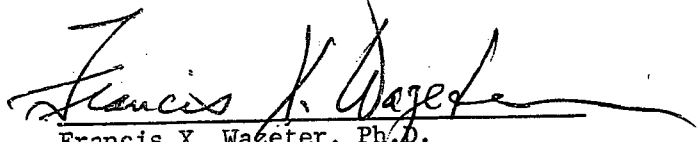


HLO-0191-65

International Research and Development Corporation

SPONSOR: E. I. duPont de Nemours and Company
COMPOUND: [REDACTED]
SUBJECT: 90-Day Feeding Study in the Beagle Dog.


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Date: November 30, 1965

[REDACTED]
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I. SYNOPSIS

In a 90-day oral toxicity study [REDACTED] was fed 7 days each week to male and female beagle dogs at dietary levels of 100, 500 or 2500 ppm. After 35 days of feeding, the 500 ppm. and 2500 ppm. dietary levels were increased to 1000 ppm. and 5000 ppm., respectively for the duration of the 90 days of treatment.

No pharmacodynamic and/or gross toxic signs were observed. Detailed physical examination revealed all dogs to be essentially normal.

No adverse body weight changes occurred among any dogs used for this study. Food consumption values remained relatively constant, and average daily water intake and urine output were not meaningfully different from values obtained in the control period.

No alterations in hematologic parameters were observed which could be related to feeding the test compound.

No biologically meaningful changes occurred with respect to plasma glucose, protein, albumin, urea nitrogen or albumin-to-globulin ratios.

A biologically significant increase in plasma cholesterol was found for 5-of-6 dogs at the 2500 ppm. dietary level.

Prothrombin time determinations and serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxalacetic transaminase (SGOT) activities remained within the usual ranges at all periods of measurement. Alkaline phosphatase activities exhibited an upward trend in 2 of 6 dogs at the high dietary level.

Urinalysis did not reveal compound-related changes at any period of examination.

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II. COMPOUND

The test compound was received from E. I. duPont de Nemours and Company, Wilmington, Delaware, on June 19, 1965. It was a brown amorphous solid in containers bearing the label [REDACTED], Haskell No. 4212."

[REDACTED]

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After 90 consecutive days of compound administration, all dogs were sacrificed and subjected to necropsy examination. (see section on Pathology for detailed methodology.)

2. Laboratory Tests:

At least 3 times during the control period, and again after 1, 2 and 3 months of compound administration, blood and 24-hour urine samples were obtained for clinical laboratory studies.

a. Hematology:

Routine hematologic studies included total¹ and differential leucocyte counts, hematocrits², hemoglobin concentrations³, erythrocyte sedimentation rates⁴, and total erythrocyte counts¹.

b. Biochemical Studies:

(1) Plasma: Chemical determination on plasma routinely included quantitative tests for glucose⁵, total protein⁶, total albumin⁷, and urea nitrogen⁸. Albumin-to-globulin ratios were calculated.

¹ Coulter Particle Size Counter, Model A., Coulter Electronics, 590 W. 20th Street, Hialeah, Florida.

² Miller, S., Microcapillary Method, Textbook of Clinical Pathology, 1960, Williams and Wilkins Company, Philadelphia, Pa., p. 43.

³ Miller, S., Cyanmethemoglobin Method, Textbook of Clinical Pathology, 1960, Williams and Wilkins Company, Philadelphia, Pa., p. 35.

⁴ Miller, S., Westergren Method, Textbook of Clinical Pathology, 1960, Williams and Wilkins Company, Philadelphia, Pa., p. 48.

⁵ Hoffman, W. S., Modified Hoffman Method, J. Biol. Chem., 120: 51, 1937. (Auto Analyzer).

⁶ Stevens, D. L., Modified Biuret Method, Amer. J. Clin. Path. 7: 40, 1946. (Auto Analyzer).

⁷ Stevens, D. L., Stevens Adaptation for Auto Analyzer, J. Clin. Invest., 33: 211, 1954.

⁸ Skeggs, L. T., Diacetyl Monoxime Method, Amer. J. Clin. Path. 28: 311, 1957. (Auto Analyzer).

