	39.3 3

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
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	-8	-7	-6	-5	-4	-3	-2	-1
CONTROL	255.	334.	259.	241.	256.	310.	271.	262.
0 mg/kg	71.5	62.5	39.2	25.9	51.5	74.2	69.7	38.7
	3	3	3	3	3	3	3	3
LOW DOSE	245.	283.	154.	219.	186.	288.	211.	209.
250 mg/kg	31.8	73.4	48.3	41.3	29.9	20.1	28.8	48.0
	3	3	3	3	3	3	3	3
MEDIUM DOSE	171.	325.	178.	228.	202.	247.	211.	189.
500 mg/kg	65.6	30.9	48.0	29.3	38.0	54.3	30.4	34.5
	3	3	3	3	3	3	3	3
HIGH DOSE	291.	330.	235.	164.	248.	362.	292.	225.
1000 mg/kg	56.9	63.5	89.1	51.5	34.0	35.5	159.6	36.8
	3	3	2	3	3	3	3	2

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	1	2	3	4	5	6	7
CONTROL	305.	348.	249.	282.	363.	286.	287.
0 mg/kg	51.9	72.1	16.5	79.9	78.9	34.1	33.8
	3	3	3	3	3	3	3
LOW DOSE	255.	312.	238.	270.	325.	297.	270.
250 mg/kg	53.1	67.4	32.9	32.6	27.8	47.4	35.8
	3	3	3	3	3	3	3
MEDIUM DOSE	251.	240.	205.	255.	359.	210.	241.
500 mg/kg	124.4	4.2	38.0	34.9	120.4	33.0	39.6
	3	2	3	3	3	3	3
HIGH DOSE	344.	274.	230.	281.	261.	247.	386.
1000 mg/kg	83.4	23.5	78.0	112.1	87.7	65.1	143.8
	2	3	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	8	9	10	11	12	13	14
CONTROL	305. F	372.	326.	311.	355.	353.	323.
0 mg/kg	37.6	60.8	52.7	51.1	71.3	74.7	55.3
	3	3	3	3	3	3	3
LOW DOSE	332.	390.	309.	299.	285.	318.	316.
250 mg/kg	8.4	118.1	62.2	29.3	35.2	41.9	37.8
	3	3	3	3	3	3	3
MEDIUM DOSE	224. *	373.	229.	380.	268.	249.	315.
500 mg/kg	28.2	52.0	74.4	98.5	55.0	94.7	46.5
	3	3	3	3	3	3	3
HIGH DOSE	265.	388.	269.	420.	244.	292.	319.
1000 mg/kg	50.5	145.3	36.6	86.0	53.1	40.0	103.0
	3	3	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	15	16	17	18	19	20	21
CONTROL	250.	330.	284.	376.	401. B	318.	375.
0 mg/kg	46.2	32.7	21.5	60.7	147.6	66.5	105.1
	3	3	3	3	3	3	3
LOW DOSE	250.	275.	182.	350.	363.	298.	239.
250 mg/kg	35.3	37.1	65.4	78.6	34.7	51.2	106.5
	3	3	3	3	3	3	3
MEDIUM DOSE	211.	230.	213.	342.	401.	297.	317.
500 mg/kg	28.7	59.7	39.0	57.2	135.0	143.2	122.4
	3	3	3	3	3	3	3
HIGH DOSE	239.	270.	258.	351.	314.	342.	350.
1000 mg/kg	27.7	25.2	49.1	72.0	14.6	120.7	87.9
	3	3	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	22	23	24	25	26	27	28	29
CONTROL	324. B	311.	263.	263.	345.	337.	243.	281. Y
0 mg/kg	44.5	39.7	50.6	76.2	13.3	86.9	24.6	41.0
	3	3	3	3	3	3	3	2
LOW DOSE	375.	363.	254.	325.	305.	354.	206.	325.
250 mg/kg	28.4	51.3	56.5	38.1	44.6	47.0	48.7	
	3	3	3	3	3	3	3	1
MEDIUM DOSE	289.	406.	237.	293.	413.	295.	207.	307.
500 mg/kg	117.5	88.5	76.6	9.2	101.0	8.2	41.3	130.1
	3	3	3	3	3	3	3	2
HIGH DOSE	355.	320.	249.	301.	329.	357.	231.	304.
1000 mg/kg	10.1	46.7	44.1	66.0	38.8	86.0	29.0	
	3	3	3	3	3	3	3	1

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	-16	-15	-14	-13	-12	-11	-10	-9
CONTROL	186.	184.	206.	251.	219.	271. F	275.	244.
0 mg/kg	56.4	54.3	33.6	51.6	24.0	11.5	56.0	66.8
	3	3	3	3	3	3	3	3
LOW DOSE	132.	154.	167.	176.	169.	231.	247.	195.
250 mg/kg	97.9	16.2	55.0	78.4	7.6	30.7	32.3	67.6
	3	3	3	3	3	3	3	3
MEDIUM DOSE	124.	179.	137.	167.	169.	197. **	226.	213.
500 mg/kg	26.3	43.3	120.8	37.8	48.9	30.7	32.7	35.0
	3	3	3	3	3	3	3	3
HIGH DOSE	185.	225.	188.	234.	246.	231.	282.	250.
1000 mg/kg	33.9	49.2	12.0	54.0	63.7	16.6	26.2	20.2
	3	3	2	3	3	3	2	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	-8	-7	-6	-5	-4	-3	-2	-1
CONTROL	229.	280. FB	193.	224.	220.	278. B	279.	264. F
0 mg/kg	25.5	21.1	37.2	51.7	27.5	72.6	39.5	12.5
	3	3	3	3	3	3	3	3
LOW DOSE	148.	214. *	148.	132.	128.	207.	239.	177. *
250 mg/kg	81.9	21.8	66.7	55.6	56.5	24.3	95.8	26.4
	3	3	3	3	3	3	3	3
MEDIUM DOSE	190.	195. *	178.	136.	181.	216.	189.	147. **
500 mg/kg	76.2	2.1	12.1	44.2	47.8	7.5	59.9	52.5
	3	3	3	3	3	3	3	3
HIGH DOSE	253.	287.	197.	157.	124.	246.	246.	168. **
1000 mg/kg	54.0	57.6	29.5	42.6	31.9	109.2	67.5	27.8
	3	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
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* : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 5% LEVEL
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	1	2	3	4	5	6	7
CONTROL	271.	331.	227.	243.	310.	251.	284.
0 mg/kg	65.7	85.8	33.1	20.5	34.3	93.2	55.4
	3	3	3	3	3	3	3
LOW DOSE	271.	209.	191.	219.	264.	206.	305.
250 mg/kg	144.4	132.1	103.6	90.2	99.5	24.0	51.1
	3	3	3	3	3	3	3
MEDIUM DOSE	161.	249.	199.	157.	249.	220.	239.
500 mg/kg	25.6	75.3	15.0	40.9	56.3	77.7	58.9
	3	3	3	3	3	3	3
HIGH DOSE	289.	301.	204.	275.	280.	313.	295.
1000 mg/kg	60.7	42.9	27.0	35.6	82.7	94.0	52.0
	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE TEST SIGNIFICANT AT THE 5% LEVEL
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	8	9	10	11	12	13	14
CONTROL	336.	359.	279.	307.	291. F	298.	316.
0 mg/kg	87.0	60.3	24.9	15.3	48.6	18.7	51.2
	3	3	3	3	3	3	3
LOW DOSE	233.	324.	275.	312.	245.	243.	240.
250 mg/kg	49.1	78.8	107.7	63.2	33.6	44.4	97.9
	3	3	3	3	3	3	3
MEDIUM DOSE	193.	265.	221.	302.	205. **	204.	212.
500 mg/kg	66.6	84.9	56.3	20.3	11.4	24.1	41.7
	3	3	3	3	3	3	3
HIGH DOSE	258.	324.	257.	346.	268.	265.	222.
1000 mg/kg	10.4	37.8	58.4	34.4	15.6	70.2	28.4
	3	3	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	15	16	17	18	19	20	21
CONTROL	230.	272.	206.	303.	310.	321.	325.
0 mg/kg	67.9	57.3	30.5	40.5	68.6	25.2	58.0
	3	3	3	3	3	3	3
LOW DOSE	215.	216.	154.	316.	337.	255.	270.
250 mg/kg	77.1	43.2	58.8	74.2	77.6	101.0	74.5
	3	3	3	3	3	3	3
MEDIUM DOSE	206.	197.	165.	262.	270.	223.	162.
500 mg/kg	63.4	41.6	54.5	32.1	32.8	41.1	149.0
	3	3	3	3	3	3	3
HIGH DOSE	230.	272.	253.	258.	284.	341.	237.
1000 mg/kg	38.2	46.8	84.3	83.1	82.9	101.0	50.1
	3	3	3	3	3	3	3

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 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE FEED CONSUMPTION (g)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZE

STUDY DAY	22	23	24	25	26	27	28	29
CONTROL	291.	335.	189.	275. F	345.	226.	202. FB	203. Y
0 mg/kg	26.5	75.0	55.3	35.7	34.4	92.0	10.4	
	3	3	3	3	3	3	3	1
LOW DOSE	278.	302.	238.	248.	326.	282.	145.	229.
250 mg/kg	42.3	83.5	23.0	32.6	52.5	34.7	62.1	15.6
	3	3	3	3	3	3	3	2
MEDIUM DOSE	225.	318.	173.	168. **	290.	274.	134. *	195.
500 mg/kg	53.4	45.9	49.6	29.5	49.0	30.6	7.0	
	3	3	3	3	3	3	3	1
HIGH DOSE	332.	256.	197.	306.	351.	355.	221.	216.
1000 mg/kg	48.8	87.7	7.9	37.9	56.0	43.8	24.6	29.7
	3	2	3	3	3	3	3	2

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 4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE WATER CONSUMPTION (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	1050. B
0 mg/kg	360.6 3
LOW DOSE	1250.
250 mg/kg	50.0 3
MEDIUM DOSE	983.
500 mg/kg	225.5 3
HIGH DOSE	2150.
1000 mg/kg	1228.8 3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE WATER CONSUMPTION (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	1367.
0 mg/kg	480.5
	3
LOW DOSE	717.
250 mg/kg	76.4
	3
MEDIUM DOSE	533.
500 mg/kg	404.1
	3
HIGH DOSE	1217.
1000 mg/kg	732.0
	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
POOLED WATER CONSUMPTION (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	1208. B
0 mg/kg	417.6 6
LOW DOSE	983.
250 mg/kg	297.8 6
MEDIUM DOSE	758.
500 mg/kg	382.6 6
HIGH DOSE	1683.
1000 mg/kg	1039.1 6

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129
IN THE DOG

Dosage (mg/kg)				
Arithmetic Means and Percent of Intended Dose				
Study Week	1	2	3	4
Males				
Low Dose	232	237	211	210
% Intended Dose	92.9	94.8	84.3	83.9
Medium Dose	440	454	434	396
% Intended Dose	88.0	90.8	86.8	79.2
High Dose	840	952	910	938
% Intended Dose	84.0	95.2	91.0	93.8
Females				
Low Dose	205	214	199	177
% Intended Dose	82.1	85.7	79.5	70.7
Medium Dose	424	404	360	307
% Intended Dose	84.9	80.9	72.0	61.4
High Dose	986	989	980	893
% Intended Dose	98.6	98.9	98.0	89.3

TABLE 6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE RECTAL TEMPERATURES (DEGREES CENTIGRADE)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	38.6	38.7	39.0	38.6
0 mg/kg	0.55	0.52	0.29	0.06
	3	3	3	3
LOW DOSE	38.8	39.0	38.7	39.0
250 mg/kg	0.35	0.06	0.21	0.23
	3	3	3	3
MEDIUM DOSE	38.8	39.4	38.8	38.8
500 mg/kg	0.25	0.47	0.29	0.35
	3	3	3	3
HIGH DOSE	38.4	38.8	38.9	38.9
1000 mg/kg	0.55	0.23	0.29	0.10
	3	3	3	3

PT : PRETREATMENT

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE RECTAL TEMPERATURES (DEGREES CENTIGRADE)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	38.6 Y	39.0	38.5	39.0
0 mg/kg	0.51	0.26	0.49	0.15
	3	3	3	3
LOW DOSE	39.0	39.1	38.8	38.7
250 mg/kg	0.00	0.21	0.21	0.15
	3	3	3	3
MEDIUM DOSE	38.8	38.9	38.7	38.7
500 mg/kg	0.26	0.17	0.15	0.65
	3	3	3	3
HIGH DOSE	39.0	38.9	38.6	38.8
1000 mg/kg	0.00	0.17	0.06	0.40
	3	3	3	3

PT : PRETREATMENT

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
POOLED RECTAL TEMPERATURES (DEGREES CENTIGRADE)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	38.6	38.8	38.7	38.8
0 mg/kg	0.48	0.40	0.45	0.24
	6	6	6	6
LOW DOSE	38.9	39.0	38.8	38.8
250 mg/kg	0.24	0.15	0.19	0.22
	6	6	6	6
MEDIUM DOSE	38.8	39.1	38.7	38.7
500 mg/kg	0.23	0.41	0.21	0.47
	6	6	6	6
HIGH DOSE	38.7	38.8	38.8	38.9
1000 mg/kg	0.49	0.20	0.23	0.27
	6	6	6	6

PT : PRETREATMENT

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 7.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE ALANINE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	31.	29.	30.	29.
0 mg/kg	15.6	5.3	9.0	8.2
	3	3	3	3
LOW DOSE	23.	28.	25.	26.
250 mg/kg	3.1	8.1	4.2	6.0
	3	3	3	3
MEDIUM DOSE	27.	25.	26.	25.
500 mg/kg	5.2	6.7	6.1	6.4
	3	3	3	3
HIGH DOSE	23.	21.	21.	23.
1000 mg/kg	4.0	2.5	3.1	5.5
	3	3	3	3

PT : PRETREATMENT

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 7.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE ALANINE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	24.	28. F	28.	26.
0 mg/kg	4.5	2.6	8.4	8.5
	3	3	3	3
LOW DOSE	28.	32.	30.	32.
250 mg/kg	2.6	6.2	3.5	4.0
	3	3	3	3
MEDIUM DOSE	23.	19. *	22.	23.
500 mg/kg	3.2	2.9	4.7	7.6
	3	3	3	3
HIGH DOSE	30.	22.	25.	27.
1000 mg/kg	5.6	2.5	1.7	3.1
	3	3	3	3

PT : PRETREATMENT

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 7.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED ALANINE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	28.	29. F	29.	28.
0 mg/kg	10.9	3.8	7.8	7.7
	6	6	6	6
LOW DOSE	26.	30.	27.	29.
250 mg/kg	3.6	6.9	4.5	5.6
	6	6	6	6
MEDIUM DOSE	25.	22. *	24.	24.
500 mg/kg	4.4	5.9	5.4	6.3
	6	6	6	6
HIGH DOSE	26.	22. *	23.	25.
1000 mg/kg	5.9	2.3	3.3	4.5
	6	6	6	6

PT : PRETREATMENT

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 7.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE ASPARTATE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	21.	21.	21.	21. Y
0 mg/kg	5.3	2.5	4.9	5.1
	3	3	3	3
LOW DOSE	22.	24.	18.	20.
250 mg/kg	1.2	5.5	1.0	0.0
	3	3	3	3
MEDIUM DOSE	23.	18.	19.	19.
500 mg/kg	4.0	2.1	2.5	1.5
	3	3	3	3
HIGH DOSE	20.	19.	17.	19.
1000 mg/kg	1.5	3.2	1.5	2.3
	3	3	3	3

PT : PRETREATMENT

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 7.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE ASPARTATE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	20.	22.	21.	21.
0 mg/kg	4.5	3.2	6.1	5.5
	3	3	3	3
LOW DOSE	22.	27.	20.	23.
250 mg/kg	1.5	14.8	3.1	2.1
	3	3	3	3
MEDIUM DOSE	23.	17.	20.	20.
500 mg/kg	2.6	5.2	4.2	2.3
	3	3	3	3
HIGH DOSE	21.	21.	20.	21.
1000 mg/kg	3.2	2.0	1.0	0.6
	3	3	3	3

PT : PRETREATMENT

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 7.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED ASPARTATE AMINOTRANSFERASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	20.	22. B	21.	21.
0 mg/kg	4.5	2.7	5.0	4.8
	6	6	6	6
LOW DOSE	22.	25.	19.	21.
250 mg/kg	1.3	10.2	2.4	2.0
	6	6	6	6
MEDIUM DOSE	23.	18.	20.	20.
500 mg/kg	3.1	3.6	3.1	1.8
	6	6	6	6
HIGH DOSE	21.	20.	19.	20.
1000 mg/kg	2.4	2.7	1.9	1.9
	6	6	6	6

PT : PRETREATMENT

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 7.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE ALKALINE PHOSPHATASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	53.	42.	38.	38.
0 mg/kg	6.2	9.9	3.8	8.1
	3	3	3	3
LOW DOSE	47.	37.	36.	34.
250 mg/kg	11.9	5.1	6.6	5.6
	3	3	3	3
MEDIUM DOSE	58.	43.	43.	42.
500 mg/kg	9.6	4.4	5.1	3.0
	3	3	3	3
HIGH DOSE	40.	33.	32.	32.
1000 mg/kg	10.4	4.7	6.4	7.6
	3	3	3	3

PT : PRETREATMENT

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 7.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE ALKALINE PHOSPHATASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	53.	44.	49.	50.
0 mg/kg	10.7	11.6	18.6	19.0
	3	3	3	3
LOW DOSE	45.	38.	38.	40.
250 mg/kg	9.2	10.0	10.8	14.6
	3	3	3	3
MEDIUM DOSE	51.	38.	38.	37.
500 mg/kg	9.0	13.0	4.7	5.7
	3	3	3	3
HIGH DOSE	54.	45.	52.	53.
1000 mg/kg	9.5	13.1	17.9	19.1
	3	3	3	3

PT : PRETREATMENT

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 7.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED ALKALINE PHOSPHATASE (U/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	53.	43.	44.	44.
0 mg/kg	7.8 6	9.7 6	13.6 6	14.6 6
LOW DOSE	46.	37.	37.	37.
250 mg/kg	9.6 6	7.1 6	8.1 6	10.5 6
MEDIUM DOSE	54.	41.	41.	40.
500 mg/kg	9.3 6	9.1 6	5.0 6	4.8 6
HIGH DOSE	47.	39.	42.	42.
1000 mg/kg	11.8 6	11.0 6	16.3 6	17.5 6

PT : PRETREATMENT

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 7.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE CHOLESTEROL (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	3.5	3.2	3.2	3.8 B
0 mg/kg	0.68	0.76	0.30	0.57
	3	3	3	3
LOW DOSE	3.2	2.7	2.9	3.2
250 mg/kg	0.15	0.23	0.06	0.06
	3	3	3	3
MEDIUM DOSE	3.8	3.1	3.5	3.9
500 mg/kg	0.35	0.26	0.50	0.53
	3	3	3	3
HIGH DOSE	3.1	3.1	3.0	3.4
1000 mg/kg	0.10	0.40	0.31	0.10
	3	3	3	3

PT : PRETREATMENT

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 7.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE CHOLESTEROL (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	3.6	3.0	3.4	4.0
0 mg/kg	0.72	0.82	0.76	0.68
	3	3	3	3
LOW DOSE	3.3	3.0	2.8	3.4
250 mg/kg	0.70	0.95	0.75	0.82
	3	3	3	3
MEDIUM DOSE	3.0	2.6	2.9	3.5
500 mg/kg	0.71	0.26	0.69	1.05
	3	3	3	3
HIGH DOSE	3.5	2.9	3.3	3.8
1000 mg/kg	0.67	0.26	0.06	0.44
	3	3	3	3

PT : PRETREATMENT

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 7.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED CHOLESTEROL (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	3.5	3.1	3.3	3.9
0 mg/kg	0.63	0.72	0.53	0.57
	6	6	6	6
LOW DOSE	3.2	2.8	2.8	3.3
250 mg/kg	0.46	0.64	0.48	0.53
	6	6	6	6
MEDIUM DOSE	3.4	2.9	3.2	3.7
500 mg/kg	0.64	0.36	0.62	0.78
	6	6	6	6
HIGH DOSE	3.3	3.0	3.2	3.6
1000 mg/kg	0.49	0.32	0.28	0.36
	6	6	6	6

PT : PRETREATMENT

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 7.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE TOTAL BILIRUBIN (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12o	15	28
CONTROL	1.8	2.7	4.4	4.1	5.7	3.8
0 mg/kg	0.5	0.8	1.2	0.9	1.9	1.2
	3	3	3	3	3	3
LOW DOSE	2.3	2.6	5.0	3.7	4.2	3.5
250 mg/kg	0.7	0.4	1.0	0.8	1.1	1.1
	3	3	3	3	3	3
MEDIUM DOSE	2.2	2.7	4.7	4.7	4.9	4.2
500 mg/kg	0.3	1.1	2.1	2.0	1.9	1.0
	3	3	3	3	3	3
HIGH DOSE	2.4	2.4	5.4	5.4	4.6	4.7
1000 mg/kg	0.6	0.7	1.3	1.8	1.1	0.7
	3	3	3	3	3	3

PT : PRETREATMENT
o : REANALYSIS OF SERUM COLLECTED DAY 12

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 7.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE TOTAL BILIRUBIN (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12o	15	28
CONTROL	2.0	3.0	7.1	7.4	6.9	5.7
0 mg/kg	1.2	0.3	3.1	2.4	1.5	0.6
	3	3	3	3	3	3
LOW DOSE	1.8	2.7	6.0	5.7	5.0	4.6
250 mg/kg	1.3	1.1	2.1	1.6	0.8	0.6
	3	3	3	3	3	3
MEDIUM DOSE	3.2	2.3	6.6	6.1	5.5	5.3
500 mg/kg	1.0	0.5	1.7	2.3	3.5	1.3
	3	3	3	3	3	3
HIGH DOSE	2.8	2.4	5.1	4.7	5.0	5.0
1000 mg/kg	0.3	1.0	1.0	1.5	1.4	1.3
	3	3	3	3	3	3

PT : PRETREATMENT
o : REANALYSIS OF SERUM COLLECTED DAY 12

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 7.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED TOTAL BILIRUBIN (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12a	15	28
CONTROL	1.9	2.8	5.8	5.8	6.3	4.7
0 mg/kg	0.8	0.6	2.5	2.4	1.7	1.3
	6	6	6	6	6	6
LOW DOSE	2.1	2.7	5.5	4.7	4.6	4.1
250 mg/kg	1.0	0.7	1.6	1.5	0.9	1.0
	6	6	6	6	6	6
MEDIUM DOSE	2.7	2.5	5.7	5.4	5.2	4.8
500 mg/kg	0.9	0.8	2.0	2.1	2.5	1.2
	6	6	6	6	6	6
HIGH DOSE	2.6	2.4	5.2	5.0	4.8	4.9
1000 mg/kg	0.5	0.8	1.0	1.5	1.2	0.9
	6	6	6	6	6	6

PT : PRETREATMENT
a : REANALYSIS OF SERUM COLLECTED DAY 12

F : ONWAY 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 7.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE GLUCOSE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	5.9	6.5 B	4.8	4.8
0 mg/kg	0.20	2.66	1.25	0.46
	3	3	3	3
LOW DOSE	5.7	5.4	5.2	5.2
250 mg/kg	0.47	0.60	0.32	0.21
	3	3	3	3
MEDIUM DOSE	5.3	5.0	5.2	5.3
500 mg/kg	0.15	0.55	0.12	0.99
	3	3	3	3
HIGH DOSE	5.2	4.8	4.5	4.5
1000 mg/kg	0.50	0.36	0.55	0.49
	3	3	3	3

PT : PRETREATMENT

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 7.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE GLUCOSE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	5.4	5.3	4.8	4.9
0 mg/kg	0.76	0.40	0.25	0.75
	3	3	3	3
LOW DOSE	5.2	5.4	4.3	4.8
250 mg/kg	0.15	0.40	0.72	0.26
	3	3	3	3
MEDIUM DOSE	5.1	4.8	5.0	4.9
500 mg/kg	0.47	0.25	0.20	0.65
	3	3	3	3
HIGH DOSE	5.2	4.8	4.5	5.1
1000 mg/kg	0.64	0.35	0.45	0.40
	3	3	3	3

PT : PRETREATMENT

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 7.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED GLUCOSE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	5.6	5.9 B	4.8 B	4.8
0 mg/kg	0.58	1.82	0.81	0.56
	6	6	6	6
LOW DOSE	5.5	5.4	4.7	5.0
250 mg/kg	0.42	0.46	0.69	0.32
	6	6	6	6
MEDIUM DOSE	5.2	4.9	5.1	5.1
500 mg/kg	0.33	0.39	0.17	0.77
	6	6	6	6
HIGH DOSE	5.2	4.8	4.5	4.8
1000 mg/kg	0.52	0.32	0.45	0.50
	6	6	6	6

PT : PRETREATMENT

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 7.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE UREA (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12a	15	28
CONTROL	3.7	4.2	10.9 B	10.6	10.6	9.5
0 mg/kg	1.6	0.8	2.3	1.8	1.3	1.5
	3	3	3	3	3	3
LOW DOSE	3.0	3.8	8.9	8.8	9.8	8.2
250 mg/kg	0.2	0.4	0.6	0.4	0.6	0.8
	3	3	3	3	3	3
MEDIUM DOSE	3.4	3.6	9.6	9.5	9.7	8.5
500 mg/kg	0.8	0.3	0.2	0.3	0.8	0.7
	3	3	3	3	3	3
HIGH DOSE	3.4	3.7	9.8	9.7	9.6	8.6
1000 mg/kg	0.9	0.9	0.9	0.6	2.0	1.6
	3	3	3	3	3	3

PT : PRETREATMENT

o : REANALYSIS OF SERUM COLLECTED DAY 12

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 7.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE UREA (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12 ^a	15	28
CONTROL	3.3	3.9	9.6 Y	9.8	10.4	9.1
0 mg/kg	0.6	1.3	1.3	2.1	2.3	2.4
	3	3	3	3	3	3
LOW DOSE	3.7	3.3	9.4	9.4	9.0	7.9
250 mg/kg	1.0	0.5	0.9	0.7	1.1	1.8
	3	3	3	3	3	3
MEDIUM DOSE	3.0	3.6	9.1	8.8	9.2	8.3
500 mg/kg	0.5	0.5	0.0	0.3	1.6	0.3
	3	3	3	3	3	3
HIGH DOSE	3.1	3.6	9.3	9.5	9.7	9.2
1000 mg/kg	0.3	0.4	1.2	1.7	1.5	1.0
	3	3	3	3	3	3