III. CLINICAL STUDIES

A. METHODS:

1. General Procedure:

Twelve male and 12 female young, purebred beagle dogs in apparent good health, were used for a 90-day feeding study of [REDACTED]

The dogs were separated into one control and 3 treated groups of 3 males and 3 females each, and were housed individually in metabolism cages in temperature and humidity controlled quarters throughout the course of study. Powdered Purina Dog Chow without [REDACTED] and the same chow with the prescribed dietary levels of the test compound were available, as was water, at all times to the respective groups of dogs. Food consumption and individual body weights were measured and recorded once each week. Water intake and urine output were measured and recorded daily during each clinical laboratory test interval week.

Prior to the initiation of the compound administration phase of this study, stool flotation studies were conducted for the detection of intestinal parasites. Positive findings were followed by appropriate vermifuge therapy.

During the control period and again during the period of compound administration, all dogs were subjected to detailed physical examination. Heart sounds were examined by five point auscultation; pulse rates were determined by palpation; the ocular fundi were viewed for abnormalities; and reflexes were evaluated.

In addition to the routine physical examination described above, all dogs were observed several times daily, 7 days each week, for signs of pharmacodynamic and/or toxic effects.

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Although no gross compound-related lesions were observed at necropsy, a slight compound-related liver weight increase occurred at the middle and high dietary levels. Compound-related microscopic lesions consisted of hypertrophy of centrilobular liver parenchymal cells in 4-of-6 dogs from the 5000 ppm. dietary level group. No compound-related lesions were seen in other tissues from these dogs or in livers from dogs at the lower dietary levels.

(2) Liver Function: Plasma alkaline phosphatase activity⁹, prothrombin time¹⁰ determinations, serum glutamic oxalacetic (SGOT) and serum glutamic pyruvic (SGPT) transaminase activities¹¹, and cholesterol¹² determinations, were used as an indication of liver function. In addition, serum albumin electrophoretic patterns (cellulose strip method) were obtained once during the control period and again after one and 3 months of compound administration¹³.

(3) Urinalysis: Observations for abnormality in gross appearance and color and qualitative tests for the detection of bilirubin¹⁴, occult blood,^{15,16,17} albumin,^{18,19,20,21} and glucose,^{21,22,23} were conducted on the 24-hour urine specimen. Urinary pH,²⁴ specific gravity and volume were measured, and the urinary sediments were examined microscopically.

⁹ Marsh, W., Modified King-Armstrong Method, Clin. Chem. 5: 119, 1959. (Auto Analyzer).

¹⁰ Quick, A. J., Hemorrhagic Diseases, 1957, Lea & Febiger, Phila., Pa.

¹¹ Reitman, S., and Frankel, S., Colorimetric Method for the Determination of Serum Transaminase Activity, Am. J. of Clin. Path., 28: 56, 1957.

¹² Hycel Cholesterol Procedures - Hycel, Inc., Houston, Texas, Revised Dec. 1962.

¹³ "Sephrore 111", Gelman Technical Manual No. 51199-A, 1963.

¹⁴ "Ictotest" (Ames Reagent Tablets).

¹⁵ "Hemastix" (Ames Reagent Strips).

¹⁶ "Hematest" (Ames Reagent Tablets).

¹⁷ "Occultest" (Ames Reagent Tablets).

¹⁸ "Albustix" (Ames Reagent Strips).

¹⁹ "Bumintest" (Ames Reagent Tablets).

²⁰ Heller's Ring Test, Practical Physiologic Chemistry, Hawk, Oser and and Summerson, 13th Ed., p. 830.

²¹ "Combistix" (Ames Reagent Strips).

²² "Clinistix" (Ames Reagent Strips).

²³ "Clinitest" (Ames Reagent Tablets).

²⁴ Beckman Expanded Scale pH Meter, Model No. 76.

c. Special Sampling:

Twenty-four hour urine and fecal samples were obtained from all dogs during the period of compound administration. These were frozen and delivered to the sponsor for analysis of [REDACTED] content. Similarly, representative tissue samples (see section on Pathology) were provided following necropsy examination.