PT : PRETREATMENT
^a : REANALYSIS OF SERUM COLLECTED DAY 12
 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 7.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED UREA (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	12a	15	28
CONTROL	3.5	4.1	10.3 B	10.2 B	10.5	9.3
0 mg/kg	1.1	1.0	1.8	1.8	1.7	1.8
	6	6	6	6	6	6
LOW DOSE	3.3	3.5	9.2	9.1	9.4	8.1
250 mg/kg	0.7	0.5	0.7	0.6	0.9	1.3
	6	6	6	6	6	6
MEDIUM DOSE	3.2	3.6	9.4	9.1	9.4	8.4
500 mg/kg	0.6	0.4	0.3	0.5	1.1	0.5
	6	6	6	6	6	6
HIGH DOSE	3.3	3.7	9.6	9.6	9.7	8.9
1000 mg/kg	0.6	0.6	1.0	1.1	1.6	1.2
	6	6	6	6	6	6

PT : PRETREATMENT
o : REANALYSIS OF SERUM COLLECTED DAY 12

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 7.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE CREATININE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	67.	70.	64.	64.
0 mg/kg	9.3	15.4	3.1	1.0
	3	3	3	3
LOW DOSE	62.	67.	63.	66.
250 mg/kg	4.9	8.3	3.8	6.5
	3	3	3	3
MEDIUM DOSE	66.	66.	58.	67.
500 mg/kg	5.9	10.0	13.1	4.7
	3	3	3	3
HIGH DOSE	68.	67.	62.	68.
1000 mg/kg	6.4	8.5	5.6	6.0
	3	3	3	3

PT : PRETREATMENT

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 7.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE CREATININE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	66.	66.	62.	66.
0 mg/kg	11.2	6.4	7.8	10.5
	3	3	3	3
LOW DOSE	70.	66.	63.	65.
250 mg/kg	10.5	13.3	11.9	10.5
	3	3	3	3
MEDIUM DOSE	70.	68.	62.	63.
500 mg/kg	11.6	11.5	7.6	6.7
	3	3	3	3
HIGH DOSE	58.	66.	64.	65.
1000 mg/kg	6.1	9.3	5.5	4.7
	3	3	3	3

PT : PRETREATMENT

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 7.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED CREATININE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	67.	68.	63.	65.
0 mg/kg	9.2	10.8	5.5	6.8
	6	6	6	6
LOW DOSE	66.	67.	63.	66.
250 mg/kg	8.5	10.0	7.9	7.8
	6	6	6	6
MEDIUM DOSE	68.	67.	60.	65.
500 mg/kg	8.5	9.7	9.8	5.8
	6	6	6	6
HIGH DOSE	63.	66.	63.	67.
1000 mg/kg	7.7	8.0	5.1	5.0
	6	6	6	6

PT : PRETREATMENT

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 7.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE SODIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	148.	148.	146. Y	147.
0 mg/kg	2.5	4.9	1.2	2.0
	3	3	3	3
LOW DOSE	148.	146.	144.	146.
250 mg/kg	2.9	1.5	1.5	2.0
	3	3	3	3
MEDIUM DOSE	148.	146.	145.	146.
500 mg/kg	1.2	3.0	0.0	5.5
	3	3	3	3
HIGH DOSE	148.	147.	145.	145.
1000 mg/kg	0.6	2.5	2.0	4.2
	3	3	3	3

PT : PRETREATMENT

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 7.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE SODIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	146.	147.	147.	147.
0 mg/kg	1.5	1.5	3.5	3.8
	3	3	3	3
LOW DOSE	146.	150.	148.	146.
250 mg/kg	1.0	4.2	2.5	1.5
	3	3	3	3
MEDIUM DOSE	146.	147.	147.	149.
500 mg/kg	2.1	1.7	0.6	3.5
	3	3	3	3
HIGH DOSE	146.	147.	147.	147.
1000 mg/kg	3.0	3.0	4.2	3.2
	3	3	3	3

PT : PRETREATMENT

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 7.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED SODIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	147.	148.	146.	147.
0 mg/kg	2.4	3.4	2.4	2.7
	6	6	6	6
LOW DOSE	147.	148.	146.	146.
250 mg/kg	2.1	3.8	2.9	1.6
	6	6	6	6
MEDIUM DOSE	147.	147.	146.	148.
500 mg/kg	1.7	2.3	1.0	4.4
	6	6	6	6
HIGH DOSE	147.	147.	146.	146.
1000 mg/kg	2.3	2.5	3.1	3.5
	6	6	6	6

PT : PRETREATMENT

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 7.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE POTASSIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	4.9	4.5	4.8	4.8
0 mg/kg	0.31	0.46	0.06	0.12
	3	3	3	3
LOW DOSE	4.9	4.5	4.7	4.6
250 mg/kg	0.53	0.29	0.35	0.06
	3	3	3	3
MEDIUM DOSE	4.7	4.5	5.0	4.8
500 mg/kg	0.21	0.23	0.15	0.30
	3	3	3	3
HIGH DOSE	4.7	4.6	5.3	4.9
1000 mg/kg	0.25	0.20	0.31	0.45
	3	3	3	3

PT : PRETREATMENT

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 7.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE POTASSIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	4.4	4.5	5.0	4.8
0 mg/kg	0.40	0.36	0.25	0.60
	3	3	3	3
LOW DOSE	4.3	5.0	4.7	4.5
250 mg/kg	0.10	1.23	0.12	0.10
	3	3	3	3
MEDIUM DOSE	4.9	4.5	4.9	5.0
500 mg/kg	0.65	0.26	0.12	0.12
	3	3	3	3
HIGH DOSE	4.4	4.5	4.7	4.6
1000 mg/kg	0.23	0.17	0.44	0.21
	3	3	3	3

PT : PRETREATMENT

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 7.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED POTASSIUM (nmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	4.6	4.5 B	4.9	4.8
0 mg/kg	0.41	0.37	0.20	0.39
	6	6	6	6
LOW DOSE	4.6	4.7	4.7	4.6
250 mg/kg	0.47	0.85	0.23	0.10
	6	6	6	6
MEDIUM DOSE	4.8	4.5	4.9	4.9
500 mg/kg	0.45	0.22	0.13	0.22
	6	6	6	6
HIGH DOSE	4.6	4.6	5.0	4.8
1000 mg/kg	0.29	0.18	0.46	0.35
	6	6	6	6

PT : PRETREATMENT

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 7.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE CHLORIDE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	115.	113.	111.	110.
0 mg/kg	1.5	1.5	0.6	1.5
	3	3	3	3
LOW DOSE	113.	111.	112.	110.
250 mg/kg	0.6	1.0	2.5	1.2
	3	3	3	3
MEDIUM DOSE	113.	112.	113.	112.
500 mg/kg	1.7	3.6	2.3	1.0
	3	3	3	3
HIGH DOSE	112.	111.	113.	111.
1000 mg/kg	1.0	3.1	2.1	1.5
	3	3	3	3

PT : PRETREATMENT

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 7.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE CHLORIDE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	111.	109. Y	112.	109.
0 mg/kg	1.0	0.0	2.1	0.6
	3	3	3	3
LOW DOSE	113.	112.	110.	109.
250 mg/kg	2.1	4.6	2.6	1.5
	3	3	3	3
MEDIUM DOSE	114.	114.	111.	113.
500 mg/kg	1.2	1.7	4.9	2.1
	3	3	3	3
HIGH DOSE	114.	112.	113.	109.
1000 mg/kg	1.5	3.5	3.5	4.5
	3	3	3	3

PT : PRETREATMENT

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 7.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED CHLORIDE (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	113.	111.	111.	110.
0 mg/kg	2.3 6	2.2 6	1.5 6	1.2 6
LOW DOSE	113.	111.	111.	110.
250 mg/kg	1.4 6	3.0 6	2.5 6	1.3 6
MEDIUM DOSE	113.	113.	112.	112.
500 mg/kg	1.4 6	2.8 6	3.7 6	1.5 6
HIGH DOSE	113.	112.	113.	110.
1000 mg/kg	1.5 6	3.0 6	2.6 6	3.2 6

PT : PRETREATMENT

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 7.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE CALCIUM (nmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	2.75	2.74 F	2.66	2.55
0 mg/kg	0.040	0.051	0.044	0.062
	3	3	3	3
LOW DOSE	2.76	2.56 **	2.62	2.53
250 mg/kg	0.064	0.084	0.029	0.055
	3	3	3	3
MEDIUM DOSE	2.75	2.56 **	2.63	2.57
500 mg/kg	0.020	0.051	0.080	0.075
	3	3	3	3
HIGH DOSE	2.72	2.62 *	2.63	2.51
1000 mg/kg	0.087	0.031	0.036	0.036
	3	3	3	3

PT : PRETREATMENT

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 7.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE CALCIUM (nmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	2.75	2.66 B	2.73	2.56 B
0 mg/kg	0.061	0.070	0.085	0.086
	3	3	3	3
LOW DOSE	2.73	2.76	2.70	2.61
250 mg/kg	0.056	0.206	0.084	0.065
	3	3	3	3
MEDIUM DOSE	2.72	2.57	2.62	2.48
500 mg/kg	0.086	0.098	0.051	0.148
	3	3	3	3
HIGH DOSE	2.79	2.67	2.67	2.57
1000 mg/kg	0.020	0.012	0.042	0.044
	3	3	3	3

PT : PRETREATMENT

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 7.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED CALCIUM (mmol/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	2.75	2.70 B	2.69	2.56
0 mg/kg	0.046	0.071	0.071	0.040
	6	6	6	6
LOW DOSE	2.75	2.66	2.66	2.57
250 mg/kg	0.056	0.178	0.071	0.072
	6	6	6	6
MEDIUM DOSE	2.73	2.57	2.63	2.52
500 mg/kg	0.059	0.070	0.061	0.117
	6	6	6	6
HIGH DOSE	2.76	2.64	2.65	2.54
1000 mg/kg	0.067	0.034	0.040	0.049
	6	6	6	6

PT : PRETREATMENT

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 7.13.
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE TOTAL PROTEIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	57.	63.	64.	65.
0 mg/kg	1.2	4.6	2.5	3.2
	3	3	3	3
LOW DOSE	62.	62.	68.	67.
250 mg/kg	4.7	3.6	4.9	5.8
	3	3	3	3
MEDIUM DOSE	58.	60.	67.	67.
500 mg/kg	3.6	0.6	4.6	2.1
	3	3	3	3
HIGH DOSE	58.	61.	66.	67.
1000 mg/kg	3.5	2.1	6.1	5.3
	3	3	3	3

PT : PRETREATMENT

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 7.13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE TOTAL PROTEIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	58.	59.	69.	67.
0 mg/kg	2.1	3.5	3.0	2.6
	3	3	3	3
LOW DOSE	57.	61.	67.	68.
250 mg/kg	3.5	3.1	1.0	2.1
	3	3	3	3
MEDIUM DOSE	58.	55.	64.	61.
500 mg/kg	1.0	5.0	2.9	1.5
	3	3	3	3
HIGH DOSE	57.	59.	66.	65.
1000 mg/kg	3.5	4.4	5.0	4.6
	3	3	3	3

PT : PRETREATMENT

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 7.13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED TOTAL PROTEIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	58.	61.	67.	66.
0 mg/kg	1.8	4.1	3.6	2.8
	6	6	6	6
LOW DOSE	60.	61.	68.	68.
250 mg/kg	4.4	3.1	3.3	3.9
	6	6	6	6
MEDIUM DOSE	58.	57.	66.	64.
500 mg/kg	2.4	4.2	3.7	3.7
	6	6	6	6
HIGH DOSE	57.	60.	66.	66.
1000 mg/kg	3.2	3.2	5.0	4.5
	6	6	6	6

PT : PRETREATMENT

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 7.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE ALBUMIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	33.	33.	33.	32. Y
0 mg/kg	0.6	2.6	1.2	1.5
	3	3	3	3
LOW DOSE	33.	31.	31.	31.
250 mg/kg	1.5	2.3	0.6	1.2
	3	3	3	3
MEDIUM DOSE	31.	29.	30.	30.
500 mg/kg	1.5	1.5	2.9	1.0
	3	3	3	3
HIGH DOSE	33.	32.	31.	32.
1000 mg/kg	1.2	0.6	0.6	0.0
	3	3	3	3

PT : PRETREATMENT

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 7.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE ALBUMIN (g/L)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	34. Y	33.	32.	33.
0 mg/kg	1.0	1.2	3.8	1.5
	3	3	3	3
LOW DOSE	34.	35.	34.	36.
250 mg/kg	1.0	2.1	2.1	0.6
	3	3	3	3
MEDIUM DOSE	33.	30.	32.	31.
500 mg/kg	0.0	1.5	0.6	1.7
	3	3	3	3
HIGH DOSE	34.	32.	33.	33.
1000 mg/kg	1.0	2.3	2.5	2.5
	3	3	3	3

PT : PRETREATMENT

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 7.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED ALBUMIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	34.	33. F	33.	33.
0 mg/kg	0.8 6	1.8 6	2.6 6	1.4 6
LOW DOSE	33.	33.	33.	34.
250 mg/kg	1.4 6	2.9 6	2.1 6	2.5 6
MEDIUM DOSE	32.	30. **	31.	31.
500 mg/kg	1.6 6	1.4 6	2.0 6	1.4 6
HIGH DOSE	33.	32.	32.	33.
1000 mg/kg	1.2 6	1.5 6	2.0 6	1.8 6

PT : PRETREATMENT

F : ONWAY 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 7.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE GLOBULIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	23.	30.	31.	33.
0 mg/kg	1.5 3	2.1 3	2.6 3	3.6 3
LOW DOSE	29.	31.	37.	36.
250 mg/kg	6.1 3	5.9 3	5.2 3	6.9 3
MEDIUM DOSE	27.	30.	37.	37.
500 mg/kg	4.0 3	2.1 3	3.1 3	2.9 3
HIGH DOSE	25.	29.	35.	35.
1000 mg/kg	3.6 3	2.6 3	6.4 3	5.3 3

PT : PRETREATMENT

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 7.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE GLOBULIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	24.	27.	37.	34.
0 mg/kg	3.1 3	4.5 3	4.5 3	4.0 3
LOW DOSE	23.	26.	33.	32.
250 mg/kg	4.5 3	1.7 3	2.1 3	2.6 3
MEDIUM DOSE	25.	25.	33.	30.
500 mg/kg	1.0 3	3.6 3	2.3 3	1.2 3
HIGH DOSE	23.	27.	33.	32.
1000 mg/kg	3.1 3	3.5 3	4.4 3	5.0 3

PT : PRETREATMENT

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 7.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
POOLED GLOBULIN (g/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	24.	28.	34.	34.
0 mg/kg	2.2 6	3.5 6	4.5 6	3.5 6
LOW DOSE	26.	29.	35.	34.
250 mg/kg	5.7 6	4.8 6	4.3 6	5.2 6
MEDIUM DOSE	26.	28.	35.	34.
500 mg/kg	2.9 6	3.9 6	3.3 6	4.3 6
HIGH DOSE	24.	28.	34.	34.
1000 mg/kg	3.3 6	3.1 6	5.0 6	4.9 6

PT : PRETREATMENT

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 7.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
MALE A/G RATIO
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	1.43	1.11	1.08	0.99
0 mg/kg	0.113	0.039	0.116	0.135
	3	3	3	3
LOW DOSE	1.16	1.01	0.86	0.89
250 mg/kg	0.261	0.239	0.120	0.184
	3	3	3	3
MEDIUM DOSE	1.14	0.97	0.83	0.81
500 mg/kg	0.216	0.120	0.099	0.091
	3	3	3	3
HIGH DOSE	1.32	1.10	0.92	0.93
1000 mg/kg	0.193	0.115	0.161	0.131
	3	3	3	3

PT : PRETREATMENT

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 7.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
FEMALE A/G RATIO
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	1.42	1.25	0.90	0.96
0 mg/kg	0.228	0.263	0.194	0.160
	3	3	3	3
LOW DOSE	1.50	1.34	1.06	1.12
250 mg/kg	0.332	0.102	0.123	0.106
	3	3	3	3
MEDIUM DOSE	1.32	1.20	0.97	1.02
500 mg/kg	0.053	0.112	0.053	0.064
	3	3	3	3
HIGH DOSE	1.52	1.23	1.02	1.06
1000 mg/kg	0.183	0.169	0.159	0.200
	3	3	3	3

PT : PRETREATMENT

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 7.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

SERUM CLINICAL CHEMISTRY

POOLED A/G RATIO

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	1.42	1.18	0.99	0.98
0 mg/kg	0.161	0.186	0.175	0.133
	6	6	6	6
LOW DOSE	1.33	1.17	0.96	1.01
250 mg/kg	0.325	0.243	0.153	0.183
	6	6	6	6
MEDIUM DOSE	1.23	1.08	0.90	0.92
500 mg/kg	0.172	0.161	0.105	0.142
	6	6	6	6
HIGH DOSE	1.42	1.16	0.97	0.99
1000 mg/kg	0.198	0.147	0.153	0.168
	6	6	6	6

PT : PRETREATMENT

F : ONEMAN 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 DOG
HEMATOLOGY
MALE HEMOGLOBIN (g/dL)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	16.7	16.7	16.4	15.7
0 mg/kg	0.72	1.27	0.60	0.70
	3	3	3	3
LOW DOSE	16.1	16.4	16.3	15.3
250 mg/kg	0.29	1.05	0.32	0.38
	3	3	3	3
MEDIUM DOSE	15.7	16.3	16.3	16.2
500 mg/kg	0.81	0.81	0.98	0.76
	3	3	3	3
HIGH DOSE	16.2	15.8	16.3	16.0
1000 mg/kg	2.49	1.57	1.68	1.74
	3	3	3	3

PT : PRETREATMENT

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 DOG
HEMATOLOGY
FEMALE HEMOGLOBIN (g/dL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	17.6	17.1	17.8	16.7
0 mg/kg	0.47	1.07	0.76	0.06
	3	3	3	3
LOW DOSE	16.8	16.3	16.5	15.7
250 mg/kg	0.93	1.43	0.75	0.85
	3	3	3	3
MEDIUM DOSE	17.5	15.3	15.9	15.4
500 mg/kg	0.91	0.65	0.78	0.80
	3	3	3	3
HIGH DOSE	16.9	16.2	16.4	16.4
1000 mg/kg	0.86	1.11	1.11	0.74
	3	3	3	3

PT : PRETREATMENT

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 DOG
HEMATOLOGY
POOLED HEMOGLOBIN (g/dL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	17.1	16.9	17.1	16.2
0 mg/kg	0.72	1.07	1.01	0.72
	6	6	6	6
LOW DOSE	16.4	16.4	16.4	15.5
250 mg/kg	0.71	1.12	0.54	0.64
	6	6	6	6
MEDIUM DOSE	16.6	15.8	16.1	15.8
500 mg/kg	1.25	0.83	0.83	0.83
	6	6	6	6
HIGH DOSE	16.5	16.0	16.4	16.2
1000 mg/kg	1.71	1.23	1.27	1.21
	6	6	6	6

PT : PRETREATMENT

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 DOG
HEMATOLOGY
MALE HEMATOCRIT (L/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.493	0.485	0.478	0.458
0 mg/kg	0.0205	0.0477	0.0130	0.0191
	3	3	3	3
LOW DOSE	0.474	0.464	0.469	0.441
250 mg/kg	0.0087	0.0331	0.0129	0.0095
	3	3	3	3
MEDIUM DOSE	0.461	0.460	0.475	0.469
500 mg/kg	0.0268	0.0278	0.0370	0.0258
	3	3	3	3
HIGH DOSE	0.482	0.453	0.476	0.470
1000 mg/kg	0.0820	0.0401	0.0515	0.0471
	3	3	3	3

PT : PRETREATMENT

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 DOG
HEMATOLOGY
FEMALE HEMATOCRIT (L/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.515	0.489	0.515	0.483
0 mg/kg	0.0173	0.0384	0.0226	0.0015
	3	3	3	3
LOW DOSE	0.493	0.465	0.478	0.451
250 mg/kg	0.0309	0.0547	0.0282	0.0280
	3	3	3	3
MEDIUM DOSE	0.515	0.442	0.464	0.443
500 mg/kg	0.0321	0.0055	0.0061	0.0216
	3	3	3	3
HIGH DOSE	0.496	0.463	0.483	0.472
1000 mg/kg	0.0343	0.0340	0.0327	0.0250
	3	3	3	3

PT : PRETREATMENT

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 DOG
HEMATOLOGY
POOLED HEMATOCRIT (L/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.504	0.487	0.497	0.470
0 mg/kg	0.0207	0.0388	0.0261	0.0181
	6	6	6	6
LOW DOSE	0.483	0.464	0.473	0.446
250 mg/kg	0.0227	0.0404	0.0202	0.0195
	6	6	6	6
MEDIUM DOSE	0.488	0.451	0.470	0.456
500 mg/kg	0.0397	0.0204	0.0245	0.0256
	6	6	6	6
HIGH DOSE	0.489	0.458	0.479	0.471
1000 mg/kg	0.0568	0.0337	0.0388	0.0337
	6	6	6	6

PT : PRETREATMENT

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 8.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE RED BLOOD CELL COUNT (X10E12/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	7.52	7.44	7.32	7.04
0 mg/kg	0.180 3	0.723 3	0.254 3	0.145 3
LOW DOSE	7.04	6.94	6.98	6.58
250 mg/kg	0.273 3	0.656 3	0.310 3	0.262 3
MEDIUM DOSE	6.96	6.98	7.14	7.07
500 mg/kg	0.516 3	0.501 3	0.699 3	0.532 3
HIGH DOSE	7.24	6.84	7.15	7.12
1000 mg/kg	1.096 3	0.454 3	0.589 3	0.535 3

PT : PRETREATMENT

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 8.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE RED BLOOD CELL COUNT (X10E12/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	7.57	7.26	7.59	7.13
0 mg/kg	0.329	0.477	0.163	0.204
	3	3	3	3
LOW DOSE	7.40	7.04	7.20	6.81
250 mg/kg	0.442	0.648	0.314	0.229
	3	3	3	3
MEDIUM DOSE	7.63	6.64	6.93	6.63
500 mg/kg	0.316	0.251	0.272	0.097
	3	3	3	3
HIGH DOSE	7.44	6.96	7.19	6.99
1000 mg/kg	0.407	0.344	0.561	0.406
	3	3	3	3

PT : PRETREATMENT

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 8.3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED RED BLOOD CELL COUNT (X10E12/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	7.55	7.35	7.46	7.09
0 mg/kg	0.239	0.556	0.242	0.165
	6	6	6	6
LOW DOSE	7.22	6.99	7.09	6.70
250 mg/kg	0.382	0.586	0.303	0.252
	6	6	6	6
MEDIUM DOSE	7.30	6.81	7.04	6.85
500 mg/kg	0.531	0.401	0.488	0.420
	6	6	6	6
HIGH DOSE	7.34	6.90	7.17	7.05
1000 mg/kg	0.747	0.366	0.515	0.430
	6	6	6	6

PT : PRETREATMENT

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 8.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE MEAN CORPUSCULAR VOLUME (fL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	65.5	65.1	65.2	64.9
0 mg/kg	1.18	0.32	0.87	1.30
	3	3	3	3
LOW DOSE	67.3	66.8	67.1	66.9
250 mg/kg	1.45	1.60	1.35	1.39
	3	3	3	3
MEDIUM DOSE	66.3	65.9	66.6	66.4
500 mg/kg	1.44	1.19	1.35	1.31
	3	3	3	3
HIGH DOSE	66.3	66.0	66.4	65.9
1000 mg/kg	1.88	2.26	2.35	2.12
	3	3	3	3

PT : PRETREATMENT

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 8.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE MEAN CORPUSCULAR VOLUME (fL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	68.0	67.3	67.7	67.7
0 mg/kg	1.93	2.58	2.04	1.79
	3	3	3	3
LOW DOSE	66.5	65.8	66.3	66.1
250 mg/kg	1.31	1.88	2.13	2.27
	3	3	3	3
MEDIUM DOSE	67.4	66.6	66.9	66.8
500 mg/kg	2.27	1.95	1.91	2.32
	3	3	3	3
HIGH DOSE	66.7	66.4	67.3	67.5
1000 mg/kg	4.69	3.46	3.27	2.26
	3	3	3	3

PT : PRETREATMENT

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 8.4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED MEAN CORPUSCULAR VOLUME (fL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	66.7	66.2	66.5	66.3
0 mg/kg	1.97	2.04	1.97	2.06
	6	6	6	6
LOW DOSE	66.9	66.3	66.7	66.5
250 mg/kg	1.31	1.65	1.65	1.74
	6	6	6	6
MEDIUM DOSE	66.9	66.3	66.8	66.6
500 mg/kg	1.80	1.50	1.49	1.70
	6	6	6	6
HIGH DOSE	66.5	66.2	66.8	66.7
1000 mg/kg	3.20	2.62	2.59	2.15
	6	6	6	6

PT : PRETREATMENT

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 8.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY

MALE MEAN CORPUSCULAR HEMOGLOBIN (pg)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	22.2	22.5	22.3	22.2
0 mg/kg	0.36	0.72	0.60	0.64
	3	3	3	3
LOW DOSE	22.9	23.6	23.3	23.2
250 mg/kg	0.50	0.72	0.61	0.52
	3	3	3	3
MEDIUM DOSE	22.6	23.3	22.9	23.0
500 mg/kg	0.51	0.56	0.82	0.68
	3	3	3	3
HIGH DOSE	22.3	23.1	22.7	22.4
1000 mg/kg	0.38	0.83	0.82	0.78
	3	3	3	3

PT : PRETREATMENT

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 8.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE MEAN CORPUSCULAR HEMOGLOBIN (pg)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	23.2	23.5	23.4	23.5
0 mg/kg	0.75	0.60	0.64	0.69
	3	3	3	3
LOW DOSE	22.7	23.2	23.0	23.0
250 mg/kg	0.59	0.47	0.76	0.55
	3	3	3	3
MEDIUM DOSE	23.0	23.1	22.9	23.2
500 mg/kg	0.65	1.46	1.10	0.90
	3	3	3	3
HIGH DOSE	22.7	23.2	22.9	23.4
1000 mg/kg	1.37	1.31	0.78	0.66
	3	3	3	3

PT : PRETREATMENT

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 8.5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

HEMATOLOGY

POOLED MEAN CORPUSCULAR HEMOGLOBIN (pg)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	22.7	23.0	22.9	22.9
0 mg/kg	0.77	0.82	0.83	0.92
	6	6	6	6
LOW DOSE	22.8	23.4	23.1	23.1
250 mg/kg	0.51	0.59	0.65	0.49
	6	6	6	6
MEDIUM DOSE	22.8	23.2	22.9	23.1
500 mg/kg	0.55	0.99	0.87	0.72
	6	6	6	6
HIGH DOSE	22.5	23.1	22.8	22.9
1000 mg/kg	0.92	0.99	0.72	0.85
	6	6	6	6

PT : PRETREATMENT

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 8.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY

MALE MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	33.9 B	34.5	34.2	34.3
0 mg/kg	0.06	0.98	0.59	0.75
	3	3	3	3
LOW DOSE	34.0	35.3	34.7	34.6
250 mg/kg	0.06	0.29	0.26	0.72
	3	3	3	3
MEDIUM DOSE	34.1	35.4	34.4	34.6
500 mg/kg	0.25	0.45	0.58	0.32
	3	3	3	3
HIGH DOSE	33.6	34.9	34.2	34.0
1000 mg/kg	0.46	0.58	0.17	0.64
	3	3	3	3

PT : PRETREATMENT

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 8.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	34.1	35.0	34.6 B	34.7
0 mg/kg	0.30	0.55	0.10	0.15
	3	3	3	3
LOW DOSE	34.0	35.2	34.6	34.8
250 mg/kg	0.32	0.98	0.46	0.32
	3	3	3	3
MEDIUM DOSE	34.0	34.7	34.2	34.7
500 mg/kg	0.36	1.27	1.30	0.25
	3	3	3	3
HIGH DOSE	34.0	34.9	34.0	34.6
1000 mg/kg	0.50	0.35	0.46	0.40
	3	3	3	3

PT : PRETREATMENT

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 8.6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY

POOLED MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	34.0	34.7	34.4	34.5
0 mg/kg	0.23	0.76	0.44	0.53
	6	6	6	6
LOW DOSE	34.0	35.3	34.7	34.7
250 mg/kg	0.21	0.65	0.34	0.51
	6	6	6	6
MEDIUM DOSE	34.0	35.0	34.3	34.6
500 mg/kg	0.28	0.93	0.90	0.26
	6	6	6	6
HIGH DOSE	33.8	34.9	34.1	34.3
1000 mg/kg	0.48	0.43	0.33	0.58
	6	6	6	6

PT : PRETREATMENT

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 8.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE WHITE BLOOD CELL COUNT (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	11.3 B	9.9	12.3	11.5
0 mg/kg	0.70	2.75	0.36	0.98
	3	3	3	3
LOW DOSE	10.8	10.0	15.2	13.4
250 mg/kg	1.70	1.49	2.37	1.33
	3	3	3	3
MEDIUM DOSE	11.4	11.4	14.4	13.1
500 mg/kg	0.51	6.24	1.57	1.42
	3	3	3	3
HIGH DOSE	12.9	10.4	15.3	12.7
1000 mg/kg	4.88	3.18	1.51	1.28
	3	3	3	3

PT : PRETREATMENT

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 8.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE WHITE BLOOD CELL COUNT (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	10.4	10.2	13.2	16.8 F
0 mg/kg	1.13	1.76	0.81	2.95
	3	3	3	3
LOW DOSE	8.9	8.6	12.1	10.6 **
250 mg/kg	0.85	1.42	0.40	1.91
	3	3	3	3
MEDIUM DOSE	11.9	10.5	12.8	12.3 *
500 mg/kg	3.36	4.35	2.94	2.18
	3	3	3	3
HIGH DOSE	9.2	9.1	11.9	10.6 **
1000 mg/kg	1.82	2.33	0.64	1.50
	3	3	3	3

PT : PRETREATMENT

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 8.7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED WHITE BLOOD CELL COUNT (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	10.9 B	10.1	12.8	14.1
0 mg/kg	0.97	2.07	0.76	3.51
	6	6	6	6
LOW DOSE	9.9	9.3	13.6	12.0
250 mg/kg	1.58	1.50	2.25	2.13
	6	6	6	6
MEDIUM DOSE	11.7	10.9	13.6	12.7
500 mg/kg	2.17	4.84	2.28	1.70
	6	6	6	6
HIGH DOSE	11.0	9.7	13.6	11.7
1000 mg/kg	3.86	2.59	2.15	1.68
	6	6	6	6

PT : PRETREATMENT

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 8.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

HEMATOLOGY

MALE IMMATURE NEUTROPHIL (%)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE IMMATURE NEUTROPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.8
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED IMMATURE NEUTROPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE MATURE NEUTROPHIL (%)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	62.	52.	61.	61.
0 mg/kg	4.5	2.0	7.5	8.6
	3	3	3	3
LOW DOSE	63.	58.	65.	62.
250 mg/kg	2.6	12.5	6.1	5.8
	3	3	3	3
MEDIUM DOSE	54.	56.	60.	50.
500 mg/kg	12.5	22.6	7.8	9.5
	3	3	3	3
HIGH DOSE	63.	69.	61.	65.
1000 mg/kg	5.5	8.7	3.2	6.4
	3	3	3	3

PT : PRETREATMENT

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 8.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE MATURE NEUTROPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	63.	60.	64.	70.
0 mg/kg	6.7	3.1	6.9	4.9
	3	3	3	3
LOW DOSE	55.	62.	60.	50.
250 mg/kg	10.8	11.1	2.3	17.8
	3	3	3	3
MEDIUM DOSE	51.	56.	55.	54.
500 mg/kg	11.2	4.0	10.4	10.4
	3	3	3	3
HIGH DOSE	51.	53.	63.	51.
1000 mg/kg	4.7	5.9	6.4	4.0
	3	3	3	3

PT : PRETREATMENT

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 8.9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED MATURE NEUTROPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	63.	56.	63.	65.
0 mg/kg	5.2	5.1	6.6	8.0
	6	6	6	6
LOW DOSE	59.	60.	63.	56.
250 mg/kg	8.3	10.8	5.0	13.5
	6	6	6	6
MEDIUM DOSE	53.	56.	57.	52.
500 mg/kg	10.7	14.5	8.7	9.2
	6	6	6	6
HIGH DOSE	57.	61.	62.	58.
1000 mg/kg	8.3	11.0	4.7	9.3
	6	6	6	6

PT : PRETREATMENT

F : ONWAY 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 8.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE LYMPHOCYTE (%)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	29.	39.	31.	30.
0 mg/kg	4.0	5.5	7.8	8.5
	3	3	3	3
LOW DOSE	27.	32.	28.	31.
250 mg/kg	5.2	12.6	8.1	3.5
	3	3	3	3
MEDIUM DOSE	35.	35.	33.	39.
500 mg/kg	9.0	16.9	5.6	4.4
	3	3	3	3
HIGH DOSE	28.	24.	31.	27.
1000 mg/kg	4.5	8.5	5.0	3.6
	3	3	3	3

PT : PRETREATMENT

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 8.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE LYMPHOCYTE (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	29.	30. FY	29.	23.
0 mg/kg	6.7	1.5	6.1	3.5
	3	3	3	3
LOW DOSE	36.	27.	34.	37.
250 mg/kg	12.3	6.2	3.5	8.7
	3	3	3	3
MEDIUM DOSE	36.	29.	31.	38.
500 mg/kg	7.5	0.0	8.1	8.9
	3	3	3	3
HIGH DOSE	41.	36. *	28.	39.
1000 mg/kg	7.2	2.1	5.6	9.1
	3	3	3	3

PT : PRETREATMENT

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 8.10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED LYMPHOCYTE (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	29.	34.	30.	26.
0 mg/kg	4.9	6.1	6.3	6.9
	6	6	6	6
LOW DOSE	32.	29.	31.	34.
250 mg/kg	9.8	9.2	6.3	6.7
	6	6	6	6
MEDIUM DOSE	36.	32.	32.	39.
500 mg/kg	7.4	11.1	6.3	6.3
	6	6	6	6
HIGH DOSE	35.	30.	30.	33.
1000 mg/kg	8.6	8.9	5.1	8.9
	6	6	6	6

PT : PRETREATMENT

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 B.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE MONOCYTE (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	7.	7.	6.	7.
0 mg/kg	1.5	3.6	0.6	3.8
	3	3	3	3
LOW DOSE	7.	7.	3.	6.
250 mg/kg	2.3	2.1	1.2	2.1
	3	3	3	3
MEDIUM DOSE	8.	3.	5.	8.
500 mg/kg	2.1	1.5	1.2	4.9
	3	3	3	3
HIGH DOSE	6.	6.	4.	6.
1000 mg/kg	1.5	1.5	2.1	3.5
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE MONOCYTE (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	5.	6.	6.	7.
0 mg/kg	3.6	1.5	0.6	3.6
	3	3	3	3
LOW DOSE	4.	6.	3.	8.
250 mg/kg	2.1	3.6	0.6	4.0
	3	3	3	3
MEDIUM DOSE	7.	8.	8.	5.
500 mg/kg	4.2	3.0	2.6	1.5
	3	3	3	3
HIGH DOSE	5.	7.	7.	8.
1000 mg/kg	3.8	1.0	2.9	3.1
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.11
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED MONOCYTE (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	6.	6.	6.	7.
0 mg/kg	2.6	2.6	0.5	3.3
	6	6	6	6
LOW DOSE	6.	6.	3.	7.
250 mg/kg	2.6	2.7	0.9	3.2
	6	6	6	6
MEDIUM DOSE	8.	6.	7.	7.
500 mg/kg	2.9	3.3	2.3	3.8
	6	6	6	6
HIGH DOSE	5.	6.	6.	7.
1000 mg/kg	2.6	1.4	2.8	3.1
	6	6	6	6

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE EOSINOPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	3.	2.	2.	2.
0 mg/kg	2.1	0.6	1.2	3.2
	3	3	3	3
LOW DOSE	3.	4.	3.	2.
250 mg/kg	2.3	2.1	2.0	0.6
	3	3	3	3
MEDIUM DOSE	3.	6.	2.	2.
500 mg/kg	2.1	4.4	2.0	1.2
	3	3	3	3
HIGH DOSE	3.	1.	3.	2.
1000 mg/kg	4.6	0.6	1.0	1.0
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE EOSINOPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	2.	4.	1.	0.
0 mg/kg	2.3	2.1	1.2	0.6
	3	3	3	3
LOW DOSE	5.	5.	3.	5.
250 mg/kg	1.5	4.0	4.0	5.0
	3	3	3	3
MEDIUM DOSE	5.	7.	7.	4.
500 mg/kg	3.1	4.0	2.1	2.3
	3	3	3	3
HIGH DOSE	4.	3.	1.	3.
1000 mg/kg	4.0	3.1	0.6	2.6
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED EOSINOPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	3.	3.	2.	1.
0 mg/kg	2.0	1.8	1.2	2.3
	6	6	6	6
LOW DOSE	4.	4.	3.	4.
250 mg/kg	2.1	2.9	2.9	3.8
	6	6	6	6
MEDIUM DOSE	4.	6.	4.	3.
500 mg/kg	2.6	3.8	3.1	1.8
	6	6	6	6
HIGH DOSE	3.	2.	2.	3.
1000 mg/kg	3.9	2.3	1.2	1.9
	6	6	6	6

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE BASOPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.6
	3	3	3	3
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE BASOPHIL (%)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	3	3	3	3

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED BASOPHIL (%)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	0.	0.	0.	0.
0 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6
LOW DOSE	0.	0.	0.	0.
250 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6
MEDIUM DOSE	0.	0.	0.	0.
500 mg/kg	0.0	0.0	0.0	0.4
	6	6	6	6
HIGH DOSE	0.	0.	0.	0.
1000 mg/kg	0.0	0.0	0.0	0.0
	6	6	6	6

PT : PRETREATMENT

DATA NOT STATISTICALLY ANALYZED

TABLE 8.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE PLATELET (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	431.	422.	454.	475.
0 mg/kg	46.5	78.1	51.7	14.8
	3	3	3	3
LOW DOSE	344.	326.	325.	373.
250 mg/kg	76.4	82.5	56.8	66.0
	3	3	3	3
MEDIUM DOSE	403.	335.	389.	404.
500 mg/kg	83.9	103.7	105.1	79.0
	3	3	3	3
HIGH DOSE	394.	392.	449.	426.
1000 mg/kg	37.6	37.4	56.7	35.8
	3	3	3	3

PT : PRETREATMENT

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 B.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE PLATELET (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	314.	290.	330.	375.
0 mg/kg	28.0	29.7	47.8	22.6
	3	3	3	3
LOW DOSE	316.	300.	378.	348.
250 mg/kg	31.3	31.4	30.9	77.1
	3	3	3	3
MEDIUM DOSE	427.	391.	402.	431.
500 mg/kg	64.5	76.8	69.0	65.0
	3	3	3	3
HIGH DOSE	382.	382.	430.	453.
1000 mg/kg	102.4	115.7	63.9	99.3
	3	3	3	3

PT : PRETREATMENT

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 8.14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED PLATELET (X10E9/L)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	373.	356.	392.	425.
0 mg/kg	72.5	89.4	81.2	57.5
	6	6	6	6
LOW DOSE	330.	313.	351.	361.
250 mg/kg	54.5	57.6	50.1	65.6
	6	6	6	6
MEDIUM DOSE	415.	363.	395.	418.
500 mg/kg	68.1	87.3	79.8	66.5
	6	6	6	6
HIGH DOSE	388.	387.	440.	440.
1000 mg/kg	69.3	77.1	55.0	68.4
	6	6	6	6

PT : PRETREATMENT

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 8.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY

MALE ACTIVATED PARTIAL THROMBOPLASTIN TIME (SECONDS)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	8.6	8.3	9.1	9.1
0 mg/kg	0.60	0.90	0.25	0.17
	3	3	3	3
LOW DOSE	8.9	9.0	9.3	9.3
250 mg/kg	0.42	0.45	0.15	0.75
	3	3	3	3
MEDIUM DOSE	8.8	8.9	9.5	9.5
500 mg/kg	0.36	0.25	0.51	0.40
	3	3	3	3
HIGH DOSE	9.3	9.7	9.9	9.9
1000 mg/kg	0.81	1.02	0.98	1.36
	3	3	3	3

PT : PRETREATMENT

F : ONWAY 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 8.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

HEMATOLOGY

FEMALE ACTIVATED PARTIAL THROMBOPLASTIN TIME (SECONDS)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	9.2	9.0	9.6	9.2
0 mg/kg	0.12	0.26	0.42	0.65
	3	3	3	3
LOW DOSE	9.0	8.9	9.2	9.2
250 mg/kg	0.46	0.42	0.25	0.31
	3	3	3	3
MEDIUM DOSE	8.9	9.1	9.1	9.1
500 mg/kg	0.70	0.38	0.23	0.25
	3	3	3	3
HIGH DOSE	8.9	9.1	9.3	9.4
1000 mg/kg	0.50	0.25	0.45	0.12
	3	3	3	3

PT : PRETREATMENT

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 8.15
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

HEMATOLOGY

POOLED ACTIVATED PARTIAL THROMBOPLASTIN TIME (SECONDS)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	8.9	8.7	9.3 B	9.1
0 mg/kg	0.50	0.70	0.41	0.43
	6	6	6	6
LOW DOSE	8.9	8.9	9.3	9.3
250 mg/kg	0.40	0.40	0.19	0.52
	6	6	6	6
MEDIUM DOSE	8.9	9.0	9.3	9.3
500 mg/kg	0.50	0.31	0.40	0.37
	6	6	6	6
HIGH DOSE	9.1	9.4	9.6	9.6
1000 mg/kg	0.65	0.74	0.77	0.92
	6	6	6	6

PT : PRETREATMENT

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 8.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
MALE PROTHROMBIN TIME (SECONDS)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	6.4	6.1	6.3	6.2 B
0 mg/kg	0.31	0.29	0.29	0.20
	3	3	3	3
LOW DOSE	6.3	6.0	6.2	6.2
250 mg/kg	0.15	0.20	0.10	0.06
	3	3	3	3
MEDIUM DOSE	6.4	6.1	6.4	6.3
500 mg/kg	0.21	0.10	0.15	0.10
	3	3	3	3
HIGH DOSE	6.7	6.4	6.6	6.8
1000 mg/kg	0.81	0.67	0.67	0.72
	3	3	3	3

PT : PRETREATMENT

F : ONWAY 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 8.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
FEMALE PROTHROMBIN TIME (SECONDS)

ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	6.4	6.2	6.4	6.3
0 mg/kg	0.46	0.17	0.15	0.26
	3	3	3	3
LOW DOSE	6.6	6.2	6.4	6.4
250 mg/kg	0.32	0.36	0.36	0.45
	3	3	3	3
MEDIUM DOSE	6.3	6.0	6.3	6.2
500 mg/kg	0.21	0.15	0.06	0.15
	3	3	3	3
HIGH DOSE	6.3	5.9	6.2	6.3
1000 mg/kg	0.21	0.06	0.10	0.21
	3	3	3	3

PT : PRETREATMENT

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 8.16
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
HEMATOLOGY
POOLED PROTHROMBIN TIME (SECONDS)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	1	12	28
CONTROL	6.4	6.1	6.3 B	6.3 B
0 mg/kg	0.35	0.23	0.23	0.22
	6	6	6	6
LOW DOSE	6.4	6.1	6.3	6.3
250 mg/kg	0.28	0.28	0.26	0.31
	6	6	6	6
MEDIUM DOSE	6.3	6.0	6.3	6.3
500 mg/kg	0.21	0.14	0.12	0.12
	6	6	6	6
HIGH DOSE	6.5	6.2	6.4	6.5
1000 mg/kg	0.58	0.50	0.49	0.55
	6	6	6	6

PT : PRETREATMENT

F : ONWAY 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
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
URINALYSIS
MALE REFRACTIVE INDEX +
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	12-13	27-28
CONTROL	1.353	1.351	1.355
0 mg/kg	0.0029	0.0081	0.0051
	3	3	3
LOW DOSE	1.354	1.350	1.352
250 mg/kg	0.0035	0.0076	0.0080
	3	3	3
MEDIUM DOSE	1.349	1.353	1.353
500 mg/kg	0.0043	0.0076	0.0035
	3	3	3
HIGH DOSE	1.350	1.358	1.357
1000 mg/kg	0.0056	0.0023	0.0023
	3	3	3

PT : PRETREATMENT

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
+ : REFRACTIVITY X10E-4 + 1.333

TABLE 9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
URINALYSIS
FEMALE REFRACTIVE INDEX +
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	12-13	27-28
CONTROL	1.352	1.351	1.353
0 mg/kg	0.0040	0.0043	0.0059
	3	3	3
LOW DOSE	1.346	1.354	1.355
250 mg/kg	0.0050	0.0039	0.0029
	3	3	3
MEDIUM DOSE	1.347	1.352	1.353
500 mg/kg	0.0057	0.0106	0.0055
	3	3	3
HIGH DOSE	1.347	1.353	1.352
1000 mg/kg	0.0066	0.0078	0.0100
	3	3	3

PT : PRETREATMENT

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

+ : REFRACTIVITY $\times 10^{-4} + 1.333$

TABLE 9
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
URINALYSIS
POOLED REFRACTIVE INDEX +
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	PT	12-13	27-28
CONTROL	1.352	1.351	1.354
0 mg/kg	0.0031	0.0058	0.0050
	6	6	6
LOW DOSE	1.350	1.352	1.353
250 mg/kg	0.0061	0.0060	0.0056
	6	6	6
MEDIUM DOSE	1.348	1.352	1.353
500 mg/kg	0.0046	0.0083	0.0041
	6	6	6
HIGH DOSE	1.348	1.355	1.354
1000 mg/kg	0.0057	0.0056	0.0070
	6	6	6

PT : PRETREATMENT

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
+ : REFRACTIVITY $\times 10^{-4} + 1.333$

TABLE 10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE URINE VOLUME (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	397.
0 mg/kg	179.5
	3
LOW DOSE	510.
250 mg/kg	40.0
	3
MEDIUM DOSE	527.
500 mg/kg	161.7
	3
HIGH DOSE	800.
1000 mg/kg	385.9
	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE URINE VOLUME (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	773.
0 mg/kg	364.7 3
LOW DOSE	277.
250 mg/kg	144.7 3
MEDIUM DOSE	227.
500 mg/kg	145.7 3
HIGH DOSE	420.
1000 mg/kg	191.6 3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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 10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
POOLED URINE VOLUME (mL)
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

STUDY DAY	22-23
CONTROL	585.
0 mg/kg	329.7
	6
LOW DOSE	393.
250 mg/kg	159.2
	6
MEDIUM DOSE	377.
500 mg/kg	214.4
	6
HIGH DOSE	610.
1000 mg/kg	342.9
	6

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
B : BARTLETT-BOX HOMOGENEITY OF VARIANCE 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

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)
 STUDY NUMBER: SA2449
 PATHOLOGIST(S): CURT PORT, DVM, PHD
 STUDY START DATE: 18-OCT-84

PRINTED: 1-FEB-85
 PAGE: 1

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

NOTES: ANIMALS = ALL DEAD									
CTLS = CONTROLS FROM GROUP(S): 1									
ANIMAL SEX:									
DOSAGE GROUP:									
NO. IN GROUP:									
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SEARLE RESEARCH & DEVELOPMENT										LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)										PRINTED: 1-FEB-85					
PRODUCT SAFETY ASSESSMENT										STUDY NUMBER: SA2449										PAGE: 2					
SKOKIE, ILLINOIS 60077										PATHOLOGIST(S): CURT PORT, DVM, PHD															
SPECIES: DOG/BEAGLE										STUDY START DATE: 18-OCT-84										STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX					
NOTES: ANIMALS = ALL DEAD										— ANIMALS —										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	
										3		3		3		3		3		3		3			
INT LG-CECUM										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
INT LG-COLON										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
INT LG-RECTUM										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
KIDNEY										3		3		3		3		3		3		3			
—MINERALIZATION, MEDULLA										1996				2014				1999		2011		2017			
										1997				2015											
										1998				2016											
										NUMBER EXAMINED:															
LARYNX										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
LIVER										3		3		3		3		3		3		3			
—FOCAL LYMPHOCYTIC AGGREGATIONS														2014								2017			
										NUMBER EXAMINED:															
LYMPH N-MANDIB										3		3		3		3		3		3		3			
—ERYTHROPHAGOCYTOSIS																				2013					
										NUMBER EXAMINED:															
—HEMOSIDEROSIS																				2013					
										NUMBER EXAMINED:															
LYMPH N-MESENER										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
LUNG										3		3		3		3		3		3		3			
										NUMBER EXAMINED:															
MAMMARY GLAND																		3		2		3			
										NUMBER EXAMINED:															
NICITATING MEMB										0		0		1		0		0		0		0			
—INFLAMMATION														2009											
										NUMBER EXAMINED:															
OVARY																		3		3		3			
										NUMBER EXAMINED:															

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)
 STUDY NUMBER: SA2449
 PATHOLOGIST(S): CURT PORT, DVM, PHD
 STUDY START DATE: 18-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

PRINTED: 1-FEB-85
 PAGE: 3

NOTES: ANIMALS = ALL DEAD CTLS = CONTROLS FROM GROUP(S): 1		ANIMAL SEX:		— ANIMALS —		AFFECTED —	
T I S S U E S W I T H F I N D I N G S		DOSAGE GROUP: NO. IN GROUP:		CTLS 2 3 4		CTLS 2 3 4	
				3 3 3 3		3 3 3 3	
PANCREAS	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
PITUITARY GLAND	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
-CYST				1996 2010		1999 2006 2000 2007	
PERIPHERAL NERVE	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
PROSTATE	NUMBER EXAMINED:		3 3 3 3			
PARATHYROID	NUMBER EXAMINED:		2 2 3 2		3 3 3 3	2 3
-CYST(S)							2017
SPINAL CORD	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
SALIVARY GLAND	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
SKIN	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
SKELETAL MUSCLE	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
SPLEEN	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
STOMACH	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
TESTIS	NUMBER EXAMINED:		3 3 3 3			
-GERMINAL EPITHELIAL DEGENERATION.				1998			
-TUBULAR HYPOPLASIA				2014 2016			
THYROID GLAND	NUMBER EXAMINED:		3 3 3 3		3 3 3 3	3 3
-CYST(S)							2011 2019

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

LESION INCIDENCE BY ANIMAL NUMBER(ALL FINDING)
 STUDY NUMBER: SA2449
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 STUDY START DATE: 18-OCT-84

PRINTED: 1-FEB-85
 PAGE: 4

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

NOTES: ANIMALS = ALL DEAD CTLs = CONTROLS FROM GROUP(S): 1		ANIMAL SEX:		— ANIMALS —		AFFECTED —	
T I S S U E S W I T H F I N D I N G S		DOSAGE GROUP: NO. IN GROUP:		— MALES — CTLs 2 3 3 3 3 4		— FEMALES — CTLs 2 3 3 3 3 4	
THYROID GLAND	NUMBER EXAMINED:	3	3	3	3	3	3
—C-CELL HYPERPLASIA						2012	
THYMUS	NUMBER EXAMINED:	3	3	3	3	3	3
—CYST(S)				2014			
				2016			
TONGUE	NUMBER EXAMINED:	3	3	3	3	3	3
TRACHEA	NUMBER EXAMINED:	3	3	3	3	3	3
URINARY BLADDER	NUMBER EXAMINED:	3	3	3	3	3	3
UTERUS	NUMBER EXAMINED:					3	3
VAGINA	NUMBER EXAMINED:					3	3
—LYMPHOID FOLLICLE						3	3
						2013	

TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	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	11.3	76.9	7.0	96.	8.6	12.6
0 mg/kg	2.00	4.01	1.62	19.1	1.25	2.99
	3	3	3	3	3	3
LOW DOSE	11.3	83.5	7.5	96.	8.5	11.5
250 mg/kg	1.23	3.87	1.22	22.0	1.49	3.06
	3	3	3	3	3	3
MEDIUM DOSE	11.5	81.5	7.2	91.	7.9	11.3
500 mg/kg	1.26	5.09	1.23	10.7	0.40	1.95
	3	3	3	3	3	3
HIGH DOSE	10.8	80.3	7.5	83.	7.6	10.3
1000 mg/kg	2.20	8.49	1.11	18.1	0.29	1.67
	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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Y : HOMOGENEITY OF VARIANCE TEST NOT DONE
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TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	WT	L I V E R		WT	K I D N E Y	
			ORG/FBW X10E-2	ORG/BRN		ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL 0 mg/kg	11.3	352.	3.1	4.6	76.	6.7	10.0
	2.00	49.5	0.13	0.87	14.5	0.16	2.37
	3	3	3	3	3	3	3
LOW DOSE 250 mg/kg	11.3	285.	2.5	3.4	71.	6.3	8.6
	1.23	39.8	0.12	0.62	15.5	1.05	2.05
	3	3	3	3	3	3	3
MEDIUM DOSE 500 mg/kg	11.5	306.	2.7	3.8	61.	5.3	7.4
	1.26	26.1	0.32	0.35	9.3	1.16	0.91
	3	3	3	3	3	3	3
HIGH DOSE 1000 mg/kg	10.8	306.	2.9	3.8	58.	5.4	7.2
	2.20	20.0	0.40	0.30	11.4	0.70	0.74
	3	3	3	3	3	3	3