3. Compound Administration:

The test compound [REDACTED] was incorporated into the basic laboratory diet (powdered Purina Dog Chow) and fed to the respective groups of dogs throughout the study. The 3 treated groups of dogs were fed diets containing [REDACTED] at initial concentrations of 100, 500, or 2500 ppm. for a continuous period of 35 days. From the 6th week of compound administration to the termination of the study the 500 ppm. dietary level was increased to 1000 ppm. and the 2500 ppm. dietary level was increased to 5000 ppm. The dogs at the lowest dietary level continued to receive a diet containing 100 ppm. of the test agent throughout the study. The diets were freshly prepared each week and were constantly available to the dogs in self-feeding hoppers.

The control group of 3 male and 3 female dogs was maintained on a regimen identical to that of the treated groups except that the powdered basic laboratory diet did not contain [REDACTED]

B. RESULTS:

1. Behavior, Appearance and Mortality:

No alterations in behavior or appearance which could be considered to be compound-related were seen among any of the control or treated dogs employed in this study.

Incidental alterations. included one female dog (65-038) in [REDACTED]

the control group that exhibited 3 small 1-to-2 cm. areas of alopecia on the back throughout the study; one male dog (65-072, 100 ppm.) that exhibited slight alopecia of the right rear leg during the last half of the study; one female dog (65-085, 100 ppm.) that exhibited an enlarged right Harderian gland throughout the study; one male dog (65-087, 1000 ppm.) that exhibited conjunctivitis and opacity of the right cornea during the last 4 compound administration weeks; and one female dog (65-094, 1000 ppm.) that exhibited slight dermatitis of the right foreleg during the last month of compound administration.

All dogs survived the 90-day period of compound administration.

2. Physical Examination:

Routine physical examinations conducted during the study revealed all dogs to be essentially normal in behavior and appearance at all times. Heart sounds were not unusual; pulse rates were normal; reflexes were unimpaired and fundoscopic examination of the eyegrounds revealed no changes.

3. Body Weight (Table 1):

All control and treated dogs exhibited essentially normal body weights throughout the 90-day period of treatment. No differences in body weight gain were seen between the control and the treated groups of dogs.

4. Food Consumption (Table 2):

All dogs consumed essentially the same quantities of food each week during the compound administration period as they did during the control period. No differences in food consumption were seen between the control and the treated groups of dogs.

5. Compound Consumption:

Compound consumption was calculated in mg./kg./day based on the average food consumption and body weight of each animal. The results of these calculations appear in Table 3.

6. Water Intake and Urine Output (Table 4):

Although considerable variation in average daily water intake and urine output was found for most dogs employed in this study, the values obtained during the period of treatment were not consistently different from values obtained during the corresponding control period. No biologically meaningful differences were found between the control and test animals.

7. Laboratory Tests (Tables 5 through 28-A):

a. Hematology:

No compound-related hematologic changes occurred among dogs used for this study.

Incidental changes, not related to compound administration, included low borderline hemoglobin and hematocrit values and mild to marked hypochromasia of the erythrocytes. The incidence of occurrence was similarly distributed in the control and treated groups, particularly in the control examination periods and in the first examination (1 month) interval after the beginning of treatment. These values tended to fall into the usual acceptable ranges as the study progressed.

An elevated total leucocyte count was observed in Dog 65-083 (control; male) and Dog 65-078 (male; 500 ppm.) in the final control examination period prior to treatment, and Dog 65-092 (female; 500 ppm.) after 3 months of compound administration.

A decrease in the polymorphonuclear leucocyte-to-lymphocyte

ratio was observed at one or more periods of examination in 3-of-6 control dogs and 9-of-18 treated dogs during the period of study.

An occasional elevation in erythrocyte sedimentation rate was observed in the control and treated groups of dogs at one of the control periods of examination. One dog (65-187, male; 500 ppm.) exhibited an elevation in this parameter in the treatment period. This was observed at the 60-day examination period and had returned to normal by the terminal examination.

b. Biochemical Studies:

(1) Plasma: No compound-related changes in plasma biochemistry were found among dogs used for this study.

(2) Liver Function Tests: A dose-related increase in plasma cholesterol was found in 5-of-6 dogs after 3 months of compound administration at the 2500 - 5000 ppm. level. No consistent biologically meaningful changes in plasma cholesterol were found at the lower dietary levels (Table 28-A).

In addition, a slight upward trend in plasma alkaline phosphatase activity was noted for Dogs 65-090 (male) and 65-099 (male) at the 2500 - 5000 ppm. level.