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TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	A D R E N A L		T H Y R O I D			
		WT	ORG/FBW X10E-5	ORG/BRN X10E-3	WT	ORG/FBW X10E-5	ORG/BRN X10E-3
CONTROL	11.3	1.03	9.1	13.6	0.93	8.4	12.1
0 mg/kg	2.00	0.237	1.12	3.68	0.091	1.46	1.53
	3	3	3	3	3	3	3
LOW DOSE	11.3	1.22	10.8	14.7	0.99	8.8	11.9
250 mg/kg	1.23	0.175	0.38	2.68	0.164	0.68	2.36
	3	3	3	3	3	3	3
MEDIUM DOSE	11.5	1.27	11.0	15.7	1.09	9.5	13.4
500 mg/kg	1.26	0.150	0.13	2.61	0.166	1.53	2.05
	3	3	3	3	3	3	3
HIGH DOSE	10.8	1.03	9.7	12.8	0.93	8.9	11.7
1000 mg/kg	2.20	0.136	1.49	0.35	0.079	2.58	2.27
	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	— P I T U I T A R Y — WT	ORG/FBW X10E-6	ORG/BRN X10E-4	— S T O M A C H — WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	11.3	0.080	7.2	10.4	96.5	8.6	12.6
0 mg/kg	2.00	0.0060	0.75	1.29	17.29	0.27	2.84
	3	3	3	3	3	3	3
LOW DOSE	11.3	0.076	6.8	9.2	92.4	8.2	11.1
250 mg/kg	1.23	0.0180	1.58	2.40	8.20	0.48	1.45
	3	3	3	3	3	3	3
MEDIUM DOSE	11.5	0.059	5.2	7.2	83.5	7.2	10.3
500 mg/kg	1.26	0.0123	1.41	1.60	14.31	0.80	2.03
	3	3	3	3	3	3	3
HIGH DOSE	10.8	0.067	6.2	8.3	83.9	7.8	10.4
1000 mg/kg	2.20	0.0132	0.17	1.38	15.23	0.45	1.21
	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	THY MUS WT WT	ORG/FBW X10E-4	ORG/ERN X10E-2	SALIVARY GL WT	ORG/FBW X10E-3	ORG/ERN X10E-1
CONTROL	11.3	4.8	4.3	6.3	17.6	1.6	2.3
0 mg/kg	2.00	1.75	1.50	2.43	1.99	0.26	0.33
	3	3	3	3	3	3	3
LOW DOSE	11.3	8.0	7.1	9.6	18.3	1.6	2.2
250 mg/kg	1.23	1.72	1.34	2.22	3.97	0.20	0.55
	3	3	3	3	3	3	3
MEDIUM DOSE	11.5	11.7	9.9	14.7	16.6	1.4	2.0
500 mg/kg	1.26	6.10	4.29	8.02	0.70	0.13	0.20
	3	3	3	3	3	3	3
HIGH DOSE	10.8	9.2	8.0	11.2	15.4	1.4	1.9
1000 mg/kg	2.20	5.86	3.69	6.90	3.20	0.16	0.24
	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	TESTIS WT	ORG/FBW X10E-4	ORG/BRN X10E-2	PROSTATE WT	ORG/FBW X10E-4	ORG/BRN X10E-2	EPIDIDYMISS WT	ORG/FBW X10E-4	ORG/BRN X10E-2
CONTROL	11.3	15.8	14.4	2.1	5.5	5.1	7.1	3.85	3.4	5.0
0 mg/kg	2.00	2.89	3.66	0.40	1.97	2.49	2.33	0.562	0.34	0.96
	3	3	3	3	3	3	3	3	3	3
LOW DOSE	11.3	16.7	15.2	2.0	10.4	9.1	12.6	4.18	3.7	5.1
250 mg/kg	1.23	3.84	5.32	0.36	3.38	2.13	4.51	1.205	0.76	1.63
	3	3	3	3	3	3	3	3	3	3
MEDIUM DOSE	11.5	13.1	11.1	1.6	7.1	6.5	8.5	4.18	3.6	5.1
500 mg/kg	1.26	5.78	3.81	0.77	4.79	5.10	5.17	1.015	0.79	1.28
	3	3	3	3	3	3	3	3	3	3
HIGH DOSE	10.8	14.6	13.6	1.8	7.2	6.6	8.6	3.76	3.4	4.7
1000 mg/kg	2.20	3.60	3.36	0.52	5.00	4.58	5.33	1.098	0.36	1.25
	3	3	3	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	— B R A I N — WT	ORG/FBW X10E-3	— H E A R T — WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	9.7	71.7	7.4	87.	9.0	12.2
0 mg/kg	0.83	2.63	0.43	7.1	0.47	0.94
	3	3	3	3	3	3
LOW DOSE	9.7	77.7	8.1	78.	8.1	10.1
250 mg/kg	1.14	8.05	1.67	2.1	0.71	1.29
	3	3	3	3	3	3
MEDIUM DOSE	8.7	78.6	9.2	71.	8.3	9.1
500 mg/kg	1.06	12.16	2.20	11.4	1.74	0.75
	3	3	3	3	3	3
HIGH DOSE	9.4	83.2	8.8	81.	8.6	9.8
1000 mg/kg	0.21	6.62	0.73	9.0	0.78	1.57
	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	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	9.7	285.	2.9	4.0	52.	5.3	7.2
0 mg/kg	0.83	34.6	0.10	0.38	8.1	0.39	0.97
	3	3	3	3	3	3	3
LOW DOSE	9.7	260.	2.7	3.4	53.	5.4	6.9
250 mg/kg	1.14	33.8	0.27	0.70	9.9	0.41	1.99
	3	3	3	3	3	3	3
MEDIUM DOSE	8.7	230.	2.7	3.0	48.	5.6	6.2
500 mg/kg	1.06	22.5	0.27	0.54	1.5	0.75	0.83
	3	3	3	3	3	3	3
HIGH DOSE	9.4	281.	3.0	3.4	51.	5.4	6.1
1000 mg/kg	0.21	18.0	0.16	0.15	2.1	0.13	0.43
	3	3	3	3	3	3	3

F : ONEWAY ANALYSIS OF VARIANCE SIGNIFICANT AT THE 5% LEVEL
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TABLE 12.2
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FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	WT	A D R E N A L		WT	T H Y R O I D	
			ORG/FBW X10E-5	ORG/BRN X10E-3		ORG/FBW X10E-5	ORG/BRN X10E-3
CONTROL	9.7	1.20	12.4	16.7	0.84	8.7	11.7
0 mg/kg	0.83	0.215	1.24	2.45	0.146	1.48	1.71
	3	3	3	3	3	3	3
LOW DOSE	9.7	1.20	12.4	15.6	0.99	10.4	12.9
250 mg/kg	1.14	0.075	0.77	2.59	0.197	2.61	2.81
	3	3	3	3	3	3	3
MEDIUM DOSE	8.7	1.03	12.1	13.1	0.79	9.2	10.3
500 mg/kg	1.06	0.148	3.03	0.89	0.025	0.96	2.00
	3	3	3	3	3	3	3
HIGH DOSE	9.4	1.09	11.5	13.1	0.81	8.6	9.7
1000 mg/kg	0.21	0.195	1.92	1.51	0.160	1.64	1.19
	3	3	3	3	3	3	3

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 12.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	— P I T U I T A R Y — WT	ORG/FBW X10E-6	ORG/BRN X10E-4	— S T O M A C H — WT	ORG/FBW X10E-3	ORG/BRN X10E-1
CONTROL	9.7	0.073	7.5	10.2	82.4	8.6	11.5
0 mg/kg	0.83	0.0231	1.69	2.95	6.51	0.98	0.74
	3	3	3	3	3	3	3
LOW DOSE	9.7	0.072	7.3	9.4	79.9	8.3	10.4
250 mg/kg	1.14	0.0142	0.57	2.86	10.60	0.86	2.17
	3	3	3	3	3	3	3
MEDIUM DOSE	8.7	0.063	7.4	8.0	81.7	9.5	10.6
500 mg/kg	1.06	0.0108	1.70	0.49	3.74	0.77	1.98
	3	3	3	3	3	3	3
HIGH DOSE	9.4	0.078	8.3	9.5	77.4	8.2	9.3
1000 mg/kg	0.21	0.0095	0.88	1.81	9.20	0.81	1.08
	3	3	3	3	3	3	3

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
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

TABLE 12.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	THY M U S WT ORG/FBW X10E-4	ORG/BRN X10E-2	S A L I V A R Y WT ORG/FBW X10E-3	G L ORG/BRN X10E-1		
CONTROL	9.7	8.0	8.3	11.1	13.5	1.4	1.9 B
0 mg/kg	0.83	2.06	1.94	2.54	0.56	0.06	0.04
	3	3	3	3	3	3	3
LOW DOSE	9.7	10.2	10.5	13.3	14.7	1.5	1.9
250 mg/kg	1.14	2.01	1.51	3.64	3.36	0.22	0.61
	3	3	3	3	3	3	3
MEDIUM DOSE	8.7	7.9	8.8	10.9	11.7	1.4	1.5
500 mg/kg	1.06	4.75	4.20	8.27	0.85	0.26	0.19
	3	3	3	3	3	3	3
HIGH DOSE	9.4	13.0	13.8	15.9	14.4	1.5	1.7
1000 mg/kg	0.21	4.64	4.69	6.22	2.87	0.28	0.24
	3	3	3	3	3	3	3

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 12.2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE ORGAN WEIGHTS (g) AND RATIOS
ARITHMETIC MEANS WITH STANDARD DEVIATIONS AND GROUP SIZES

	FINAL BODY WT kg	WT	O V A R Y		WT	U T E R U S	
			ORG/FBW X10E-5	ORG/BRN X10E-2		ORG/FBW X10E-4	ORG/BRN X10E-2
CONTROL	9.7	1.14	11.6	1.6 B	9.9 B	9.6 B	13.6 B
0 mg/kg	0.83	0.399	3.00	0.51	13.14	12.20	17.77
	3	3	3	3	3	3	3
LOW DOSE	9.7	0.98	10.3	1.3	3.2	3.3	4.1
250 mg/kg	1.14	0.055	1.67	0.07	0.85	1.05	0.97
	3	3	3	3	3	3	3
MEDIUM DOSE	8.7	1.26	14.3	1.7	7.0	7.4	10.1
500 mg/kg	1.06	0.494	3.99	0.95	8.34	8.25	13.15
	3	3	3	3	3	3	3
HIGH DOSE	9.4	0.96	10.1	1.1	3.7	3.9	4.3
1000 mg/kg	0.21	0.140	1.46	0.08	2.27	2.51	2.58
	3	3	3	3	3	3	3

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
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*** : T-TEST AGAINST CONTROL SIGNIFICANT AT THE 0.1% LEVEL

APPENDIX A, TABLE 1

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

MALE BODY WEIGHTS (kg)

INDIVIDUAL VALUES

STUDY DAY	PT	PT	-1	7	14	21	29-30
CONTROL - 0 mg/kg							
84-1996	9.2	9.1	9.1	9.1	9.3	9.3	9.3
84-1997	11.2	11.0	10.7	10.6	11.1	11.2	11.2
84-1998	13.5	13.2	13.3	13.3	13.5	13.5	13.3
LOW DOSE - 250 mg/kg							
84-2002	10.2	10.0	9.8	9.7	10.0	10.0	9.9
84-2003	12.4	12.4	12.1	12.0	12.1	12.2	12.3
84-2004	12.4	12.3	11.8	11.9	12.0	12.1	11.6
MEDIUM DOSE - 500 mg/kg							
84-2008	12.5	12.5	12.2	12.4	12.3	12.9	12.7
84-2009	12.2	12.0	11.9	11.6	11.8	11.7	11.7
84-2010	10.1	10.0	9.9	9.8	9.9	9.9	10.2
HIGH DOSE - 1000 mg/kg							
84-2014	8.4	8.5	8.6	8.5	8.5	8.6	8.7
84-2015	12.6	12.6	12.6	12.5	12.7	13.2	13.1
84-2016	10.7	10.5	10.4	10.2	10.5	10.6	10.7

PT : PRETREATMENT

APPENDIX A, TABLE 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
FEMALE BODY WEIGHT (kg)
INDIVIDUAL VALUES

STUDY DAY	PT	PT	-1	7	14	21	29-30
CONTROL - 0 mg/kg							
84-1999	10.1	10.3	10.2	10.2	10.4	10.5	10.6
84-2000	9.2	9.1	9.1	9.2	9.4	9.5	9.4
84-2001	8.8	8.8	8.9	8.7	9.2	9.1	9.0
LOW DOSE - 250 mg/kg							
84-2005	9.6	9.4	9.1	8.8	9.2	8.8	9.2
84-2006	11.0	10.8	10.8	10.6	10.8	11.3	11.0
84-2007	9.3	9.0	8.9	8.8	9.0	8.9	8.9
MEDIUM DOSE - 500 mg/kg							
84-2011	9.9	9.7	9.2	9.1	9.1	8.9	8.5
84-2012	10.3	10.1	10.2	10.1	10.2	10.0	9.8
84-2013	8.0	7.9	7.7	7.6	7.6	7.7	7.7
HIGH DOSE - 1000 mg/kg							
84-2017	9.2	9.1	8.9	8.9	9.0	9.2	9.2
84-2018	10.5	10.3	9.9	9.8	9.8	9.6	9.5
84-2019	9.6	9.5	9.6	9.6	9.5	9.8	9.6

PT : PRETREATMENT

APPENDIX A, TABLE 2

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

MALE BODY WEIGHT CHANGE (kg) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	-1	7	14	21	29-30
CONTROL - 0 mg/kg					
84-1996	0.0	0.0	0.2	0.0	0.0
84-1997	-0.3	-0.1	0.5	0.1	0.0
84-1998	0.1	0.0	0.2	0.0	-0.2
LOW DOSE - 250 mg/kg					
84-2002	-0.2	-0.1	0.3	0.0	-0.1
84-2003	-0.3	-0.1	0.1	0.1	0.1
84-2004	-0.5	0.1	0.1	0.1	-0.5
MEDIUM DOSE - 500 mg/kg					
84-2008	-0.3	0.2	-0.1	0.6	-0.2
84-2009	-0.1	-0.3	0.2	-0.1	0.0
84-2010	-0.1	-0.1	0.1	0.0	0.3
HIGH DOSE - 1000 mg/kg					
84-2014	0.1	-0.1	0.0	0.1	0.1
84-2015	0.0	-0.1	0.2	0.5	-0.1
84-2016	-0.1	-0.2	0.3	0.1	0.1

APPENDIX A, TABLE 2

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

FEMALE BODY WEIGHT CHANGE (kg) FROM PRECEDING PERIOD

INDIVIDUAL VALUES

STUDY DAY	-1	7	14	21	29-30
CONTROL - 0 mg/kg					
84-1999	-0.1	0.0	0.2	0.1	0.1
84-2000	0.0	0.1	0.2	0.1	-0.1
84-2001	0.1	-0.2	0.5	-0.1	-0.1
LOW DOSE - 250 mg/kg					
84-2005	-0.3	-0.3	0.4	-0.4	0.4
84-2006	0.0	-0.2	0.2	0.5	-0.3
84-2007	-0.1	-0.1	0.2	-0.1	0.0
MEDIUM DOSE - 500 mg/kg					
84-2011	-0.5	-0.1	0.0	-0.2	-0.4
84-2012	0.1	-0.1	0.1	-0.2	-0.2
84-2013	-0.2	-0.1	0.0	0.1	0.0
HIGH DOSE - 1000 mg/kg					
84-2017	-0.2	0.0	0.1	0.2	0.0
84-2018	-0.4	-0.1	0.0	-0.2	-0.1
84-2019	0.1	0.0	-0.1	0.3	-0.2

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	-16	-15	-14	-13	-12	-11	-10	-9
CONTROL - 0 mg/kg								
84-1996	88.	179.	188.	258.	205.	236.	265.	304.
84-1997	198.	252.	209.	238.	221.	221.	274.	301.
84-1998	181.	145.	303.	278.	349.	321.	347.	372.
LOW DOSE - 250 mg/kg								
84-2002	158.	167.	254.	242.	208.	181.	277.	254.
84-2003	287.	284.	210.	304.	239.	330.	276.	307.
84-2004	175.	162.	249.	261.	172.	260.	323.	240.
MEDIUM DOSE - 500 mg/kg								
84-2008	215.	261.	373.	279.	257.	401.	309.	270.
84-2009	133.	159.	231.	209.	217.	174.	299.	253.
84-2010	276.	201.	305.	216.	210.	263.	295.	309.
HIGH DOSE - 1000 mg/kg								
84-2014	218.	215.	262.	252.	201.	209.	297.	273.
84-2015	338.	354.	186.	435.	259.	408.	339.	271.
84-2016	176.	211.	269.	261.	202.	226.	305.	340.

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	-8	-7	-6	-5	-4	-3	-2	-1
CONTROL - 0 mg/kg								
84-1996	189.	276.	228.	233.	206.	250.	277.	239.
84-1997	245.	325.	246.	220.	254.	287.	337.	241.
84-1998	331.	400.	303.	270.	309.	393.	198.	307.
LOW DOSE - 250 mg/kg								
84-2002	280.	307.	103.	267.	220.	305.	198.	208.
84-2003	237.	342.	199.	196.	165.	266.	244.	258.
84-2004	218.	201.	160.	195.	172.	294.	191.	162.
MEDIUM DOSE - 500 mg/kg								
84-2008	227.	316.	124.	260.	159.	217.	177.	199.
84-2009	188.	299.	194.	220.	230.	215.	236.	218.
84-2010	99.	359.	216.	203.	218.	310.	219.	151.
HIGH DOSE - 1000 mg/kg								
84-2014	277.	276.	ND	187.	255.	364.	476.	ND
84-2015	354.	400.	298.	105.	278.	397.	200.	199.
84-2016	243.	314.	172.	200.	211.	326.	199.	251.

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	1	2	3	4	5	6	7
CONTROL - 0 mg/kg							
84-1996	250.	296.	233.	242.	277.	266.	282.
84-1997	312.	317.	266.	230.	380.	325.	256.
84-1998	353.	430.	248.	374.	432.	266.	323.
LOW DOSE - 250 mg/kg							
84-2002	195.	354.	201.	301.	335.	261.	311.
84-2003	295.	347.	263.	236.	347.	280.	245.
84-2004	276.	234.	251.	273.	294.	351.	254.
MEDIUM DOSE - 500 mg/kg							
84-2008	393.	243.	244.	264.	498.	243.	269.
84-2009	199.	237.	168.	216.	287.	210.	259.
84-2010	161.	ND	204.	284.	292.	177.	196.
HIGH DOSE - 1000 mg/kg							
84-2014	ND	272.	245.	187.	162.	310.	313.
84-2015	403.	251.	300.	405.	329.	252.	552.
84-2016	285.	298.	146.	251.	292.	180.	294.

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	8	9	10	11	12	13	14
CONTROL - 0 mg/kg							
84-1996	309.	302.	300.	302.	295.	282.	260.
84-1997	341.	412.	292.	366.	337.	346.	348.
84-1998	266.	402.	387.	265.	434.	431.	362.
LOW DOSE - 250 mg/kg							
84-2002	337.	385.	365.	332.	326.	270.	349.
84-2003	322.	511.	242.	287.	266.	343.	325.
84-2004	336.	275.	320.	277.	264.	342.	275.
MEDIUM DOSE - 500 mg/kg							
84-2008	248.	418.	246.	467.	225.	196.	337.
84-2009	231.	316.	294.	273.	249.	358.	262.
84-2010	193.	385.	148.	400.	330.	192.	347.
HIGH DOSE - 1000 mg/kg							
84-2014	225.	288.	229.	450.	204.	331.	233.
84-2015	249.	555.	301.	487.	223.	251.	433.
84-2016	322.	322.	276.	323.	304.	293.	290.

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	15	16	17	18	19	20	21
CONTROL - 0 mg/kg							
84-1996	197.	294.	274.	311.	274.	292.	317.
84-1997	282.	338.	309.	387.	366.	394.	311.
84-1998	271.	358.	270.	431.	563.	269.	496.
LOW DOSE - 250 mg/kg							
84-2002	209.	257.	254.	323.	395.	240.	215.
84-2003	272.	318.	126.	439.	326.	319.	355.
84-2004	268.	251.	167.	289.	367.	336.	146.
MEDIUM DOSE - 500 mg/kg							
84-2008	201.	219.	244.	378.	557.	461.	245.
84-2009	243.	294.	225.	276.	317.	233.	247.
84-2010	188.	176.	169.	372.	330.	197.	458.
HIGH DOSE - 1000 mg/kg							
84-2014	207.	257.	309.	337.	327.	287.	335.
84-2015	254.	254.	254.	429.	316.	480.	444.
84-2016	256.	299.	211.	287.	298.	258.	270.

APPENDIX B

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

MALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	22	23	24	25	26	27	28	29
CONTROL - 0 mg/kg								
84-1996	296.	316.	211.	256.	330.	237.	266.	252.
84-1997	300.	348.	312.	342.	348.	389.	245.	310.
84-1998	375.	269.	267.	190.	356.	386.	217.	DEAD
LOW DOSE - 250 mg/kg								
84-2002	393.	406.	256.	328.	348.	355.	182.	DEAD
84-2003	389.	376.	310.	362.	308.	400.	262.	325.
84-2004	342.	306.	197.	286.	259.	306.	174.	DEAD
MEDIUM DOSE - 500 mg/kg								
84-2008	421.	471.	163.	288.	514.	288.	195.	215.
84-2009	250.	305.	316.	288.	312.	293.	253.	DEAD
84-2010	196.	441.	232.	304.	413.	304.	173.	399.
HIGH DOSE - 1000 mg/kg								
84-2014	367.	342.	200.	236.	299.	307.	217.	304.
84-2015	350.	266.	263.	368.	316.	456.	264.	DEAD
84-2016	349.	351.	285.	300.	373.	307.	211.	DEAD

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	-16	-15	-14	-13	-12	-11	-10	-9
CONTROL - 0 mg/kg								
84-1999	248.	214.	232.	273.	225.	284.	335.	316.
84-2000	138.	216.	218.	192.	240.	267.	224.	232.
84-2001	171.	121.	168.	288.	193.	262.	266.	184.
LOW DOSE - 250 mg/kg								
84-2005	23.	146.	105.	86.	174.	210.	212.	118.
84-2006	212.	144.	210.	217.	160.	266.	276.	243.
84-2007	162.	173.	186.	226.	172.	216.	252.	225.
MEDIUM DOSE - 500 mg/kg								
84-2011	139.	228.	185.	173.	200.	232.	222.	232.
84-2012	140.	147.	0.	202.	195.	176.	196.	173.
84-2013	94.	161.	227.	127.	113.	182.	261.	235.
HIGH DOSE - 1000 mg/kg								
84-2017	191.	201.	179.	213.	173.	246.	263.	242.
84-2018	149.	282.	196.	193.	290.	233.	ND	235.
84-2019	216.	193.	ND	295.	275.	213.	300.	273.

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	-8	-7	-6	-5	-4	-3	-2	-1
CONTROL - 0 mg/kg								
84-1999	255.	267.	235.	278.	237.	247.	234.	251.
84-2000	204.	304.	178.	175.	188.	361.	309.	276.
84-2001	228.	268.	165.	218.	234.	226.	293.	265.
LOW DOSE - 250 mg/kg								
84-2005	56.	190.	72.	70.	72.	179.	168.	148.
84-2006	177.	218.	173.	150.	127.	220.	348.	182.
84-2007	212.	233.	198.	177.	185.	222.	201.	200.
MEDIUM DOSE - 500 mg/kg								
84-2011	255.	196.	185.	173.	171.	217.	177.	106.
84-2012	106.	193.	185.	148.	139.	223.	254.	206.
84-2013	208.	197.	164.	87.	233.	208.	136.	128.
HIGH DOSE - 1000 mg/kg								
84-2017	219.	269.	167.	119.	160.	174.	232.	150.
84-2018	315.	240.	199.	203.	111.	193.	186.	200.
84-2019	224.	351.	226.	149.	100.	372.	319.	154.

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	1	2	3	4	5	6	7
CONTROL - 0 mg/kg							
84-1999	217.	268.	224.	220.	281.	283.	242.
84-2000	344.	429.	262.	260.	348.	324.	347.
84-2001	251.	297.	196.	248.	302.	146.	264.
LOW DOSE - 250 mg/kg							
84-2005	148.	85.	94.	126.	178.	179.	277.
84-2006	430.	195.	300.	306.	241.	216.	364.
84-2007	235.	348.	178.	226.	373.	224.	274.
MEDIUM DOSE - 500 mg/kg							
84-2011	185.	181.	182.	151.	207.	146.	187.
84-2012	134.	236.	208.	201.	313.	213.	303.
84-2013	164.	330.	208.	120.	227.	301.	227.
HIGH DOSE - 1000 mg/kg							
84-2017	226.	286.	235.	234.	296.	245.	242.
84-2018	295.	267.	186.	290.	353.	273.	297.
84-2019	347.	349.	191.	300.	190.	420.	346.

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	8	9	10	11	12	13	14
CONTROL - 0 mg/kg							
84-1999	335.	312.	289.	319.	275.	277.	299.
84-2000	423.	427.	298.	313.	346.	312.	374.
84-2001	249.	338.	251.	290.	253.	306.	276.
LOW DOSE - 250 mg/kg							
84-2005	247.	252.	171.	286.	223.	261.	132.
84-2006	178.	311.	386.	384.	229.	192.	323.
84-2007	273.	408.	267.	266.	284.	275.	265.
MEDIUM DOSE - 500 mg/kg							
84-2011	129.	234.	156.	279.	197.	229.	191.
84-2012	262.	200.	256.	312.	218.	181.	185.
84-2013	188.	361.	251.	316.	200.	202.	260.
HIGH DOSE - 1000 mg/kg							
84-2017	261.	283.	284.	306.	283.	277.	245.
84-2018	266.	357.	297.	365.	252.	329.	230.
84-2019	246.	333.	190.	366.	270.	190.	190.

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	15	16	17	18	19	20	21
CONTROL - 0 mg/kg							
84-1999	280.	289.	237.	305.	306.	348.	324.
84-2000	258.	321.	176.	343.	380.	317.	383.
84-2001	153.	286.	205.	262.	243.	298.	267.
LOW DOSE - 250 mg/kg							
84-2005	130.	166.	111.	231.	282.	153.	212.
84-2006	280.	237.	130.	366.	426.	355.	244.
84-2007	236.	244.	221.	352.	304.	258.	354.
MEDIUM DOSE - 500 mg/kg							
84-2011	162.	210.	110.	297.	240.	210.	194.
84-2012	178.	150.	166.	255.	265.	190.	0.
84-2013	279.	230.	219.	234.	305.	269.	293.
HIGH DOSE - 1000 mg/kg							
84-2017	259.	245.	207.	350.	319.	249.	233.
84-2018	245.	245.	201.	234.	343.	324.	289.
84-2019	187.	326.	350.	189.	189.	449.	189.

APPENDIX B

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

FEMALE FEED CONSUMPTION (g)

INDIVIDUAL VALUES

STUDY DAY	22	23	24	25	26	27	28	29
CONTROL - 0 mg/kg								
84-1999	301.	309.	251.	234.	370.	225.	214.	203.
84-2000	311.	420.	144.	301.	360.	318.	199.	DEAD
84-2001	261.	277.	173.	289.	306.	134.	194.	DEAD
LOW DOSE - 250 mg/kg								
84-2005	268.	229.	239.	233.	297.	245.	108.	218.
84-2006	324.	393.	261.	285.	387.	314.	111.	DEAD
84-2007	241.	284.	215.	225.	295.	286.	217.	240.
MEDIUM DOSE - 500 mg/kg								
84-2011	254.	335.	122.	201.	304.	241.	134.	DEAD
84-2012	257.	266.	221.	144.	236.	301.	127.	195.
84-2013	163.	353.	176.	159.	331.	281.	141.	DEAD
HIGH DOSE - 1000 mg/kg								
84-2017	309.	318.	206.	263.	318.	307.	242.	237.
84-2018	299.	ND	191.	323.	416.	364.	227.	DEAD
84-2019	388.	194.	194.	333.	320.	393.	194.	195.

APPENDIX C

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

INDIVIDUAL VALUES

WATER CONSUMPTION (mL)

STUDY DAY 22-23

CONTROL - 0 mg/kg

MALES

84-1996	750
84-1997	950
84-1998	1450

FEMALES

84-1999	1800
84-2000	1450
84-2001	850

LOW DOSE - 250 mg/kg

MALES

84-2002	1200
84-2003	1300
84-2004	1250

FEMALES

84-2005	700
84-2006	650
84-2007	800

MEDIUM DOSE - 500 mg/kg

MALES

84-2008	750
84-2009	1000
84-2010	1200

FEMALES

84-2011	900
84-2012	100
84-2013	600

HIGH DOSE - 1000 mg/kg

MALES

84-2014	1650
84-2015	3550
84-2016	1250

FEMALES

84-2017	550
84-2018	1100
84-2019	2000

APPENDIX D

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

MALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	1	2	3	4	5	6	7
LOW DOSE - 250 mg/kg							
84-2002	249.	247.	208.	249.	247.	245.	247.
84-2003	247.	248.	232.	233.	248.	247.	249.
84-2004	218.	197.	181.	215.	250.	199.	219.
MEDIUM DOSE - 500 mg/kg							
84-2008	500.	498.	498.	498.	498.	498.	496.
84-2009	277.	382.	239.	376.	496.	387.	420.
84-2010	407.	ND	417.	475.	480.	447.	495.
HIGH DOSE - 1000 mg/kg							
84-2014	ND	419.	407.	855.	436.	733.	994.
84-2015	996.	992.	1000.	996.	996.	996.	1000.
84-2016	976.	971.	702.	774.	933.	865.	966.

APPENDIX D

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

MALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	8	9	10	11	12	13	14
LOW DOSE - 250 mg/kg							
84-2002	249.	249.	247.	247.	237.	246.	246.
84-2003	249.	249.	238.	247.	248.	248.	230.
84-2004	230.	248.	245.	236.	190.	233.	167.
MEDIUM DOSE - 500 mg/kg							
84-2008	500.	500.	496.	498.	454.	353.	478.
84-2009	358.	498.	455.	496.	407.	364.	425.
84-2010	492.	495.	378.	495.	492.	490.	408.
HIGH DOSE - 1000 mg/kg							
84-2014	1000.	994.	994.	1000.	1000.	994.	994.
84-2015	996.	996.	1000.	996.	888.	996.	1000.
84-2016	956.	971.	868.	946.	779.	863.	755.

APPENDIX D

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

MALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	15	16	17	18	19	20	21
LOW DOSE - 250 mg/kg							
84-2002	171.	184.	239.	250.	245.	246.	206.
84-2003	228.	202.	130.	250.	248.	240.	248.
84-2004	172.	139.	152.	245.	249.	246.	133.
MEDIUM DOSE - 500 mg/kg							
84-2008	280.	297.	496.	498.	498.	500.	498.
84-2009	413.	254.	356.	462.	394.	392.	439.
84-2010	475.	444.	427.	497.	495.	497.	497.
HIGH DOSE - 1000 mg/kg							
84-2014	994.	988.	876.	418.	1000.	994.	994.
84-2015	1000.	1000.	996.	1000.	1000.	1000.	992.
84-2016	843.	629.	719.	871.	843.	967.	981.

APPENDIX D

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

MALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	22	23	24	25	26	27	28	29
LOW DOSE - 250 mg/kg								
84-2002	250.	246.	168.	210.	241.	229.	144.	DEAD
84-2003	247.	248.	216.	244.	248.	241.	163.	219.
84-2004	238.	193.	140.	162.	200.	208.	180.	DEAD
MEDIUM DOSE - 500 mg/kg								
84-2008	502.	500.	0.	500.	498.	393.	159.	283.
84-2009	389.	474.	318.	417.	410.	357.	327.	DEAD
84-2010	495.	495.	348.	482.	492.	442.	409.	429.
HIGH DOSE - 1000 mg/kg								
84-2014	994.	994.	988.	994.	994.	994.	1000.	988.
84-2015	996.	1000.	996.	996.	1000.	1000.	1000.	DEAD
84-2016	995.	991.	533.	896.	953.	943.	448.	DEAD

APPENDIX D

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

FEMALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	1	2	3	4	5	6	7
LOW DOSE - 250 mg/kg							
84-2005	118.	117.	129.	173.	245.	246.	246.
84-2006	236.	171.	144.	189.	138.	194.	221.
84-2007	249.	249.	250.	250.	249.	250.	250.
MEDIUM DOSE - 500 mg/kg							
84-2011	500.	492.	323.	318.	429.	283.	291.
84-2012	328.	495.	355.	490.	498.	456.	471.
84-2013	497.	494.	380.	386.	490.	490.	445.
HIGH DOSE - 1000 mg/kg							
84-2017	989.	989.	893.	994.	1000.	994.	1000.
84-2018	990.	990.	934.	995.	990.	995.	990.
84-2019	995.	995.	995.	1000.	990.	995.	995.

APPENDIX D

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

FEMALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	8	9	10	11	12	13	14
LOW DOSE - 250 mg/kg							
84-2005	247.	247.	243.	249.	205.	193.	188.
84-2006	189.	235.	217.	164.	63.	158.	160.
84-2007	250.	250.	250.	249.	249.	247.	249.
MEDIUM DOSE - 500 mg/kg							
84-2011	341.	418.	346.	492.	239.	335.	195.
84-2012	446.	495.	495.	490.	359.	240.	386.
84-2013	500.	493.	493.	500.	332.	408.	487.
HIGH DOSE - 1000 mg/kg							
84-2017	994.	994.	1000.	1000.	994.	994.	910.
84-2018	995.	1000.	995.	995.	990.	990.	995.
84-2019	995.	990.	990.	990.	990.	990.	990.

APPENDIX D

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

FEMALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	15	16	17	18	19	20	21
LOW DOSE - 250 mg/kg							
84-2005	177.	136.	151.	208.	230.	207.	186.
84-2006	145.	117.	150.	241.	244.	192.	93.
84-2007	247.	238.	217.	249.	249.	249.	250.
MEDIUM DOSE - 500 mg/kg							
84-2011	184.	225.	242.	500.	272.	242.	409.
84-2012	287.	218.	306.	498.	495.	466.	0.
84-2013	411.	421.	484.	497.	490.	480.	431.
HIGH DOSE - 1000 mg/kg							
84-2017	994.	994.	989.	994.	1000.	994.	994.
84-2018	990.	923.	770.	1000.	995.	995.	995.
84-2019	984.	995.	989.	995.	995.	995.	995.

APPENDIX D

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

FEMALE DOSAGE (mg/kg)

INDIVIDUAL VALUES

STUDY DAY	22	23	24	25	26	27	28	29
LOW DOSE - 250 mg/kg								
84-2005	199.	0.	97.	149.	165.	89.	153.	179.
84-2006	217.	240.	139.	146.	198.	145.	10.	DEAD
84-2007	249.	249.	247.	249.	249.	250.	219.	249.
MEDIUM DOSE - 500 mg/kg								
84-2011	379.	444.	213.	298.	354.	239.	261.	DEAD
84-2012	475.	493.	0.	247.	455.	430.	318.	313.
84-2013	0.	461.	0.	490.	347.	448.	123.	DEAD
HIGH DOSE - 1000 mg/kg								
84-2017	1000.	995.	533.	995.	995.	995.	571.	739.
84-2018	995.	990.	786.	828.	854.	792.	594.	DEAD
84-2019	995.	990.	990.	995.	995.	1000.	990.	990.

APPENDIX E

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

INDIVIDUAL VALUES

RECTAL TEMPERATURES (DEGREES CENTIGRADE)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	38.9	39.0	38.8	38.6
84-1997	38.0	39.0	39.3	38.7
84-1998	39.0	38.1	38.8	38.6
FEMALES				
84-1999	39.2	39.1	38.8	38.9
84-2000	38.5	39.2	38.7	39.2
84-2001	38.2	38.7	37.9	39.0
LOW DOSE - 250 mg/kg				
MALES				
84-2002	39.2	39.0	38.8	39.1
84-2003	38.5	38.9	38.5	38.7
84-2004	38.8	39.0	38.9	39.1
FEMALES				
84-2005	39.0	39.3	39.0	38.6
84-2006	39.0	39.0	38.6	38.7
84-2007	39.0	38.9	38.7	38.9
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	39.0	39.2	38.6	38.4
84-2009	38.8	39.9	38.6	38.8
84-2010	38.5	39.0	39.1	39.1
FEMALES				
84-2011	38.5	39.1	38.7	39.3
84-2012	38.9	38.8	38.5	38.0
84-2013	39.0	38.8	38.8	38.7
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	39.0	38.9	38.7	38.8
84-2015	38.0	38.9	39.2	39.0
84-2016	38.1	38.5	38.7	38.9
FEMALES				
84-2017	39.0	39.0	38.6	38.4
84-2018	39.0	39.0	38.6	39.2
84-2019	39.0	38.7	38.7	38.9

PT : PRETREATMENT

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APPENDIX F, TABLE 1

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

ALANINE AMINOTRANSFERASE (U/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	21	23	29	31
84-1997	49	33	39	36
84-1998	23	31	21	20
FEMALES				
84-1999	20	26	23	18
84-2000	24	27	24	25
84-2001	29	31	38	35
LOW DOSE- 250 mg/kg				
MALES				
84-2002	26	37	26	25
84-2003	20	22	20	20
84-2004	24	24	28	32
FEMALES				
84-2005	29	39	32	36
84-2006	25	27	26	28
84-2007	30	30	32	31
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	33	33	33	32
84-2009	24	22	22	21
84-2010	24	21	23	21
FEMALES				
84-2011	21	17	18	20
84-2012	22	17	20	18
84-2013	27	22	27	32
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	18	19	18	17
84-2015	25	24	24	28
84-2016	25	21	20	23
FEMALES				
84-2017	36	20	27	30
84-2018	29	25	24	26
84-2019	25	22	24	24

PT : PRETREATMENT

APPENDIX F, TABLE 2

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

ASPARTATE AMINOTRANSFERASE (U/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	23	18	23	22
84-1997	25	21	24	25
84-1998	15	23	15	15
FEMALES				
84-1999	15	21	14	15
84-2000	24	26	26	25
84-2001	20	20	22	24
LOW DOSE- 250 mg/kg				
MALES				
84-2002	21	30	19	20
84-2003	23	21	18	20
84-2004	21	20	17	20
FEMALES				
84-2005	21	44	21	22
84-2006	22	20	23	25
84-2007	24	17	17	21
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	24	20	22	21
84-2009	19	16	17	19
84-2010	27	19	19	18
FEMALES				
84-2011	20	11	15	19
84-2012	24	20	21	19
84-2013	25	20	23	23
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	18	21	16	18
84-2015	20	15	17	18
84-2016	21	20	19	22
FEMALES				
84-2017	25	19	20	22
84-2018	19	21	19	21
84-2019	20	23	21	21

PT : PRETREATMENT

APPENDIX F, TABLE 3

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

ALKALINE PHOSPHATASE (U/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	48	35	35	29
84-1997	51	37	36	45
84-1998	60	53	42	39
FEMALES				
84-1999	44	33	34	31
84-2000	65	56	70	69
84-2001	51	42	44	49
LOW DOSE- 250 mg/kg				
MALES				
84-2002	52	38	42	40
84-2003	33	31	29	29
84-2004	55	41	37	33
FEMALES				
84-2005	43	38	41	38
84-2006	37	28	26	27
84-2007	55	48	47	56
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	54	45	44	45
84-2009	51	38	37	39
84-2010	69	46	47	42
FEMALES				
84-2011	50	38	40	39
84-2012	60	51	42	42
84-2013	42	25	33	31
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	34	31	27	25
84-2015	34	29	29	30
84-2016	52	38	39	40
FEMALES				
84-2017	43	31	31	31
84-2018	60	46	61	64
84-2019	59	57	63	64

PT : PRETREATMENT

APPENDIX F, TABLE 4

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

CHOLESTEROL (nmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	3.3	2.9	2.9	3.2
84-1997	3.0	2.7	3.2	4.3
84-1998	4.3	4.1	3.5	4.0
FEMALES				
84-1999	3.2	2.3	2.9	3.8
84-2000	3.1	2.8	3.1	3.5
84-2001	4.4	3.9	4.3	4.8
LOW DOSE- 250 mg/kg				
MALES				
84-2002	3.3	2.4	2.8	3.2
84-2003	3.0	2.8	2.9	3.3
84-2004	3.2	2.8	2.9	3.2
FEMALES				
84-2005	3.6	3.9	2.8	3.6
84-2006	2.5	2.0	2.1	2.5
84-2007	3.8	3.0	3.6	4.1
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	3.8	3.0	3.4	4.1
84-2009	3.4	2.9	3.0	3.3
84-2010	4.1	3.4	4.0	4.3
FEMALES				
84-2011	2.4	2.5	2.1	2.5
84-2012	3.8	2.9	3.3	4.6
84-2013	2.9	2.4	3.3	3.4
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	3.2	3.5	2.7	3.3
84-2015	3.0	2.7	2.9	3.4
84-2016	3.1	3.1	3.3	3.5
FEMALES				
84-2017	3.7	2.6	3.4	4.3
84-2018	4.1	3.1	3.3	3.5
84-2019	2.8	3.0	3.3	3.6

PT : PRETREATMENT

APPENDIX F, TABLE 5

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

TOTAL BILIRUBIN (nmol/L)

STUDY DAY	PT	1	12	12a	15	28
CONTROL - 0 mg/kg						
MALES						
84-1996	1.5	1.7	5.6	5.2	5.4	3.3
84-1997	2.3	3.1	4.4	3.4	7.7	5.1
84-1998	1.5	3.2	3.3	3.8	3.9	2.9
FEMALES						
84-1999	0.6	3.0	10.3	9.8	7.9	6.3
84-2000	2.7	3.3	4.2	5.0	5.2	5.5
84-2001	2.7	2.8	6.8	7.5	7.6	5.2
LOW DOSE- 250 mg/kg						
MALES						
84-2002	1.7	2.7	6.2	4.7	5.2	4.8
84-2003	2.1	2.1	4.4	3.2	4.4	2.7
84-2004	3.1	2.9	4.5	3.3	3.1	3.1
FEMALES						
84-2005	2.8	4.0	8.2	7.1	5.7	4.0
84-2006	0.3	2.1	5.8	5.9	5.0	5.2
84-2007	2.4	2.1	4.1	4.0	4.2	4.7
MEDIUM DOSE- 500 mg/kg						
MALES						
84-2008	2.2	1.8	5.4	5.3	5.9	5.0
84-2009	2.5	2.4	2.3	2.4	2.7	3.0
84-2010	2.0	3.9	6.4	6.3	6.0	4.5
FEMALES						
84-2011	2.3	2.4	7.5	6.2	1.9	6.4
84-2012	3.1	1.7	4.6	3.7	5.8	3.9
84-2013	4.3	2.7	7.7	8.3	8.9	5.7
HIGH DOSE- 1000 mg/kg						
MALES						
84-2014	2.4	1.9	6.7	7.4	4.3	5.1
84-2015	2.9	2.1	5.3	4.1	5.8	5.1
84-2016	1.8	3.2	4.2	4.6	3.6	3.9
FEMALES						
84-2017	2.9	1.3	4.0	3.1	3.4	4.3
84-2018	3.1	2.6	5.2	4.8	6.1	6.5
84-2019	2.5	3.3	6.0	6.1	5.5	4.3

PT : PRETREATMENT
a : REANALYSIS OF SERUM COLLECTED DAY 12

APPENDIX F, TABLE 6

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

GLUCOSE (mmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	5.7	4.9	3.6	4.5
84-1997	6.1	5.1	6.1	4.5
84-1998	5.9	9.6	4.8	5.3
FEMALES				
84-1999	4.5	5.7	4.6	4.9
84-2000	5.7	4.9	4.8	4.1
84-2001	5.9	5.4	5.1	5.6
LOW DOSE- 250 mg/kg				
MALES				
84-2002	5.2	4.8	4.8	5.0
84-2003	6.1	6.0	5.3	5.4
84-2004	5.9	5.4	5.4	5.3
FEMALES				
84-2005	5.2	5.9	3.7	4.9
84-2006	5.1	5.2	4.1	4.5
84-2007	5.4	5.2	5.1	5.0
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	5.3	4.7	5.3	4.8
84-2009	5.1	4.6	5.1	4.6
84-2010	5.4	5.6	5.1	6.4
FEMALES				
84-2011	5.6	5.1	4.8	5.6
84-2012	4.9	4.6	5.0	4.9
84-2013	4.7	4.8	5.2	4.3
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	5.2	4.5	4.2	4.2
84-2015	4.7	4.7	4.1	5.1
84-2016	5.7	5.2	5.1	4.3
FEMALES				
84-2017	5.5	5.1	4.5	5.0
84-2018	4.5	4.8	5.0	5.5
84-2019	5.7	4.4	4.1	4.7

PT : PRETREATMENT

APPENDIX F, TABLE 7

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

UREA (nmol/L)

STUDY DAY	PT	1	12	12o	15	28
CONTROL - 0 mg/kg						
MALES						
84-1996	5.5	4.9	13.5	12.6	12.1	11.2
84-1997	2.8	4.4	10.2	10.3	10.2	8.9
84-1998	2.8	3.4	9.0	9.0	9.5	8.3
FEMALES						
84-1999	2.8	3.0	8.5	8.1	8.8	6.9
84-2000	4.0	5.4	11.0	12.2	13.1	11.6
84-2001	3.0	3.4	9.4	9.2	9.4	8.8
LOW DOSE- 250 mg/kg						
MALES						
84-2002	2.8	3.9	9.3	9.1	9.3	8.0
84-2003	2.9	3.4	9.2	8.9	10.5	9.1
84-2004	3.2	4.2	8.2	8.4	9.5	7.6
FEMALES						
84-2005	4.8	3.2	10.3	9.9	9.0	8.8
84-2006	3.0	2.8	8.6	8.6	7.9	5.8
84-2007	3.3	3.8	9.3	9.6	10.1	9.1
MEDIUM DOSE- 500 mg/kg						
MALES						
84-2008	4.0	3.6	9.6	9.1	8.9	7.7
84-2009	3.6	3.8	9.8	9.6	10.4	8.6
84-2010	2.5	3.3	9.5	9.7	9.7	9.1
FEMALES						
84-2011	2.6	3.0	9.1	8.4	7.6	8.1
84-2012	2.8	3.9	9.1	8.9	9.2	8.1
84-2013	3.6	3.8	9.1	9.0	10.7	8.7
HIGH DOSE- 1000 mg/kg						
MALES						
84-2014	4.3	4.7	10.8	10.4	11.9	10.2
84-2015	3.4	3.2	9.3	9.3	8.0	8.6
84-2016	2.6	3.2	9.3	9.3	9.0	7.0
FEMALES						
84-2017	3.3	3.3	10.2	9.9	9.5	9.3
84-2018	3.3	4.0	9.8	10.9	11.3	10.2
84-2019	2.7	3.5	8.0	7.6	8.4	8.2

PT : PRETREATMENT
o : REANALYSIS OF SERUM COLLECTED DAY 12

APPENDIX F, TABLE 8

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

CREATININE (mmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	59	63	61	64
84-1997	64	60	67	63
84-1998	77	88	65	65
FEMALES				
84-1999	58	61	53	56
84-2000	79	73	68	77
84-2001	62	63	64	66
LOW DOSE- 250 mg/kg				
MALES				
84-2002	59	58	61	59
84-2003	60	70	60	66
84-2004	68	74	67	72
FEMALES				
84-2005	81	81	76	76
84-2006	60	57	53	55
84-2007	70	59	59	65
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	70	76	68	69
84-2009	68	65	62	71
84-2010	59	56	43	62
FEMALES				
84-2011	62	69	65	61
84-2012	83	79	67	70
84-2013	64	56	53	57
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	75	76	68	74
84-2015	65	66	61	67
84-2016	63	59	57	62
FEMALES				
84-2017	65	70	67	67
84-2018	54	72	68	69
84-2019	55	55	58	60

PT : PRETREATMENT

APPENDIX F, TABLE 9

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

SODIUM (mmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	146	145	145	145
84-1997	151	146	145	149
84-1998	148	154	147	147
FEMALES				
84-1999	146	145	143	144
84-2000	144	147	147	151
84-2001	147	148	150	145
LOW DOSE- 250 mg/kg				
MALES				
84-2002	146	144	143	146
84-2003	146	147	146	148
84-2004	151	146	144	144
FEMALES				
84-2005	147	155	148	146
84-2006	146	149	146	145
84-2007	145	147	151	148
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	147	146	145	146
84-2009	149	149	145	152
84-2010	147	143	145	141
FEMALES				
84-2011	144	146	146	147
84-2012	148	149	147	147
84-2013	147	146	147	153
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	149	144	143	142
84-2015	148	149	145	144
84-2016	148	147	147	150
FEMALES				
84-2017	143	144	142	145
84-2018	146	150	148	151
84-2019	149	147	150	146

PT : PRETREATMENT

APPENDIX F, TABLE 10

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

POTASSIUM (nmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	4.8	4.8	4.7	4.7
84-1997	5.2	4.8	4.8	4.9
84-1998	4.6	4.0	4.8	4.7
FEMALES				
84-1999	4.0	4.4	4.7	4.7
84-2000	4.8	4.9	5.0	5.4
84-2001	4.4	4.2	5.2	4.2
LOW DOSE- 250 mg/kg				
MALES				
84-2002	4.3	4.3	4.4	4.7
84-2003	5.3	4.3	5.1	4.6
84-2004	5.1	4.8	4.7	4.6
FEMALES				
84-2005	4.2	6.4	4.6	4.6
84-2006	4.4	4.5	4.8	4.5
84-2007	4.3	4.1	4.8	4.4
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	4.6	4.8	5.0	4.8
84-2009	4.9	4.4	5.1	5.1
84-2010	4.5	4.4	4.8	4.5
FEMALES				
84-2011	4.2	4.3	4.8	5.1
84-2012	5.5	4.8	5.0	4.9
84-2013	4.9	4.4	4.8	4.9
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	4.7	4.8	5.6	5.4
84-2015	4.5	4.4	5.0	4.9
84-2016	5.0	4.6	5.2	4.5
FEMALES				
84-2017	4.5	4.4	4.9	4.7
84-2018	4.5	4.7	5.0	4.8
84-2019	4.1	4.4	4.2	4.4

PT : PRETREATMENT

APPENDIX F, TABLE 11

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

CHLORIDE (mmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	116	113	111	109
84-1997	113	111	111	112
84-1998	115	114	110	110
FEMALES				
84-1999	111	109	110	109
84-2000	110	109	111	109
84-2001	112	109	114	110
LOW DOSE- 250 mg/kg				
MALES				
84-2002	112	112	109	111
84-2003	113	110	114	111
84-2004	113	111	112	109
FEMALES				
84-2005	115	117	109	109
84-2006	111	109	108	108
84-2007	112	109	113	111
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	112	115	112	112
84-2009	115	113	116	113
84-2010	112	108	112	111
FEMALES				
84-2011	115	116	114	115
84-2012	113	113	105	111
84-2013	113	113	113	112
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	113	114	111	111
84-2015	112	112	114	112
84-2016	111	108	115	109
FEMALES				
84-2017	114	116	109	104
84-2018	115	112	116	113
84-2019	112	109	113	109

PT : PRETREATMENT

APPENDIX F, TABLE 12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
INDIVIDUAL VALUES
CALCIUM (nmol/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	2.79	2.70	2.71	2.53
84-1997	2.71	2.73	2.64	2.62
84-1998	2.76	2.80	2.63	2.50
FEMALES				
84-1999	2.68	2.61	2.76	2.56
84-2000	2.76	2.63	2.63	2.56
84-2001	2.80	2.74	2.79	2.57
LOW DOSE- 250 mg/kg				
MALES				
84-2002	2.69	2.51	2.64	2.53
84-2003	2.80	2.52	2.59	2.47
84-2004	2.80	2.66	2.64	2.58
FEMALES				
84-2005	2.74	3.00	2.80	2.68
84-2006	2.67	2.66	2.65	2.61
84-2007	2.78	2.63	2.66	2.55
MEDIUM DOSE- 500 mg/kg				
MALES				
84-2008	2.73	2.62	2.71	2.64
84-2009	2.77	2.55	2.55	2.58
84-2010	2.75	2.52	2.64	2.49
FEMALES				
84-2011	2.70	2.60	2.63	2.35
84-2012	2.81	2.65	2.66	2.64
84-2013	2.64	2.46	2.56	2.44
HIGH DOSE- 1000 mg/kg				
MALES				
84-2014	2.65	2.59	2.59	2.47
84-2015	2.82	2.61	2.64	2.54
84-2016	2.70	2.65	2.66	2.52
FEMALES				
84-2017	2.79	2.66	2.68	2.55
84-2018	2.77	2.68	2.62	2.54
84-2019	2.81	2.66	2.70	2.62

PT : PRETREATMENT

APPENDIX F, TABLE 13
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
INDIVIDUAL VALUES
TOTAL PROTEIN (g/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	58	60	67	64
84-1997	56	60	64	69
84-1998	56	68	62	63
FEMALES				
84-1999	59	59	72	68
84-2000	60	63	69	69
84-2001	56	56	66	64
LOW DOSE - 250 mg/kg				
MALES				
84-2002	67	66	74	74
84-2003	60	61	66	64
84-2004	58	59	65	64
FEMALES				
84-2005	54	64	68	66
84-2006	57	58	66	67
84-2007	61	60	67	70
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	55	59	66	65
84-2009	57	60	63	68
84-2010	62	60	72	69
FEMALES				
84-2011	59	60	66	63
84-2012	57	54	61	60
84-2013	58	50	66	61
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	54	59	62	63
84-2015	58	60	63	65
84-2016	61	63	73	73
FEMALES				
84-2017	53	54	61	60
84-2018	60	61	67	68
84-2019	57	62	71	68