Prothrombin time determinations and serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxalacetic transaminase (SGOT) values remained within the usual acceptable ranges at all periods of examination for all groups of dogs in this study. No unusual changes were noted in the serum albumin electrophoretic patterns.

(3) Urinalysis: Urinalysis examination failed to reveal changes which were considered to be related to treatment with [REDACTED]

Incidental findings, not related to compound administration, included slight bilirubinuria for one control (65-086, male) and 3 treated (65-078, 65-079 and 65-087, males) dogs at the 2-month examination period. Bilirubinuria again was found at the terminal examination, for one of these dogs (65-079, male; 500 - 1000 ppm.)

IV. PATHOLOGICAL STUDIES

A. METHODS:

1. Gross Examination:

At the completion of the compound administration period, all dogs were anesthetized with sodium pentobarbital, sacrificed by exsanguination and subjected to necropsy examination. Major organs were weighed and representative tissues were collected into 10 per cent buffered neutral formalin for subsequent histologic processing and microscopic examination. Fresh specimens of brain, liver, kidneys, spleen, fat, muscle, testes and blood were collected from each dog, frozen and forwarded to the sponsor.

2. Microscopic Examination:

The following tissues from each of the control and 5000 ppm. dosage group dogs were paraffin embedded, sectioned, stained with hematoxylin and eosin and examined microscopically:

brain	aorta	pancreas
spinal cord	spleen	liver
peripheral nerve	lymph node	gall bladder
eye	thymus	kidney
pituitary	bone marrow	urinary bladder
thyroid	salivary gland	testes or ovary
parathyroid	esophagus	prostate or uterus
adrenal	stomach	skeletal muscle
trachea	small intestine	skin
lung	large intestine	bone
heart		

Liver sections from all 100 and 1000 ppm. dosage level dogs were also processed as above and examined microscopically.

B. RESULTS:

1. Gross Pathology (Table 29) and Organ Weights (Table 30):

No compound-related gross pathologic lesions were observed in any dogs subjected to necropsy examination. Organ weights of treated dogs were within the normal range except the liver weights of the 5000 ppm. dosage group dogs which were slightly increased. The liver weights of the 1000 ppm. dosage group dogs were also greater than the liver weights of the control dogs in this study although they were still within the normal range.

2. Histopathology (Tables 31 and 32):

Compound-related changes were limited to the liver of 3-of-3 male and 1-of-3 female dogs from the 5000 ppm. dosage level group. These changes consisted of slight hypertrophy of centrilobular parenchymal cells. The cytoplasm of affected cells was more homogeneous and less coarsely granular than the cytoplasm of hepatocytes at the periphery of the lobule or of hepatocytes in control livers. These changes were not seen in any of the livers from the 100 or 1000 ppm. dosage level dogs.

██████████: Ninety-Day Feeding Study in the Dog.

TABLE 1. Individual Weekly Body Weights, Kilograms.