APPENDIX F, TABLE 14
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
SERUM CLINICAL CHEMISTRY
INDIVIDUAL VALUES
ALBUMIN (g/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	33	31	34	34
84-1997	34	32	32	32
84-1998	33	36	34	31
FEMALES				
84-1999	34	32	35	33
84-2000	33	32	28	31
84-2001	35	34	34	34
LOW DOSE - 250 mg/kg				
MALES				
84-2002	31	28	31	30
84-2003	34	32	32	32
84-2004	33	32	31	32
FEMALES				
84-2005	35	37	36	36
84-2006	34	34	35	36
84-2007	33	33	32	35
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	32	31	32	31
84-2009	29	28	27	29
84-2010	31	29	32	30
FEMALES				
84-2011	33	31	32	32
84-2012	33	30	31	29
84-2013	33	28	32	32
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	32	32	31	32
84-2015	34	32	32	32
84-2016	32	31	31	32
FEMALES				
84-2017	33	31	33	33
84-2018	34	31	31	31
84-2019	35	35	36	36

APPENDIX F, TABLE 15

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

GLOBULIN (g/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	25	29	33	30
84-1997	22	28	32	37
84-1998	23	32	28	32
FEMALES				
84-1999	25	27	37	35
84-2000	27	31	41	38
84-2001	21	22	32	30
LOW DOSE - 250 mg/kg				
MALES				
84-2002	36	38	43	44
84-2003	26	29	34	32
84-2004	25	27	34	32
FEMALES				
84-2005	19	27	32	30
84-2006	23	24	31	31
84-2007	28	27	35	35
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	23	28	34	34
84-2009	28	32	36	39
84-2010	31	31	40	39
FEMALES				
84-2011	26	29	34	31
84-2012	24	24	30	31
84-2013	25	22	34	29
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	22	27	31	31
84-2015	24	28	31	33
84-2016	29	32	42	41
FEMALES				
84-2017	20	23	28	27
84-2018	26	30	36	37
84-2019	22	27	35	32

APPENDIX F, TABLE 16

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

SERUM CLINICAL CHEMISTRY

INDIVIDUAL VALUES

A/G RATIO

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	1.32	1.07	1.03	1.13
84-1997	1.55	1.14	1.00	0.86
84-1998	1.43	1.13	1.21	0.97
FEMALES				
84-1999	1.36	1.19	0.95	0.94
84-2000	1.22	1.03	0.68	0.82
84-2001	1.67	1.55	1.06	1.13
LOW DOSE - 250 mg/kg				
MALES				
84-2002	0.86	0.74	0.72	0.68
84-2003	1.31	1.10	0.94	1.00
84-2004	1.32	1.19	0.91	1.00
FEMALES				
84-2005	1.84	1.37	1.13	1.20
84-2006	1.48	1.42	1.13	1.16
84-2007	1.18	1.22	0.91	1.00
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	1.39	1.11	0.94	0.91
84-2009	1.04	0.88	0.75	0.74
84-2010	1.00	0.94	0.80	0.77
FEMALES				
84-2011	1.27	1.07	0.94	1.03
84-2012	1.38	1.25	1.03	0.94
84-2013	1.32	1.27	0.94	1.10
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	1.45	1.19	1.00	1.03
84-2015	1.42	1.14	1.03	0.97
84-2016	1.10	0.97	0.74	0.78
FEMALES				
84-2017	1.65	1.35	1.18	1.22
84-2018	1.31	1.03	0.86	0.84
84-2019	1.59	1.30	1.03	1.13

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

HEMATOLOGY

INDIVIDUAL VALUES

HEMOGLOBIN (g/dL)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	16.5	16.1	15.8	15.0
84-1997	17.5	15.9	16.3	16.4
84-1998	16.1	18.2	17.0	15.7
FEMALES				
84-1999	18.1	18.3	18.5	16.8
84-2000	17.4	16.4	17.0	16.7
84-2001	17.2	16.5	18.0	16.7
LOW DOSE - 250 mg/kg				
MALES				
84-2002	15.8	15.3	15.9	15.1
84-2003	16.3	17.4	16.4	15.7
84-2004	16.3	16.4	16.5	15.0
FEMALES				
84-2005	17.8	17.9	17.4	16.6
84-2006	16.0	16.0	16.1	15.6
84-2007	16.5	15.1	16.1	14.9
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	15.6	15.8	16.0	15.9
84-2009	15.0	15.8	15.5	15.7
84-2010	16.6	17.2	17.4	17.1
FEMALES				
84-2011	16.7	14.7	15.0	15.4
84-2012	17.4	15.3	16.5	14.6
84-2013	18.5	16.0	16.1	16.2
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	14.3	14.7	15.2	14.8
84-2015	19.0	17.6	18.2	18.0
84-2016	15.2	15.1	15.4	15.2
FEMALES				
84-2017	16.1	15.0	16.3	16.1
84-2018	16.7	16.3	15.4	15.8
84-2019	17.8	17.2	17.6	17.2

PT : PRETREATMENT

APPENDIX G, TABLE 2

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

HEMATOLOGY

INDIVIDUAL VALUES

HEMATOCRIT (L/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	0.488	0.470	0.470	0.447
84-1997	0.516	0.446	0.471	0.480
84-1998	0.476	0.538	0.493	0.447
FEMALES				
84-1999	0.534	0.533	0.534	0.483
84-2000	0.511	0.462	0.490	0.484
84-2001	0.500	0.472	0.521	0.481
LOW DOSE - 250 mg/kg				
MALES				
84-2002	0.464	0.429	0.454	0.430
84-2003	0.480	0.495	0.474	0.448
84-2004	0.478	0.467	0.478	0.444
FEMALES				
84-2005	0.526	0.526	0.510	0.479
84-2006	0.465	0.447	0.458	0.450
84-2007	0.487	0.421	0.465	0.423
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	0.454	0.442	0.461	0.457
84-2009	0.439	0.446	0.447	0.452
84-2010	0.491	0.492	0.517	0.499
FEMALES				
84-2011	0.485	0.437	0.460	0.441
84-2012	0.512	0.448	0.471	0.423
84-2013	0.549	0.442	0.461	0.466
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	0.421	0.430	0.442	0.444
84-2015	0.575	0.499	0.535	0.524
84-2016	0.449	0.429	0.450	0.441
FEMALES				
84-2017	0.465	0.429	0.471	0.461
84-2018	0.491	0.463	0.458	0.455
84-2019	0.533	0.497	0.520	0.501

PT : PRETREATMENT

APPENDIX G, TABLE 3

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

HEMATOLOGY

INDIVIDUAL VALUES

RED BLOOD CELL COUNT (X10E12/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	7.47	7.26	7.27	6.97
84-1997	7.72	6.83	7.10	7.21
84-1998	7.37	8.24	7.60	6.95
FEMALES				
84-1999	7.77	7.78	7.78	7.04
84-2000	7.75	7.17	7.48	7.36
84-2001	7.19	6.84	7.52	6.98
LOW DOSE - 250 mg/kg				
MALES				
84-2002	6.75	6.26	6.63	6.34
84-2003	7.29	7.57	7.21	6.86
84-2004	7.09	6.99	7.11	6.55
FEMALES				
84-2005	7.79	7.78	7.48	7.07
84-2006	6.92	6.74	6.86	6.70
84-2007	7.49	6.59	7.26	6.65
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	6.93	6.76	6.93	6.83
84-2009	6.46	6.62	6.57	6.70
84-2010	7.49	7.55	7.92	7.68
FEMALES				
84-2011	7.27	6.55	6.90	6.65
84-2012	7.79	6.92	7.22	6.52
84-2013	7.84	6.44	6.68	6.71
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	6.31	6.45	6.63	6.70
84-2015	8.45	7.34	7.79	7.72
84-2016	6.97	6.74	7.03	6.93
FEMALES				
84-2017	7.57	6.85	7.40	7.07
84-2018	6.98	6.69	6.55	6.55
84-2019	7.76	7.35	7.61	7.35

PT : PRETREATMENT

APPENDIX G, TABLE 4

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

HEMATOLOGY

INDIVIDUAL VALUES

MEAN CORPUSCULAR VOLUME (fL)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	65.2	64.7	64.6	64.1
84-1997	66.8	65.3	66.2	66.4
84-1998	64.5	65.2	64.8	64.2
FEMALES				
84-1999	68.6	68.5	68.6	68.6
84-2000	65.8	64.3	65.4	65.6
84-2001	69.5	69.0	69.2	68.8
LOW DOSE - 250 mg/kg				
MALES				
84-2002	68.7	68.5	68.4	67.7
84-2003	65.8	65.3	65.7	65.3
84-2004	67.4	66.7	67.2	67.7
FEMALES				
84-2005	67.4	67.5	68.2	67.7
84-2006	67.1	66.2	66.7	67.1
84-2007	65.0	63.8	64.0	63.5
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	65.5	65.4	66.5	66.8
84-2009	68.0	67.3	68.0	67.4
84-2010	65.5	65.1	65.3	64.9
FEMALES				
84-2011	66.6	66.6	66.7	66.2
84-2012	65.7	64.7	65.1	64.9
84-2013	70.0	68.6	68.9	69.4
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	66.7	66.6	66.5	66.2
84-2015	68.0	67.9	68.7	67.8
84-2016	64.3	63.5	64.0	63.6
FEMALES				
84-2017	61.4	62.5	63.6	65.0
84-2018	70.2	69.1	69.9	69.4
84-2019	68.6	67.6	68.3	68.1

PT : PRETREATMENT

APPENDIX G, TABLE 5

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

HEMATOLOGY

INDIVIDUAL VALUES

MEAN CORPUSCULAR HEMOGLOBIN (pg)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	22.1	22.1	21.7	21.5
84-1997	22.6	23.3	22.9	22.7
84-1998	21.9	22.0	22.3	22.5
FEMALES				
84-1999	23.2	23.5	23.7	23.9
84-2000	22.5	22.9	22.7	22.7
84-2001	24.0	24.1	23.9	23.9
LOW DOSE - 250 mg/kg				
MALES				
84-2002	23.4	24.4	24.0	23.8
84-2003	22.4	23.0	22.8	22.9
84-2004	23.0	23.4	23.2	22.9
FEMALES				
84-2005	22.9	23.0	23.3	23.4
84-2006	23.1	23.7	23.5	23.3
84-2007	22.0	22.8	22.1	22.4
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	22.5	23.4	23.1	23.2
84-2009	23.2	23.8	23.6	23.5
84-2010	22.2	22.7	22.0	22.2
FEMALES				
84-2011	23.0	22.5	21.8	23.1
84-2012	22.3	22.1	22.8	22.3
84-2013	23.6	24.8	24.0	24.1
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	22.6	22.8	22.9	22.0
84-2015	22.5	24.0	23.4	23.3
84-2016	21.9	22.4	21.8	21.9
FEMALES				
84-2017	21.2	21.8	22.0	22.8
84-2018	23.9	24.4	23.5	24.1
84-2019	23.0	23.4	23.1	23.3

PT : PRETREATMENT

APPENDIX G, TABLE 6

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

HEMATOLOGY

INDIVIDUAL VALUES

MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dL)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	33.8	34.2	33.5	33.6
84-1997	33.9	35.6	34.6	34.2
84-1998	33.9	33.7	34.4	35.1
FEMALES				
84-1999	33.8	34.4	34.6	34.8
84-2000	34.1	35.5	34.7	34.5
84-2001	34.4	35.0	34.5	34.7
LOW DOSE - 250 mg/kg				
MALES				
84-2002	34.0	35.6	35.0	35.1
84-2003	34.0	35.1	34.6	35.0
84-2004	34.1	35.1	34.5	33.8
FEMALES				
84-2005	33.9	34.1	34.2	34.6
84-2006	34.4	35.8	35.1	34.7
84-2007	33.8	35.8	34.5	35.2
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	34.3	35.8	34.7	34.7
84-2009	34.1	35.4	34.7	34.8
84-2010	33.8	34.9	33.7	34.2
FEMALES				
84-2011	34.4	33.7	32.7	34.9
84-2012	33.9	34.2	35.0	34.4
84-2013	33.7	36.1	34.9	34.7
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	33.9	34.2	34.4	33.3
84-2015	33.1	35.2	34.1	34.4
84-2016	33.9	35.2	34.1	34.4
FEMALES				
84-2017	34.5	34.9	34.5	35.0
84-2018	34.0	35.3	33.6	34.7
84-2019	33.5	34.6	33.9	34.2

PT : PRETREATMENT

APPENDIX G, TABLE 7

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

HEMATOLOGY

INDIVIDUAL VALUES

WHITE BLOOD CELL COUNT (X10E9/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	11.3	8.1	12.7	10.7
84-1997	10.6	8.6	12.0	12.6
84-1998	12.0	13.1	12.2	11.2
FEMALES				
84-1999	11.1	11.6	13.8	16.7
84-2000	9.1	8.2	13.6	13.9
84-2001	11.0	10.7	12.3	19.8
LOW DOSE - 250 mg/kg				
MALES				
84-2002	9.1	8.3	13.9	11.9
84-2003	12.5	11.1	13.7	14.5
84-2004	10.8	10.6	17.9	13.7
FEMALES				
84-2005	8.1	9.3	11.9	9.0
84-2006	9.8	7.0	12.6	10.0
84-2007	8.9	9.6	11.9	12.7
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	11.0	7.6	13.2	12.4
84-2009	12.0	18.6	13.9	14.7
84-2010	11.3	8.0	16.2	12.1
FEMALES				
84-2011	9.7	6.2	12.0	11.9
84-2012	15.8	14.9	16.1	14.7
84-2013	10.3	10.3	10.4	10.4
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	11.0	9.0	14.8	12.4
84-2015	9.2	8.1	14.1	11.6
84-2016	18.4	14.0	17.0	14.1
FEMALES				
84-2017	10.3	9.5	11.5	12.1
84-2018	7.1	6.6	11.5	9.1
84-2019	10.2	11.2	12.6	10.7

PT : PRETREATMENT

APPENDIX G, TABLE B

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

HEMATOLOGY

INDIVIDUAL VALUES

IMMATURE NEUTROPHIL (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	0	0	0	0
84-1997	0	0	0	0
84-1998	0	0	0	0
FEMALES				
84-1999	0	0	0	0
84-2000	0	0	0	0
84-2001	0	0	0	0
LOW DOSE - 250 mg/kg				
MALES				
84-2002	0	0	0	0
84-2003	0	0	0	0
84-2004	0	0	0	0
FEMALES				
84-2005	0	0	0	0
84-2006	0	0	0	0
84-2007	0	0	0	0
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	0	0	0	0
84-2009	0	0	0	0
84-2010	0	0	0	0
FEMALES				
84-2011	0	0	0	0
84-2012	0	0	0	0
84-2013	0	0	0	0
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	0	0	0	0
84-2015	0	0	0	0
84-2016	0	0	0	0
FEMALES				
84-2017	0	0	0	0
84-2018	0	0	0	0
84-2019	0	0	0	0

PT : PRETREATMENT

APPENDIX G, TABLE 9

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

HEMATOLOGY

INDIVIDUAL VALUES

MATURE NEUTROPHIL (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	62	52	69	59
84-1997	66	50	61	70
84-1998	57	54	54	53
FEMALES				
84-1999	56	61	56	64
84-2000	65	63	68	72
84-2001	69	57	68	73
LOW DOSE - 250 mg/kg				
MALES				
84-2002	66	44	64	55
84-2003	61	62	60	65
84-2004	62	68	72	65
FEMALES				
84-2005	52	64	59	46
84-2006	67	50	59	34
84-2007	46	72	63	69
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	42	37	51	49
84-2009	53	81	62	41
84-2010	67	50	66	60
FEMALES				
84-2011	64	57	58	62
84-2012	43	52	43	42
84-2013	47	60	63	57
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	63	67	59	69
84-2015	58	62	60	69
84-2016	69	79	65	58
FEMALES				
84-2017	56	51	66	53
84-2018	47	49	68	53
84-2019	49	60	56	46

PT : PRETREATMENT

APPENDIX G, TABLE 10

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

HEMATOLOGY

INDIVIDUAL VALUES

LYMPHOCYTE (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	29	36	22	30
84-1997	25	45	33	21
84-1998	33	35	37	38
FEMALES				
84-1999	37	30	36	25
84-2000	25	28	25	25
84-2001	26	31	26	19
LOW DOSE - 250 mg/kg				
MALES				
84-2002	24	45	27	35
84-2003	33	30	37	29
84-2004	24	20	21	29
FEMALES				
84-2005	41	29	37	39
84-2006	22	32	30	44
84-2007	45	20	34	27
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	44	49	39	42
84-2009	35	16	32	41
84-2010	26	39	28	34
FEMALES				
84-2011	28	29	32	31
84-2012	37	29	38	48
84-2013	43	29	22	35
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	33	27	32	26
84-2015	28	30	36	24
84-2016	24	14	26	31
FEMALES				
84-2017	37	38	29	35
84-2018	36	37	22	32
84-2019	49	34	33	49

PT : PRETREATMENT

APPENDIX G, TABLE 11

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

HEMATOLOGY

INDIVIDUAL VALUES

MONOCYTE (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	8	10	6	10
84-1997	7	3	5	3
84-1998	5	8	6	9
FEMALES				
84-1999	2	4	6	10
84-2000	9	7	5	3
84-2001	4	6	6	8
LOW DOSE - 250 mg/kg				
MALES				
84-2002	6	5	4	8
84-2003	6	6	2	5
84-2004	10	9	4	4
FEMALES				
84-2005	2	2	3	9
84-2006	5	9	3	12
84-2007	6	7	2	4
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	10	5	6	6
84-2009	7	2	6	14
84-2010	6	3	4	5
FEMALES				
84-2011	6	11	5	6
84-2012	12	8	10	5
84-2013	4	5	9	3
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	4	4	5	2
84-2015	6	7	2	6
84-2016	7	6	6	9
FEMALES				
84-2017	3	7	4	7
84-2018	9	8	9	11
84-2019	2	6	9	5

PT : PRETREATMENT

APPENDIX G, TABLE 12

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

HEMATOLOGY

INDIVIDUAL VALUES

EOSINOPHIL (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	1	2	3	1
84-1997	2	2	1	6
84-1998	5	3	3	0
FEMALES				
84-1999	5	5	2	1
84-2000	1	2	2	0
84-2001	1	6	0	0
LOW DOSE - 250 mg/kg				
MALES				
84-2002	4	6	5	2
84-2003	0	2	1	1
84-2004	4	3	3	2
FEMALES				
84-2005	5	5	1	6
84-2006	6	9	8	10
84-2007	3	1	1	0
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	4	9	4	3
84-2009	5	1	0	3
84-2010	1	8	2	1
FEMALES				
84-2011	2	3	5	1
84-2012	8	11	9	5
84-2013	6	6	6	5
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	0	2	4	3
84-2015	8	1	2	1
84-2016	0	1	3	2
FEMALES				
84-2017	4	4	1	5
84-2018	8	6	1	4
84-2019	0	0	2	0

PT : PRETREATMENT

APPENDIX G, TABLE 13

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

HEMATOLOGY

INDIVIDUAL VALUES

BASOPHIL (%)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	0	0	0	0
84-1997	0	0	0	0
84-1998	0	0	0	0
FEMALES				
84-1999	0	0	0	0
84-2000	0	0	0	0
84-2001	0	0	0	0
LOW DOSE - 250 mg/kg				
MALES				
84-2002	0	0	0	0
84-2003	0	0	0	0
84-2004	0	0	0	0
FEMALES				
84-2005	0	0	0	0
84-2006	0	0	0	0
84-2007	0	0	0	0
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	0	0	0	0
84-2009	0	0	0	1
84-2010	0	0	0	0
FEMALES				
84-2011	0	0	0	0
84-2012	0	0	0	0
84-2013	0	0	0	0
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	0	0	0	0
84-2015	0	0	0	0
84-2016	0	0	0	0
FEMALES				
84-2017	0	0	0	0
84-2018	0	0	0	0
84-2019	0	0	0	0

PT : PRETREATMENT

APPENDIX G, TABLE 14

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

HEMATOLOGY

INDIVIDUAL VALUES

PLATELET (X10E9/L)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	471	472	500	482
84-1997	380	332	398	458
84-1998	442	462	464	485
FEMALES				
84-1999	323	322	372	396
84-2000	337	286	340	377
84-2001	283	263	278	351
LOW DOSE - 250 mg/kg				
MALES				
84-2002	366	300	343	389
84-2003	407	418	370	429
84-2004	259	259	261	300
FEMALES				
84-2005	282	265	352	274
84-2006	321	311	369	343
84-2007	344	325	412	428
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	394	380	433	458
84-2009	491	408	465	440
84-2010	324	216	269	313
FEMALES				
84-2011	354	309	322	362
84-2012	449	461	443	491
84-2013	477	404	440	441
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	422	434	514	467
84-2015	408	378	412	410
84-2016	351	363	420	401
FEMALES				
84-2017	285	279	361	345
84-2018	489	507	487	540
84-2019	371	359	443	475

PT : PRETREATMENT

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APPENDIX G, TABLE 15

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

HEMATOLOGY

INDIVIDUAL VALUES

ACTIVATED PARTIAL THROMBOPLASTIN TIME (SECONDS)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	9.2	9.2	9.3	9.2
84-1997	8.6	8.4	8.8	8.9
84-1998	8.0	7.4	9.1	9.2
FEMALES				
84-1999	9.1	8.7	9.1	8.5
84-2000	9.3	9.1	9.9	9.8
84-2001	9.1	9.2	9.7	9.2
LOW DOSE - 250 mg/kg				
MALES				
84-2002	9.2	9.0	9.1	8.9
84-2003	8.4	8.6	9.3	8.9
84-2004	9.0	9.5	9.4	10.2
FEMALES				
84-2005	9.4	8.4	9.0	8.9
84-2006	9.1	9.0	9.5	9.3
84-2007	8.5	9.2	9.2	9.5
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	9.2	9.1	9.6	9.6
84-2009	8.5	8.9	9.9	9.1
84-2010	8.7	8.6	8.9	9.9
FEMALES				
84-2011	9.6	9.5	9.4	9.4
84-2012	9.0	8.9	9.0	9.1
84-2013	8.2	8.8	9.0	8.9
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	8.4	8.5	8.8	8.4
84-2015	9.8	10.1	10.2	10.4
84-2016	9.8	10.4	10.7	11.0
FEMALES				
84-2017	9.4	9.3	9.3	9.3
84-2018	8.9	9.1	9.7	9.5
84-2019	8.4	8.8	8.8	9.3

PT : PRETREATMENT

APPENDIX G, TABLE 16

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

HEMATOLOGY

INDIVIDUAL VALUES

PROTHROMBIN TIME (SECONDS)

STUDY DAY	PT	1	12	28
CONTROL - 0 mg/kg				
MALES				
84-1996	6.1	5.9	6.1	6.0
84-1997	6.7	6.4	6.6	6.4
84-1998	6.3	5.9	6.1	6.2
FEMALES				
84-1999	6.9	6.3	6.6	6.5
84-2000	6.3	6.0	6.3	6.4
84-2001	6.0	6.3	6.4	6.0
LOW DOSE - 250 mg/kg				
MALES				
84-2002	6.4	6.2	6.3	6.2
84-2003	6.1	6.0	6.2	6.2
84-2004	6.3	5.8	6.1	6.1
FEMALES				
84-2005	6.8	6.3	6.5	6.4
84-2006	6.7	6.5	6.7	6.8
84-2007	6.2	5.8	6.0	5.9
MEDIUM DOSE - 500 mg/kg				
MALES				
84-2008	6.5	6.2	6.5	6.4
84-2009	6.6	6.1	6.4	6.3
84-2010	6.2	6.0	6.2	6.2
FEMALES				
84-2011	6.2	6.0	6.3	6.1
84-2012	6.5	6.1	6.2	6.2
84-2013	6.1	5.8	6.3	6.4
HIGH DOSE - 1000 mg/kg				
MALES				
84-2014	6.3	6.0	6.3	6.4
84-2015	7.6	7.2	7.4	7.6
84-2016	6.1	6.1	6.2	6.3
FEMALES				
84-2017	6.5	6.0	6.3	6.5
84-2018	6.2	5.9	6.1	6.2
84-2019	6.1	5.9	6.2	6.1

PT : PRETREATMENT

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

URINALYSIS

INDIVIDUAL VALUES

REFRACTIVE INDEX +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	1.350	1.353	1.349
84-1997	1.356	1.359	1.359
84-1998	1.352	1.343	1.355
FEMALES			
84-1999	1.354	1.355	1.355
84-2000	1.347	1.346	1.346
84-2001	1.354	1.351	1.357
LOW DOSE - 250 mg/kg			
MALES			
84-2002	1.358	1.357	1.361
84-2003	1.351	1.342	1.348
84-2004	1.354	1.350	1.347
FEMALES			
84-2005	1.347	1.357	1.358
84-2006	1.350	1.356	1.354
84-2007	1.340	1.350	1.352
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	1.349	1.359	1.356
84-2009	1.345	1.344	1.349
84-2010	1.353	1.355	1.354
FEMALES			
84-2011	1.353	1.358	1.354
84-2012	1.342	1.358	1.357
84-2013	1.346	1.340	1.347
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	1.344	1.358	1.358
84-2015	1.350	1.360	1.358
84-2016	1.355	1.355	1.354
FEMALES			
84-2017	1.355	1.362	1.362
84-2018	1.344	1.348	1.342
84-2019	1.343	1.350	1.351

PT : PRETREATMENT
+ : REFRACTIVITY X10E-4 + 1.333

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APPENDIX H, TABLE 2
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

INDIVIDUAL VALUES

URINE VOLUME (mL)

STUDY DAY 22-23

CONTROL - 0 mg/kg

MALES

84-1996	260
84-1997	330
84-1998	600

FEMALES

84-1999	1050
84-2000	910
84-2001	360

LOW DOSE - 250 mg/kg

MALES

84-2002	550
84-2003	470
84-2004	510

FEMALES

84-2005	110
84-2006	350
84-2007	370

MEDIUM DOSE - 500 mg/kg

MALES

84-2008	380
84-2009	500
84-2010	700

FEMALES

84-2011	380
84-2012	90
84-2013	210

HIGH DOSE - 1000 mg/kg

MALES

84-2014	770
84-2015	1200
84-2016	430

FEMALES

84-2017	200
84-2018	550
84-2019	510

APPENDIX H, TABLE 3
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

pH +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	8.0	7.0	7.5
84-1997	6.0	7.5	6.5
84-1998	7.5	7.5	7.5
FEMALES			
84-1999	6.0	7.5	6.5
84-2000	6.5	5.0	6.0
84-2001	6.0	8.0	6.5
LOW DOSE - 250 mg/kg			
MALES			
84-2002	6.0	6.0	6.5
84-2003	8.0	6.5	7.0
84-2004	7.5	7.5	7.0
FEMALES			
84-2005	6.5	6.5	8.0
84-2006	7.5	6.5	7.0
84-2007	7.5	6.5	7.0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	7.0	6.5	6.5
84-2009	7.0	5.0	6.0
84-2010	6.5	6.0	6.0
FEMALES			
84-2011	7.0	7.0	7.5
84-2012	6.0	8.0	6.5
84-2013	6.5	5.0	8.0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	7.5	6.0	6.0
84-2015	6.0	6.0	6.0
84-2016	8.0	6.5	7.0
FEMALES			
84-2017	6.5	6.0	5.0
84-2018	5.0	5.0	5.0
84-2019	6.5	8.0	6.5

PT : PRETREATMENT

+ : MODIFIED AMES MULTISTIX GRADING SYSTEM (pH UNITS 5.0 TO 8.5)

APPENDIX H, TABLE 4
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

GLUCOSE +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0
FEMALES			
84-1999	0	0	0
84-2000	0	0	0
84-2001	0	0	0
LOW DOSE - 250 mg/kg			
MALES			
84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0
FEMALES			
84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	0
FEMALES			
84-2011	0	0	0
84-2012	0	0	0
84-2013	0	0	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0	0	0
84-2015	0	0	0
84-2016	0	0	0
FEMALES			
84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT

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

APPENDIX H, TABLE 5
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

BILIRUBIN +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0
FEMALES			
84-1999	0	0	0
84-2000	0	0	0
84-2001	0	0	0
LOW DOSE - 250 mg/kg			
MALES			
84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0
FEMALES			
84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	0
FEMALES			
84-2011	0	0	0
84-2012	0	0	0
84-2013	0	0	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0	0	0
84-2015	0	0	0
84-2016	0	0	0
FEMALES			
84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT

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

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APPENDIX H, TABLE 6
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

PROTEIN +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	2	1	2
84-1997	1	1	1
84-1998	1	1	2
FEMALES			
84-1999	1	2	2
84-2000	1	1	0
84-2001	1	1	1
LOW DOSE - 250 mg/kg			
MALES			
84-2002	1	1	1
84-2003	2	1	1
84-2004	1	1	1
FEMALES			
84-2005	1	1	2
84-2006	1	1	1
84-2007	1	1	1
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	1	1	1
84-2009	1	1	1
84-2010	1	1	1
FEMALES			
84-2011	1	1	3
84-2012	1	4	1
84-2013	2	0	1
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	1	1	1
84-2015	1	1	1
84-2016	1	1	1
FEMALES			
84-2017	1	1	1
84-2018	0	0	0
84-2019	1	1	1

PT : PRETREATMENT

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

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APPENDIX H, TABLE 7
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

KETONES +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0
FEMALES			
84-1999	0	0	0
84-2000	0	0	0
84-2001	0	0	0
LOW DOSE - 250 mg/kg			
MALES			
84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0
FEMALES			
84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	0
FEMALES			
84-2011	0	0	0
84-2012	0	0	0
84-2013	0	0	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0	0	0
84-2015	0	0	0
84-2016	0	0	0
FEMALES			
84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT
+ : MODIFIED AMES MULTISTIX GRADING SYSTEM (0 TO 3)

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APPENDIX H, TABLE B

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

URINALYSIS

INDIVIDUAL VALUES

COOULT BLOOD +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0
FEMALES			
84-1999	0	0	3
84-2000	0	0	0
84-2001	0	0	0
LOW DOSE - 250 mg/kg			
MALES			
84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0
FEMALES			
84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	0
FEMALES			
84-2011	0	0	0
84-2012	2	0	0
84-2013	3	0	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	1	0	0
84-2015	0	0	0
84-2016	0	0	0
FEMALES			
84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT

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

APPENDIX H, TABLE 9

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

URINALYSIS

INDIVIDUAL VALUES

UROBILINOGEN +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0.1	0.1	1.0
84-1997	1.0	1.0	1.0
84-1998	1.0	0.1	1.0
FEMALES			
84-1999	1.0	1.0	1.0
84-2000	0.1	0.1	0.1
84-2001	0.1	1.0	0.1
LOW DOSE - 250 mg/kg			
MALES			
84-2002	1.0	1.0	1.0
84-2003	1.0	0.1	1.0
84-2004	1.0	1.0	0.1
FEMALES			
84-2005	0.1	1.0	1.0
84-2006	0.1	0.1	1.0
84-2007	0.1	1.0	1.0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	1.0	1.0	1.0
84-2009	1.0	0.1	1.0
84-2010	0.1	1.0	1.0
FEMALES			
84-2011	1.0	1.0	1.0
84-2012	0.1	1.0	1.0
84-2013	1.0	0.1	0.1
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0.1	1.0	1.0
84-2015	0.1	0.1	1.0
84-2016	1.0	1.0	0.1
FEMALES			
84-2017	1.0	1.0	1.0
84-2018	0.1	0.1	0.1
84-2019	0.1	1.0	0.1

PT : PRETREATMENT

+ : AMES MULTISTIX GRADING SYSTEM (0.1 TO 12)

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APPENDIX H, TABLE 10
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG

URINALYSIS

INDIVIDUAL VALUES

RED BLOOD CELLS +

STUDY DAY	PT	12-13	27-28
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CONTROL - 0 mg/kg

MALES

84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0

FEMALES

84-1999	0	0	12
84-2000	0	0	0
84-2001	0	0	0

LOW DOSE - 250 mg/kg

MALES

84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0

FEMALES

84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0

MEDIUM DOSE - 500 mg/kg

MALES

84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	ND

FEMALES

84-2011	0	0	0
84-2012	80	0	0
84-2013	0	0	0

HIGH DOSE - 1000 mg/kg

MALES

84-2014	0	0	0
84-2015	0	0	0
84-2016	0	0	0

FEMALES

84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT
ND : NO DATA
+ : CELLS PER HIGH POWER FIELD

APPENDIX H, TABLE 11

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

URINALYSIS

INDIVIDUAL VALUES

WHITE BLOOD CELLS +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	3	4	0
84-1997	30	1	4
84-1998	7	0	50
FEMALES			
84-1999	0	1	0
84-2000	2	0	2
84-2001	5	1	2
LOW DOSE - 250 mg/kg			
MALES			
84-2002	80	9	8
84-2003	2	0	0
84-2004	10	6	1
FEMALES			
84-2005	170	12	5
84-2006	1	0	0
84-2007	5	2	8
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	2	1	5
84-2009	2	4	65
84-2010	3	1	ND
FEMALES			
84-2011	55	1	2
84-2012	0	8	2
84-2013	0	1	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0	0	0
84-2015	7	5	0
84-2016	80	11	110
FEMALES			
84-2017	40	7	2
84-2018	0	0	0
84-2019	1	0	2

PT : PRETREATMENT
ND : NO DATA
+ : CELLS PER HIGH POWER FIELD

APPENDIX H, TABLE 12
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
URINALYSIS
INDIVIDUAL VALUES
CASTS +

STUDY DAY	PT	12-13	27-28
CONTROL - 0 mg/kg			
MALES			
84-1996	0	0	0
84-1997	0	0	0
84-1998	0	0	0
FEMALES			
84-1999	0	0	0
84-2000	0	0	0
84-2001	0	0	0
LOW DOSE - 250 mg/kg			
MALES			
84-2002	0	0	0
84-2003	0	0	0
84-2004	0	0	0
FEMALES			
84-2005	0	0	0
84-2006	0	0	0
84-2007	0	0	0
MEDIUM DOSE - 500 mg/kg			
MALES			
84-2008	0	0	0
84-2009	0	0	0
84-2010	0	0	ND
FEMALES			
84-2011	0	0	0
84-2012	0	0	0
84-2013	0	0	0
HIGH DOSE - 1000 mg/kg			
MALES			
84-2014	0	0	0
84-2015	0	0	0
84-2016	0	0	0
FEMALES			
84-2017	0	0	0
84-2018	0	0	0
84-2019	0	0	0

PT : PRETREATMENT
ND : NO DATA
+ : CASTS PER LOW POWER FIELD

APPENDIX H, TABLE 13

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

URINALYSIS

INDIVIDUAL VALUES

CRYSTALS +

STUDY DAY	PT	12-13	27-28
-----------	----	-------	-------

CONTROL - 0 mg/kg

MALES

84-1996	1	1	0
84-1997	0	1	2
84-1998	4	1	3

FEMALES

84-1999	0	1	1
84-2000	1	1	0
84-2001	0	1	2

LOW DOSE - 250 mg/kg

MALES

84-2002	0	1	2
84-2003	1	1	3
84-2004	1	1	1

FEMALES

84-2005	0	1	1
84-2006	1	2	1
84-2007	1	1	2

MEDIUM DOSE - 500 mg/kg

MALES

84-2008	0	1	2
84-2009	2	1	0
84-2010	3	1	ND

FEMALES

84-2011	1	1	1
84-2012	0	1	0
84-2013	0	1	1

HIGH DOSE - 1000 mg/kg

MALES

84-2014	1	0	1
84-2015	0	1	1
84-2016	2	1	4

FEMALES

84-2017	0	3	0
84-2018	0	1	0
84-2019	0	1	0

PT : PRETREATMENT

ND : NO DATA

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

APPENDIX H, TABLE 14

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

URINALYSIS

INDIVIDUAL VALUES

BACTERIA +

STUDY DAY	PT	12-13	27-28
-----------	----	-------	-------

CONTROL - 0 mg/kg

MALES

84-1996	1	1	0
84-1997	4	1	1
84-1998	1	1	0

FEMALES

84-1999	4	2	1
84-2000	1	1	1
84-2001	1	1	1

LOW DOSE - 250 mg/kg

MALES

84-2002	1	1	1
84-2003	3	4	4
84-2004	1	2	3

FEMALES

84-2005	1	1	1
84-2006	1	1	0
84-2007	1	1	0

MEDIUM DOSE - 500 mg/kg

MALES

84-2008	3	2	1
84-2009	1	4	4
84-2010	4	1	ND

FEMALES

84-2011	1	1	0
84-2012	1	1	2
84-2013	4	1	3

HIGH DOSE - 1000 mg/kg

MALES

84-2014	4	2	4
84-2015	1	1	0
84-2016	4	4	3

FEMALES

84-2017	4	1	0
84-2018	4	1	2
84-2019	4	4	2

PT : PRETREATMENT

ND : NO DATA

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

APPENDIX I

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

OPHTHALMIC EXAMINATION REPORT

Methods

The ophthalmic examinations were performed November 12, 1984.

The direct and consensual pupillary light reflexes (PLR) were evaluated with the animal in its cage in Room J-362. No change in room lighting was made. The light source used was a Welch-Allyn 3.5V Halogen Handle on which was mounted a Finnoff transilluminator. Magnification (2.5X) as provided by a Donegan Optivisor^R with a #5 lens plate. The eyelids, membrana nictitans, conjunctiva, cornea, and iris were examined in each dog's eyes using a focal light source and 2.5X magnification immediately after pupillary responses were evaluated.

One to two drops of 1% tropicamide (Mydracyl^R) (Alcon Laboratories) were then placed in both eyes. Five to ten minutes after the initial examination an additional 1-2 drops of tropicamide were placed in both eyes.

The remainder of the examination was performed in room J-357 under reduced illumination. The adnexa, cornea, anterior chamber, and lens were evaluated by biomicroscopy with the Kowa SL-2 Zoom Slit Lamp. Magnification was varied from 5 to 20X.

APPENDIX I

The fundus of both eyes was then evaluated by binocular indirect ophthalmoscopy using the Fison Binocular Ophthalmoscope^R (Keeler Optical Inc.) and a Nikon 14+ or 20+ Diopter examining lens. The fundus was also evaluated using the American Optical Monocular Indirect Ophthalmoscope^R Model 305R in some animals.

Results

Control Group: The following 5 animals were normal: 84-1996, 84-1997, 84-1998, 84-1999, and 84-2001.

Animal 84-2000 had a 2x3 mm iris nevus at the 11:30 position of the peripheral superior iris of the right eye. The rest of the examination was normal.

Low Dose Group: The following 5 animals were normal: 84-2002, 84-2004, 84-2005, 84-2006, and 84-2007.

Animal 84-2003 had a peripapillary retinal fold 1/5 disk diameter in length located at the 11 o'clock position of the right eye. The rest of the examination was normal.

Medium Dose Group: The following 5 animals were normal: 84-2008, 84-2010, 84-2011, 84-2012, and 84-2013.

Animal 84-2009 had prolapse of the gland of the membrana nictitans, epiphora and conjunctival inflammation of each eye. The rest of the examination was normal.

High Dose Group: The following 5 animals were normal: 84-2014, 84-2015, 84-2016, 84-2017, and 84-2019.

Animal 84-2018 had persistent pupillary membrane

APPENDIX I

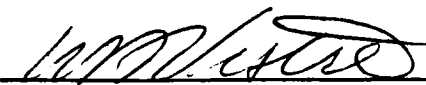
remnants on the nasal position of the iris of the right eye. The rest of the examination was normal.

Discussion

The iris nevus (animal 84-2000), retinal fold (animal 84-2003), and pupillary membrane remnants (animal 84-2018) are minor developmental defects which did not interfere with the ophthalmic examinations and are not considered significant in this study. These minor anomalies are often found in this large a group of laboratory beagles. The prolapsed glands in animal 84-2009 are due to defects in the normal ligament holding the gland in position. The epiphora and inflammation are due to irritation from the gland being in an abnormal location.

This is a relatively common finding in the laboratory beagle and is not considered significant in this study.

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

 1/28/85
W.A. Vestre, DVM, MS, Dipl., ACVO Date
Associate Professor, Ophthalmology
School of Veterinary Medicine
Purdue University

APPENDIX J

R&D PRODUCT DEVELOPMENT FUNCTION
REPORT REVIEW AND RELEASE

Page 1 of 3

DEPARTMENT: Product Development Analytical

DOCUMENT NUMBER: F-306-034-02

TITLE OF REPORT: SC-19129

TYPE OF REPORT: Analytical Summary in Support of Product Safety
Assessment Study Number 2449

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, ILLINOIS

ANALYTICAL SUMMARY

Product Development Analytical Department

Page 2 of 3

Subject: SC-19129

Summary Number: F-306-034-02

Applicable to SA Study Number: 2449

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	0.5%		
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-306-034-02

Applicable to SA Study Number: 2449

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.

APPENDIX K

EXPLANATORY NOTE TO PATHOLOGY TABLES

The following apply to the incidence tables in this study, and Appendix.

1. The groups listed on all tables as ctls (group 1), 2, 3, & 4, are the control, low (250 mg/kg), medium (500 mg/kg), and high (1000 mg/kg), groups respectively.
2. The all dead note on the microscopic observations incidence tables refers to the final sacrifice animals.
3. Terminal body weights can be found in Appendix K. 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.
4. 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 were not used in the antermortem portion of the study.

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 1

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1996/PRETEST-1 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-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
-MINERALIZATION, MEDULLA
PITUITARY GLAND
-CYST

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 2

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1997/PRETEST-
DATE OF DEATH: 16-NOV-84 2 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
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 K

S.A. 2449

3

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

HEART
-VALVULAR ENDOCARDIOSIS

KIDNEY
-MINERALIZATION, MEDULLA

PROSTATE PROSTATE IS SMALL, PROBABLY DUE TO IMMATUREITY OF THE ANIMAL.

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 3

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1998/PRETEST= 3 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 15-NOV-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. 2449

7 4

APPENDIX K

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

KIDNEY
-MINERALIZATION, MEDULLA

GALL BLADDER TISSUE IS MISSING

PARATHYROID TISSUE IS MISSING

TESTIS
-GERMINAL EPITHELIAL DEGENERATION.

PROSTATE PROSTATE IS SMALL, PROBABLY DUE TO IMMATUREITY OF ANIMAL.

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 4

STUDY START DATE: 18-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2002/PRETEST-
DATE OF DEATH: 15-NOV-84

DOSE GROUP: 2
SEX: MALE
STUDY DAY OF DEATH: 29

SACRIFICE STATUS: FINAL SACRIFICE
STUDY WEEK OF DEATH: 5
TERMINAL BODY WEIGHT: NOT TAKEN

ORGAN NAME
EPIDIDYMIS(EP)

<< GROSS ORGAN OBSERVATIONS >>
KEYWORDS / PHRASES
SMALL

SEVERITY GROSS FREE-TEXT COMMENTS
HEAD HAD A YELLOW SOFT ABSCESS

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

EPIDIDYMIS
--SPERM GRANULOMA

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 5

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2003/PRETEST-5 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 16-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 FINDINGS

TISSUE OBSERVATIONS >>
 DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS

PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 6

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2004/PRETEST= 6 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 15-NOV-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

HEART
 -CORONARY VASCULITIS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 7

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2008/PRETEST= 7 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-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 PROSTATE IS SMALL.

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 8

STUDY START DATE: 18-OCT-84
STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2009/PRETEST-
DATE OF DEATH: 15-NOV-84
SEX: MALE
STUDY DAY OF DEATH: 29
DOSE GROUP: 3
STUDY WEEK OF DEATH: 5
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

PROSTATE PROSTATE IS SMALL.

NICTITATING MEMB MISCELLANEOUS TISSUE
-INFLAMMATION

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
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STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2010/PRETEST-
 DATE OF DEATH: 16-NOV-84 9 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: FINAL SACRIFICE
 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)			NORMAL

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >>	DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
HEART		
-VALVULAR ENDOCARDIOSIS		
PITUITARY GLAND		
-CYST		

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

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STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2014/PRETEST=
 DATE OF DEATH: 16-NOV-84 STUDY DAY OF DEATH: 30 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
 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
 -MINERALIZATION, MEDULLA

LIVER
 -FOCAL LYMPHOCYTIC AGGREGATIONS

THYMUS
 -CYST(S)

PARATHYROID TISSUE IS MISSING

TESTIS
 -TUBULAR HYPOPLASIA

PROSTATE PROSTATE IS SMALL.

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 11

ANIMAL NUMBER: 84-2015/PRETEST=
 DATE OF DEATH: 15-NOV-84 STUDY DAY OF DEATH: 29 11 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
 STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX
 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
 -MINERALIZATION, MEDULLA

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 12

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2016/PRETEST-12 DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 15-NOV-84 STUDY DAY OF DEATH: 29 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

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

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >>	DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
KIDNEY -MINERALIZATION, MEDULLA		
THYMUS -CYST(S)		
TESTIS -TUBULAR HYPOPLASIA		REGIONAL HYPOPLASIA, IN ONLY ONE TESTIS

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 13

STUDY START DATE: 18-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-1999/PRETEST= 13 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-NOV-84 STUDY DAY OF DEATH: 30 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: NOT TAKEN

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

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >>
HEART	DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
-VALVULAR ENDOCARDIOSIS	
KIDNEY	
-MINERALIZATION, MEDULLA	
PITUITARY GLAND	
-CYST	

INDIVIDUAL ANIMAL DATA REPORT				STUDY NUMBER: SA2449		STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX	
SEARLE RESEARCH & DEVELOPMENT				STUDY START DATE: 18-OCT-84		PRINTED: 28-JAN-85	
PRODUCT SAFETY ASSESSMENT				SPECIES: DOG/BEAGLE		PAGE: 14	
SKOKIE, ILLINOIS 60077				DOSE GROUP: 1		SACRIFICE STATUS: FINAL SACRIFICE	
STUDY PRETEST=				STUDY WEEK OF DEATH: 5		TERMINAL BODY WEIGHT: NOT TAKEN	
DATE OF DEATH: 15-NOV-84				SEX: FEMALE		STUDY DAY OF DEATH: 29	
ORGAN NAME	<<	GROSS ORGAN	OBSERVATIONS	>>	SEVERITY	GROSS FREE-TEXT COMMENTS	
WHOLE BODY(WB)		KEYWORDS / PHRASES					
		NORMAL					
TISSUE / HISTOPATHOLOGIC FINDINGS				OBSERVATIONS >>			
<< MICROSCOPIC TISSUE				DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS			
PITUITARY GLAND							
-CYST							

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 15

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2001/PRETEST-15 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 15-NOV-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: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 16

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2005/PRETEST= 16 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 16-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

HEART
 -VALVULAR ENDOCARDIOSIS

SEARLE RESEARCH & DEVELOPMENT
 PRODUCT SAFETY ASSESSMENT
 SKOKIE, ILLINOIS 60077
 SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 17

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2006/PRETEST= 17 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 15-NOV-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

PITUITARY GLAND
 -CYST

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 18

STUDY START DATE: 18-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2007/PRETEST= 18 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-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. 2449

APPENDIX K

TISSUE / HISTOPATHOLOGIC FINDINGS	<< MICROSCOPIC TISSUE OBSERVATIONS >> DISTRIBUTION (SEVERITY) / SPECIAL COMMENTS
PITUITARY GLAND -CYST	
MAMMARY GLAND	TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 19

STUDY START DATE: 18-OCT-84

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2011/PRETEST= 19 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 15-NOV-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 K

S.A. 2449

K-20

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

KIDNEY
-MINERALIZATION, MEDULLA

THYROID GLAND
-CYST(S)

PARATHYROID TISSUE IS MISSING

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 20

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2012/PRETEST= 20 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-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

THYROID GLAND
-C-CELL HYPERPLASIA

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077
SPECIES: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 21

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2013/PRETEST= 21 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 15-NOV-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
INTESTINE(IN)	COLON, PETECHIAL HEMORRHAGE MUCOSA

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

LYMPH N-MANDIB
-ERYTHROPHAGOCYTOSIS
-HEMOSIDEROSIS

VAGINA
-LYMPHOID FOLLICLE

SEARLE RESEARCH & DEVELOPMENT
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INDIVIDUAL ANIMAL DATA REPORT
 STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
 PAGE: 22

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2017/PRETEST= 22 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
 DATE OF DEATH: 16-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
 BRAIN(BN) HYDROCEPHALUS NOTED AT TRIMMING

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

KIDNEY
 -MINERALIZATION, MEDULLA

LIVER
 -FOCAL LYMPHOCYTIC AGGREGATIONS

PARATHYROID
 -CYST(S)

BRAIN
 -DILATED VENTRICLES

SEARLE RESEARCH & DEVELOPMENT
PRODUCT SAFETY ASSESSMENT
SKOKIE, ILLINOIS 60077

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

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PAGE: 23

STUDY START DATE: 18-OCT-84
SPECIES: DOG/BEAGLE

STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER:	84-2018/PRETEST=	23 SEX:	FEMALE	DOSE GROUP:	4	SACRIFICE STATUS:	FINAL SACRIFICE
DATE OF DEATH:	15-NOV-84	STUDY DAY OF DEATH:	29	STUDY WEEK OF DEATH:	5	TERMINAL BODY WEIGHT:	NOT TAKEN

ORGAN NAME	<< GROSS KEYWORDS / PHRASES	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: DOG/BEAGLE

INDIVIDUAL ANIMAL DATA REPORT
STUDY NUMBER: SA2449

PRINTED: 28-JAN-85
PAGE: 24

STUDY START DATE: 18-OCT-84 STUDY TYPE: DIET TOXICITY/FOUR WEEK DIET TOX

ANIMAL NUMBER: 84-2019/PRETEST- 24 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: FINAL SACRIFICE
DATE OF DEATH: 16-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

HEART
-VALVULAR ENDOCARDIOSIS

THYROID GLAND
-CYST(S)

APPENDIX K, TABLE 1
FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
MALE INDIVIDUAL ORGAN WEIGHTS (g)

	BODY WT kg	BRAIN	HEART	LIVER	KIDNEY	ADRENAL	THYROID
CONTROL - 0 mg/kg							
84-1996	9.3	81.4	75.	299.	61.	0.76	0.86
84-1997	11.2	75.6	112.	360.	77.	1.16	1.03
84-1998	13.3	73.7	102.	397.	90.	1.18	0.89
LOW DOSE - 250 mg/kg							
84-2002	9.9	88.0	74.	239.	65.	1.03	0.85
84-2003	12.3	81.4	95.	309.	89.	1.37	1.17
84-2004	11.6	81.2	118.	307.	60.	1.27	0.95
MEDIUM DOSE - 500 mg/kg							
84-2008	12.7	79.4	97.	331.	65.	1.42	1.25
84-2009	11.7	77.8	98.	279.	50.	1.28	0.92
84-2010	10.2	87.3	79.	308.	67.	1.12	1.11
HIGH DOSE - 1000 mg/kg							
84-2014	8.7	71.1	64.	286.	45.	0.89	1.02
84-2015	13.1	82.1	100.	326.	63.	1.05	0.87
84-2016	10.7	87.8	85.	306.	66.	1.16	0.90

APPENDIX K, TABLE 1

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

MALE INDIVIDUAL ORGAN WEIGHTS (g)

	THYMUS	PITUITARY	STOMACH	SAL GL	TESTIS	PROSTATE	EPIDIDYMIS
CONTROL - 0 mg/kg							
84-1996	3.3	0.074	81.5	15.9	14.8	7.3	3.20
84-1997	6.7	0.079	92.5	19.8	19.1	3.4	4.22
84-1998	4.3	0.086	115.4	17.2	13.6	5.8	4.12
LOW DOSE - 250 mg/kg							
84-2002	7.7	0.068	83.4	15.0	21.0	6.6	2.80
84-2003	9.9	0.064	94.5	22.7	13.6	13.0	4.75
84-2004	6.5	0.097	99.4	17.2	15.5	11.7	5.00
MEDIUM DOSE - 500 mg/kg							
84-2008	17.7	0.045	100.0	16.6	19.2	4.3	5.21
84-2009	12.0	0.069	74.1	17.3	12.4	4.3	3.18
84-2010	5.5	0.062	76.5	15.9	7.7	12.6	4.15
HIGH DOSE - 1000 mg/kg							
84-2014	3.9	0.055	67.0	11.7	14.7	2.7	2.95
84-2015	15.5	0.081	96.5	17.3	18.1	6.4	5.01
84-2016	8.2	0.064	88.3	17.2	10.9	12.6	3.32

APPENDIX K, TABLE 1

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

MALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	BRAIN X10E-3	HEART X10E-3	LIVER X10E-2	KIDNEY X10E-3	ADRENAL X10E-5	THYROID X10E-5
CONTROL - 0 mg/kg						
84-1996	8.8	8.1	3.2	6.6	8.2	9.2
84-1997	6.8	10.0	3.2	6.9	10.4	9.2
84-1998	5.5	7.7	3.0	6.8	8.9	6.7
LOW DOSE - 250 mg/kg						
84-2002	8.9	7.5	2.4	6.6	10.4	8.6
84-2003	6.6	7.7	2.5	7.2	11.1	9.5
84-2004	7.0	10.2	2.6	5.2	10.9	8.2
MEDIUM DOSE - 500 mg/kg						
84-2008	6.3	7.6	2.6	5.1	11.2	9.8
84-2009	6.6	8.4	2.4	4.3	10.9	7.9
84-2010	8.6	7.7	3.0	6.6	11.0	10.9
HIGH DOSE - 1000 mg/kg						
84-2014	8.2	7.4	3.3	5.2	10.2	11.7
84-2015	6.3	7.6	2.5	4.8	8.0	6.6
84-2016	8.2	7.9	2.9	6.2	10.8	8.4

APPENDIX K, TABLE 1

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

MALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	THYMUS X10E-4	PITUITARY X10E-6	STOMACH X10E-3	SAL GL X10E-3	TESTIS X10E-4	PROSTATE X10E-4	EPIDIDYMIS X10E-4
CONTROL - 0 mg/kg							
84-1996	3.5	8.0	8.8	1.7	15.9	7.8	3.4
84-1997	6.0	7.1	8.3	1.8	17.1	3.0	3.8
84-1998	3.2	6.5	8.7	1.3	10.2	4.4	3.1
LOW DOSE - 250 mg/kg							
84-2002	7.8	6.9	8.4	1.5	21.2	6.7	2.8
84-2003	8.0	5.2	7.7	1.8	11.1	10.6	3.9
84-2004	5.6	8.4	8.6	1.5	13.4	10.1	4.3
MEDIUM DOSE - 500 mg/kg							
84-2008	13.9	3.5	7.9	1.3	15.1	3.4	4.1
84-2009	10.3	5.9	6.3	1.5	10.6	3.7	2.7
84-2010	5.4	6.1	7.5	1.6	7.5	12.4	4.1
HIGH DOSE - 1000 mg/kg							
84-2014	4.5	6.3	7.7	1.3	16.9	3.1	3.4
84-2015	11.8	6.2	7.4	1.3	13.8	4.9	3.8
84-2016	7.7	6.0	8.3	1.6	10.2	11.8	3.1

APPENDIX K, TABLE 1

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

MALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	HEART X10E-1	LIVER	KIDNEY X10E-1	ADRENAL X10E-3	THYROID X10E-3	THYMUS X10E-2
CONTROL - 0 mg/kg						
84-1996	9.2	3.7	7.5	9.3	10.6	4.1
84-1997	14.8	4.8	10.2	15.3	13.6	8.9
84-1998	13.8	5.4	12.2	16.0	12.1	5.8
LOW DOSE - 250 mg/kg						
84-2002	8.4	2.7	7.4	11.7	9.7	8.8
84-2003	11.7	3.8	10.9	16.8	14.4	12.2
84-2004	14.5	3.8	7.4	15.6	11.7	8.0
MEDIUM DOSE - 500 mg/kg						
84-2008	12.2	4.2	8.2	17.9	15.7	22.3
84-2009	12.6	3.6	6.4	16.5	11.8	15.4
84-2010	9.0	3.5	7.7	12.8	12.7	6.3
HIGH DOSE - 1000 mg/kg						
84-2014	9.0	4.0	6.3	12.5	14.3	5.5
84-2015	12.2	4.0	7.7	12.8	10.6	18.9
84-2016	9.7	3.5	7.5	13.2	10.3	9.3

APPENDIX K, TABLE 1

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

MALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	PITUITARY X10E-4	STOMACH X10E-1	SAL GL X10E-1	TESTIS X10E-1	PROSTATE X10E-2	EPIDIDYMIS X10E-2
CONTROL - 0 mg/kg						
84-1996	9.1	10.0	2.0	1.8	9.0	3.9
84-1997	10.4	12.2	2.6	2.5	4.5	5.6
84-1998	11.7	15.7	2.3	1.8	7.9	5.6
LOW DOSE - 250 mg/kg						
84-2002	7.7	9.5	1.7	2.4	7.5	3.2
84-2003	7.9	11.6	2.8	1.7	16.0	5.8
84-2004	11.9	12.2	2.1	1.9	14.4	6.2
MEDIUM DOSE - 500 mg/kg						
84-2008	5.7	12.6	2.1	2.4	5.4	6.6
84-2009	8.9	9.5	2.2	1.6	5.5	4.1
84-2010	7.1	8.8	1.8	0.9	14.4	4.8
HIGH DOSE - 1000 mg/kg						
84-2014	7.7	9.4	1.6	2.1	3.8	4.1
84-2015	9.9	11.8	2.1	2.2	7.8	6.1
84-2016	7.3	10.1	2.0	1.2	14.4	3.8

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN WEIGHTS (g)

	BODY WT kg	BRAIN	HEART	LIVER	KIDNEY	ADRENAL	THYROID
CONTROL - 0 mg/kg							
84-1999	10.6	73.6	85.	324.	61.	1.42	0.86
84-2000	9.4	72.8	81.	271.	47.	1.20	0.98
84-2001	9.0	68.7	86.	259.	47.	0.99	0.69
LOW DOSE - 250 mg/kg							
84-2005	9.2	77.9	76.	224.	46.	1.20	1.22
84-2006	11.0	69.6	80.	291.	64.	1.27	0.90
84-2007	8.9	85.7	77.	265.	48.	1.12	0.86
MEDIUM DOSE - 500 mg/kg							
84-2011	8.5	89.7	84.	249.	50.	1.10	0.77
84-2012	9.8	65.6	63.	235.	47.	0.86	0.82
84-2013	7.7	80.5	66.	205.	48.	1.13	0.79
HIGH DOSE - 1000 mg/kg							
84-2017	9.2	85.1	71.	274.	49.	1.02	0.81
84-2018	9.5	75.8	87.	267.	50.	0.94	0.65
84-2019	9.6	88.6	86.	301.	53.	1.31	0.97

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN WEIGHTS (g)

	THYMUS	PITUITARY	STOMACH	SAL GL	OVARY	UTERUS
CONTROL - 0 mg/kg						
84-1999	8.8	0.100	80.3	14.1	1.60	25.1
84-2000	9.6	0.060	89.7	13.4	0.93	2.2
84-2001	5.7	0.060	77.2	13.0	0.89	2.5
LOW DOSE - 250 mg/kg						
84-2005	8.1	0.065	68.6	11.5	1.01	2.3
84-2006	12.1	0.088	89.6	18.2	0.92	3.2
84-2007	10.4	0.062	81.6	14.4	1.02	4.0
MEDIUM DOSE - 500 mg/kg						
84-2011	5.6	0.075	83.2	11.6	0.92	2.3
84-2012	13.4	0.054	84.4	10.9	1.83	16.6
84-2013	4.8	0.060	77.4	12.6	1.04	2.0
HIGH DOSE - 1000 mg/kg						
84-2017	7.7	0.068	68.8	13.3	0.97	6.1
84-2018	16.1	0.087	76.3	12.3	0.81	1.6
84-2019	15.3	0.079	87.1	17.7	1.09	3.3

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	BRAIN X10E-3	HEART X10E-3	LIVER X10E-2	KIDNEY X10E-3	ADRENAL X10E-5	THYROID X10E-5
CONTROL - 0 mg/kg						
84-1999	6.9	9.0	3.1	5.8	13.4	8.1
84-2000	7.7	8.6	2.9	5.0	12.8	10.4
84-2001	7.6	9.6	2.9	5.2	11.0	7.7
LOW DOSE - 250 mg/kg						
84-2005	8.5	8.3	2.4	5.0	13.0	13.3
84-2006	6.3	7.3	2.6	5.8	11.5	8.2
84-2007	9.6	8.7	3.0	5.4	12.6	9.7
MEDIUM DOSE - 500 mg/kg						
84-2011	10.6	9.9	2.9	5.9	12.9	9.1
84-2012	6.7	6.4	2.4	4.8	8.8	8.4
84-2013	10.5	8.6	2.7	6.2	14.7	10.3
HIGH DOSE - 1000 mg/kg						
84-2017	9.3	7.7	3.0	5.3	11.1	8.8
84-2018	8.0	9.2	2.8	5.3	9.9	6.8
84-2019	9.2	9.0	3.1	5.5	13.6	10.1

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN/BODY WEIGHT RATIOS

	THYMUS X10E-4	PITUITARY X10E-6	STOMACH X10E-3	SAL GL X10E-3	OVARY X10E-5	UTERUS X10E-4
CONTROL - 0 mg/kg						
84-1999	8.3	9.4	7.6	1.3	15.1	23.7
84-2000	10.2	6.4	9.5	1.4	9.9	2.3
84-2001	6.3	6.7	8.6	1.4	9.9	2.8
LOW DOSE - 250 mg/kg						
84-2005	8.8	7.1	7.5	1.3	11.0	2.5
84-2006	11.0	8.0	8.1	1.7	8.4	2.9
84-2007	11.7	7.0	9.2	1.6	11.5	4.5
MEDIUM DOSE - 500 mg/kg						
84-2011	6.6	8.8	9.8	1.4	10.8	2.7
84-2012	13.7	5.5	8.6	1.1	18.7	16.9
84-2013	6.2	7.8	10.1	1.6	13.5	2.6
HIGH DOSE - 1000 mg/kg						
84-2017	8.4	7.4	7.5	1.4	10.5	6.6
84-2018	16.9	9.2	8.0	1.3	8.5	1.7
84-2019	15.9	8.2	9.1	1.8	11.4	3.4

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

	HEART X10E-1	LIVER	KIDNEY X10E-1	ADRENAL X10E-3	THYROID X10E-3	THYMUS X10E-2
CONTROL - 0 mg/kg						
84-1999	12.9	4.4	8.3	19.3	11.7	12.0
84-2000	11.1	3.7	6.5	16.5	13.5	13.2
84-2001	12.5	3.8	6.8	14.4	10.0	8.3
LOW DOSE - 250 mg/kg						
84-2005	9.8	2.9	5.9	15.4	15.7	10.4
84-2006	11.5	4.2	9.2	18.2	12.9	17.4
84-2007	9.0	3.1	5.6	13.1	10.0	12.1
MEDIUM DOSE - 500 mg/kg						
84-2011	9.4	2.8	5.6	12.3	8.6	6.2
84-2012	9.6	3.6	7.2	13.1	12.5	20.4
84-2013	8.2	2.5	6.0	14.0	9.8	6.0
HIGH DOSE - 1000 mg/kg						
84-2017	8.3	3.2	5.8	12.0	9.5	9.0
84-2018	11.5	3.5	6.6	12.4	8.6	21.2
84-2019	9.7	3.4	6.0	14.8	10.9	17.3

APPENDIX K, TABLE 2

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

FEMALE INDIVIDUAL ORGAN/BRAIN WEIGHT RATIOS

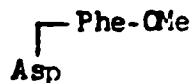
	PITUITARY X10E-4	STOMACH X10E-1	SAL GL X10E-1	OVARY X10E-2	UTERUS X10E-2
CONTROL - 0 mg/kg					
84-1999	13.6	10.9	1.9	2.2	34.1
84-2000	8.2	12.3	1.8	1.3	3.0
84-2001	8.7	11.2	1.9	1.3	3.6
LOW DOSE - 250 mg/kg					
84-2005	8.3	8.8	1.5	1.3	3.0
84-2006	12.6	12.9	2.6	1.3	4.6
84-2007	7.2	9.5	1.7	1.2	4.7
MEDIUM DOSE - 500 mg/kg					
84-2011	8.4	9.3	1.3	1.0	2.6
84-2012	8.2	12.9	1.7	2.8	25.3
84-2013	7.5	9.6	1.6	1.3	2.5
HIGH DOSE - 1000 mg/kg					
84-2017	8.0	8.1	1.6	1.1	7.2
84-2018	11.5	10.1	1.6	1.1	2.1
84-2019	8.9	9.8	2.0	1.2	3.7

APPENDIX L

PROTOCOL

1. Study Title: FOUR WEEK DIETARY ADMIX TOXICITY STUDY OF SC-19129 IN THE DOG
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 16, 1984
 - 4.2. Sacrifice: November 13-14, 1984
5. Purpose: To determine toxic effects as evidenced by clinical signs and organ damage and to provide a basis for selecting dosages for longer studies.
6. Overview of Study Design

Group	Intended Dosage (mg/kg)	Animals/Sex	Sacrifice Animals/Day
1	0	3	3
2	250	3	3
3	500	3	3
4	1000	3	3
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.
8. Test Article
 - 8.1. Chemical Structure:



- 8.2. Chemical Name: N-L- β -aspartyl-L-phenylalanine, 1-methyl ester.
- 8.3. Formulation: The appropriate amounts of test article will be mixed with diet. In order to give the intended dose, the appropriate amount of test article diet will be provided to each animal. Control animals will receive diet without compound.
- 8.4. Administration
- 8.4.1. Route: The test article will be given in the diet.
- 8.4.2. Frequency: Approximately 200 g of test article diet will be available for 1 hours each day.
- 8.4.3. Duration: 28 or 29 days.
- 8.5. Analyses:
- 8.5.1. Test article:
- 8.5.1.1. Identity, strength, purity and composition: Will be determined.
- 8.5.1.2. Stability: Will be determined.
- 8.5.2. 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.
- 8.5.3. Report: The results of these analyses will appear in a separate report provided to the Study Director by the Product Development Analytical Department.
- 8.6. Storage
- 8.6.1. Test article: Will be stored in a well-closed, light-resistant container at controlled room temperature.
- 8.6.2. Test article in carrier: Test article in diet will be stored in a plastic bag in a plastic container at controlled room temperature.

8.7. Estimated Requirements: 4.6 kg

9. Test System, Housing, and Diet

9.1. Test System

9.1.1. Species, age, and weight range: Beagle dogs (Hazleton Research Animals Inc., Cumberland, VA) of both sexes 7 to 8 months old and weighing 5 to 14 kilograms will be used. The Beagle dog has been used extensively in safety studies and a large amount of biological data is available.

9.1.2. Selection: Animals to be used in the study will be selected on the basis of acceptable findings from physical examinations, electrocardiographic examinations, clinicochemical determinations, and hematological analyses.

9.1.3. Randomization:

9.1.3.1. Assignment to dosage groups: 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 first 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 assignment produced will be reviewed for balance among the appropriate clinicochemical, hematological, and urine variables. If necessary, the randomization may be repeated to achieve better balance among the groups for these variables. 5) The groups will be assigned to dosage groups by a random permutation.

- 9.1.4. Identification: Each animal will be identified by an ear tattoo applied by the supplier and a tag, with a unique identification number, attached to a collar.

9.2. Housing

- 9.2.1. Caging: Animals will be housed individually in stainless steel cages in room J-362.

9.2.2. General environment

- 9.2.2.1. Temperature: Will be $72^{\circ} \pm 5^{\circ}\text{F}$ ($22^{\circ} \pm 3^{\circ}\text{C}$) and monitored.

- 9.2.2.2. Humidity: Will be 25% or greater and monitored.

- 9.2.2.3. Lighting: 12 hour light, 12 hour dark cycles.

9.3. Diet

- 9.3.1. Feed: Purina Certified Canine Meal 5007 containing test article will be given to the animals in the morning. The test article diet will be removed after approximately 1 hour. The animals will then receive 300g of untreated diet for 2 hours. The feed will be removed in the afternoon. Animals will be fasted overnight.

- 9.3.2. Water: Tap water from the municipal water supply will be available ad libitum.

9.3.3. Analyses

- 9.3.3.1. General: Release of each lot of feed by the manufacturer is based on analysis of composite samples from each lot which has met specifications set by the manufacturer. In addition, water is routinely analyzed for chemical and microbial impurities.

- 9.3.3.2. Special: Special analyses of feed and water will not be

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performed since no contaminants known to be capable of interfering with the study are reasonably expected to be present.

10. Clinical Observations

- 10.1. Daily Observations: Twice daily on weekdays and once daily on weekends.
- 10.2. Physical Examinations (including rectal temperatures): Once within the 2 weeks before the first dosing day, before dosing on day 1 and during weeks 2 and 4.
- 10.3. Electrocardiographic Examinations: Electrocardiograms (Leads II, aVL, V₁₀) will be taken once within the 2 weeks before the first dosing day, before dosing on day 1 and during weeks 2 and 4.
- 10.4. Body Weight and Feed Consumption
 - 10.4.1. Body weights: Will be determined three times within the two weeks before the start of dosing (the third determination being obtained the day before the first dosing day), and on days 7, 14, 29, and 30.
 - 10.4.2. Feed consumption: Determined daily beginning 2 weeks before dosing.
- 10.5. Clinical Laboratory Determinations (Blood)
 - 10.5.1. Collection: Samples of venous blood will be collected once within the 2 weeks before the first dosing day, before dosing on day 1 and during weeks 2 and 4. Samples will also be collected from moribund animals before sacrifice.
 - 10.5.2. Parameters to be determined
 - 10.5.2.1. Clinical chemistry (serum):
 - alanine aminotransferase activity
 - aspartate aminotransferase activity
 - alkaline phosphatase activity

glucose concentration
urea concentration
sodium concentration
potassium concentration
chloride concentration
calcium concentration
cholesterol concentration
total bilirubin concentration
creatinine concentration
total protein concentration
albumin (A) concentration
globulin (G) concentration
(calculated)
A/G ratio (calculated)

10.5.2.2. 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
activated partial thrombo-
plastin time
prothrombin time

10.5.3. Urine collection: Once within the 2
weeks before the first dosing day, and
during weeks 2 and 4.

10.5.3.1. Parameters to be determined:

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

10.6. Additional examinations may be done by the study
director to elucidate any observed clinical signs.

10.7. Bioavailability of Test Article:

10.7.1. Objectives: To determine 1) absorption of the test article, 2) relationship of plasma concentrations of the free acid of SC-19129 with dosage, and 3) relationship of plasma concentrations of the free acid of SC-19129 with duration of dosing.

10.7.2. Sampling Procedure: Venous blood samples (approximately 10 ml) will be collected in heparinized tubes from each animal at the following times:

- before and 2, 4, 6, and 24 hours after the start of the feeding period on days 1 and 28.

Plasma samples will be submitted to the Department of Drug Metabolism for analysis.

10.7.3. Analysis: Plasma concentrations of the free acid of SC-19129 will be determined. Appropriate pharmacokinetic evaluations will be conducted to meet the objectives listed above.

10.7.4. Report: The results of these analyses will appear in a report provided to the study director by the Drug Metabolism Department.

11. Postmortem Procedures

11.1. Animal Disposition

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

11.1.2. Animals found moribund or to be killed by design: Will be sacrificed by a lethal dose of barbiturate and necropsied.

11.2. Sacrifice Schedule: Twelve animals (3/group) will be sacrificed on days 29 and 30. For each sex within each dosage group, animals will be ranked by the last available body weight. Animals will be randomly assigned to sacrifice day.

11.3. Necropsy

11.3.1. Organ weights: The organs underlined below will be weighed for all animals killed by design. The organs of animals found dead or killed in extremis will be weighed.

11.3.2. Tissue collection

11.3.2.1. Standard:

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
gallbladder
heart
intestine, small - duodenum
intestine, small - jejunum
intestine, small - ileum
intestine, large - cecum
intestine, large - colon
intestine, large - rectum
kidney
larynx
liver
lung
lymph node, mandibular
lymph node, mesenteric
mammary gland (females only)
ovary
pancreas
peripheral nerve, sciatic
pituitary gland
prostate
salivary gland, mandibular
skeletal muscle
skin
spinal cord (cervical)
spleen
stomach
testis

thymus
thyroid gland*
tongue
trachea
urinary bladder
uterus
vagina

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

11.3.2.2. Additional specimens may be collected as determined by the study pathologist.

11.3.2.3. Fixative: Carson's fixative (buffered 10% formalin) except the testes and eyes, which will be fixed in Bouin's solution and Zenker's fixative, respectively. The testes and eyes of animals found dead will be fixed in Carson's fixative.

11.4. Histologic Examination

11.4.1. Standard: Histological sections will be prepared from the preserved specimens, stained with hematoxylin and eosin, and examined microscopically.

11.4.2. Additional sectioning, staining, and examining may be done by the pathologist to elucidate the nature of any tissue change.

12. Statistical Procedures:

12.1. Variables

body weights
body weight changes
rectal temperatures
clinical chemistry data
hematology data
urinalysis data

organ weights
organ/body weight and organ/brain weight ratios

- 12.2. Analyses: Statistical analyses of body weights and organ weights will be done separately for each sex. Analysis for all other variables will be done for each sex and for pooled sexes. For each variable, mean values and standard deviations will be determined. A one-way analysis of variance will be performed for each variable (except as listed below) 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 absolutes or urinalysis parameters except refractivity.
- 12.3. Additional analyses will be performed when necessary to augment the standard analyses described above.
13. Archiving of Materials: All raw data, supporting documents, protocol, specimens, and the final report will be transferred to the R&D Central File.

14. Protocol Approval

14.1. J. L. Allen, Ph.D.

Study Director

Product Safety Assessment: J. Allen

10-11-84

Date

14.2. F. N. Kotsonis, Ph.D.

Diplomate, A.B.T.

Director, Toxicology

Product Safety Assessment: F. Kotsonis

10/11/84

Date

14.3. D. C. Dodd, B.V.Sc.

Diplomate, A.C.V.P.

Director, Pathology

Product Safety Assessment: S. Levin for

10/12/84

Date

14.4. F. E. Kohn, Ph.D.

Senior Director,

Product Safety Assessment: F E Kohn

10/12/84

Date

APPENDIX L

PROTOCOL AMENDMENT

Effective Date - October 16, 1984

Protocol Amendment No. 1

SA 2449

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

Section 4 "Proposed Dates" has been changed to:

First dosing will occur on October 18, 1984.
Sacrifice is rescheduled for November 15-16, 1984.

Reason: The study start was postponed 2 days to allow further chemical processing of the test article.

Section 8.3 "Formulation" has been changed to:

In order to give the intended dose, the appropriate amount of test article diet (20g feed/kg body weight) will be provided to each animal.

The test article is a hydrate. Therefore, 110% of a stated dose provides the appropriate amount of compound for dosing.

Reason: The test article will be hydrated prior to use.

Section 8.4.2 Frequency of dose administration, has been changed to:

Approximately 200g of test article diet will be available for 2 hours each day.

Reason: The feeding period for the test article diet will be 2 hours instead of 1 hour to allow the animals sufficient time to consume the diet.

Section 9.3.1 "Feed" has been changed to:

The test article diet will be removed after approximately 2 hours. The animals will then receive approximately 200 - 300 g of untreated diet for 1 hour. The feed will then be removed.

S.A.2449

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Reason: The feeding period for the test article diet will be 2 hours to allow the animals sufficient time to consume the diet.

Sections 10.2 and 10.3 and 10.5.1, "Physical and Electrocardiographic Examinations and Blood Collections" have been changed to:

The pretreatment tests were performed once within the 3 weeks before the start of dosing.

Reason: The delay in start date made the pretreatment examinations more than 2 weeks before the study start.

Section 10.4.1 "Body weights" has been changed to:

Body weights will be determined three times within the three weeks before the start of dosing (the third determination being obtained the day before the first dosing day), and on days 7, 14, 21, 29 and 30.

Reason: Due to the postponement in study start, the first body weight determination was determined within 3 weeks of the start of dosing. The day 21 body weight determination was inadvertently omitted from the protocol.

Section 10.4.2 "Feed consumption" has been changed to:

Determined daily beginning 3 weeks before dosing.

Reason: Because of the delay in start date, feed consumption determinations started within 3 weeks of the study start.

 10-16-84
J.L. Allen Date
Study Director

JLA:ch

S.A.2449

L13

APPENDIX L

PROTOCOL AMENDMENT
Effective Date - October 29, 1984

Protocol Amendment No. 2

SA 2449

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

Section 10 "Clinical Observations has been changed to:

Ophthalmic examinations will be done during week 4.

Reason: It was decided that ophthalmic examinations would be done during this study.

Section 10.4.3 Water consumption determination has been added.

Water consumption will be determined for an approximate 24 hour period during week 4.

Reason: It was decided that water consumption would be measured during the study.

Section 10.5.3.2 Urine volume has been added as a urine parameter.

Urine volume will be determined for an approximate 24 hour period during week 4.

Reason: It was decided that urine volume would be determined during this study.

Section 10.7.2 "Bioavailability of Test Article" sampling has been changed to:

Venous blood samples will be collected in heparinized tubes from each animal at the following times:

- before feeding on day 1 and approximately 2, 4, 6 and 24 hours after the start of the feeding period on days 1, 15 and 28.

The volume of blood samples collected on day 1 was approximately 10 ml. Samples collected on days 15 and 28 will be approximately 7 ml.

APPENDIX L

Reason: An additional sampling day has been added (day
15).

APPROVAL:

J. L. Allen 10-29-84
J.L. Allen Date
Study Director

JLA:kp

S.A. 2449

L15

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PROTOCOL AMENDMENT
Effective Date - 11/1/84

Protocol Amendment No. 3

SA 2449

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

Section 10.5.1 Clinical Laboratory Determinations,
Collection has been changed to:

Samples of venous blood will also be collected
on Day 15 for analysis of serum urea and
bilirubin concentrations.

Reason: The values for urea and bilirubin obtained
during week 2 were generally outside of the
range of normal physiologic variation. This
unusual pattern was consistent across all
groups (including controls). To verify this
data, another blood collection will be done to
analyze for these two parameters.

APPROVAL:

 11-1-84

J. Allen
Study Director

Date

S.A. 2449

L16

QUALITY ASSURANCE STATEMENT - SA-2449 (SC-19129)

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

<u>Date of Inspec/Audit</u>	<u>Monitor</u>	<u>Date of Report to Mgmt.</u>
10/16/84 Randomization	L. Derrick	10/22/84
10/18/84 DDM Bleeds	"	"
10/19/84 Dosing	"	"
10/24/84 Body Weights	H. Schniepp	11/07/84
10/24/84 Observations	"	"
10/24/84 Dosing	"	"
11/1-2/84 DDM	"	"
11/12/84 Ophthalmic Exams	D. Howard	11/13/84
11/14/84 CC/H; Physical Exam; Rectal Temp.; EKGs; Urine Collection	D. Howard	11/14/84
10/21/84 Diet Mixing	H. Schniepp	12/04/84
11/09/84 Concentration Sampling	H. Schniepp	12/10/84
11/16/84 Homogeneity Testing; Necropsy	"	"
1/8-29/85 Audit Comparing the Raw Data Against the Draft Final Report	H. Schniepp	1/31/85

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

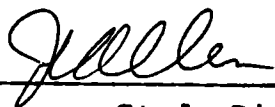
Donald D. Howard
Quality Assurance

1/31/85
Date

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GLP COMPLIANCE STATEMENT

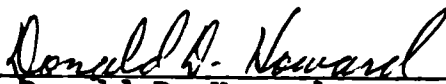
To our knowledge this study (SA-2449) (SC-19129) was conducted in compliance with the Good Laboratory Practices Regulations as set forth in part 58, 21 CFR.



Study Director

2-1-85

Date



Donald D. Howard

Dir., R&D Quality Assurance

1/31/85

Date