Dog Number	Sex	Control Period			Compound Administration Weeks											
		1	2	3	1	2	3	4	5	6	7	8	9	10	11	12
Control:																
65-038	F	7.7	7.9	8.1	8.2	8.5	8.4	8.0	8.3	8.5	8.5	8.6	8.7	8.6	8.8	8.8
65-070	M	6.5	7.2	7.9	8.6	9.5	9.9	9.8	10.5	11.1	11.8	12.2	12.4	13.4	13.4	13.8
65-081	F	4.5	4.8	5.2	6.2	6.7	7.2	6.9	7.7	8.1	8.4	8.4	9.0	9.0	9.5	9.5
65-083	M	4.4	4.5	5.2	5.7	6.3	6.7	6.3	6.9	7.5	8.1	7.8	8.3	8.7	9.1	9.1
65-086	M	4.2	4.5	5.5	6.1	6.7	7.1	7.0	7.6	8.1	8.3	8.8	9.1	9.1	9.2	9.6
65-093	F	3.7	3.9	4.1	4.5	4.8	4.9	4.7	5.2	5.3	5.5	5.7	5.7	6.2	6.3	6.7
100 ppm.:																
65-072	M	3.9	4.5	5.1	5.3	6.1	6.2	6.3	6.9	7.1	7.8	8.0	8.2	8.5	9.1	9.2
65-074	M	4.6	5.5	6.1	7.0	7.5	8.0	7.9	8.9	9.3	9.8	10.2	10.5	10.9	11.3	11.5
65-076	M	5.4	5.9	6.7	7.4	7.9	8.2	8.3	9.1	9.8	10.4	10.9	11.3	11.6	12.0	12.4
65-077	F	4.5	4.9	5.2	6.1	6.5	7.2	6.9	7.6	8.1	8.6	8.9	8.5	9.2	9.4	10.0
65-085	F	4.5	4.8	5.5	5.7	6.2	6.4	6.2	6.4	6.8	6.6	6.8	7.4	7.3	7.7	7.5
65-091	F	5.5	6.0	6.6	7.0	7.8	8.1	7.9	8.6	8.9	9.5	9.7	9.8	9.9	10.2	10.7
500 ppm.:																
65-078	M	4.5	5.0	5.5	6.0	6.7	7.2	7.1	7.9	8.2	8.8	9.2	9.6	9.7	10.1	10.4
65-079	M	3.5	3.9	4.2	4.7	5.1	5.6	5.4	6.0	6.1	6.3	6.4	6.9	6.9	7.4	7.3
65-087	M	6.4	7.3	8.1	9.2	9.8	10.5	10.4	11.0	11.4	11.8	12.6	11.5	12.8	13.7	13.9
65-092	F	3.1	3.4	3.7	4.3	4.5	4.8	4.7	5.1	5.4	5.9	6.2	5.8	6.1	6.5	6.7
65-094	F	5.5	6.1	6.7	7.3	7.8	8.2	8.3	9.1	9.4	10.0	10.3	10.3	10.9	10.8	11.4
65-095	F	4.1	4.3	4.7	5.3	5.7	6.1	5.8	6.5	6.8	7.3	7.5	7.4	8.2	8.4	8.5
2500 ppm.:																
65-088	M	3.4	3.5	3.9	4.3	4.7	5.0	4.8	5.4	5.7	6.0	6.2	6.3	6.7	6.6	7.0
65-090	M	4.7	5.3	6.1	6.7	7.3	7.9	7.9	8.5	9.1	9.6	9.7	10.1	10.7	10.9	11.3
65-096	F	4.6	5.0	5.5	6.0	6.6	7.0	7.0	7.4	7.9	8.3	8.3	8.5	8.9	9.1	9.1
65-097	F	5.1	5.5	5.8	6.4	6.9	7.5	7.4	8.2	8.8	9.4	9.5	9.8	10.2	10.7	10.7
65-098	F	3.5	3.9	4.0	4.9	5.3	5.6	5.5	6.0	6.5	6.8	6.8	7.2	7.2	7.5	7.8
65-099	M	4.3	4.8	5.4	5.5	6.1	6.5	6.5	6.9	7.4	7.5	7.9	8.0	8.5	8.7	8.7

* Increased to 1000 ppm. in the 6th week of therapy.

** Increased to 5000 ppm. in the 6th week of therapy.

Ninety-Day Feeding Study in the Dog.

TABLE 2. Average Daily Food Consumption, Grams.

Dog Number	Sex	Control Period			Compound Administration Weeks												
		1	2	3	1	2	3	4	5	6	7	8	9	10	11	12	13
Control:																	
65-038	F	210	229	256	270	234	226	264	193	157	196	196	176	212	216	225	168
65-070	M	446	378	446	407	410	366	400	458	332	182	424	385	394	361	449	304
65-081	F	278	236	315	274	304	340	280	342	289	304	326	208	269	269	344	247
65-083	M	218	204	264	271	290	288	263	294	254	283	273	185	281	284	263	209
65-086	M	307	251	354	304	329	323	287	299	266	247	260	254	286	333	358	210
65-093	F	190	139	191	216	152	215	157	203	177	209	222	163	238	228	174	178
100 ppm.:																	
65-072	M	262	279	282	250	317	334	295	325	225	259	283	235	370	281	318	209
65-074	M	283	240	357	312	328	393	347	401	333	334	342	295	355	355	341	237
65-176	M	299	353	311	339	325	343	370	404	346	381	377	347	398	382	329	353
65-077	F	196	234	248	310	300	338	288	298	286	297	321	254	319	301	266	284
65-085	F	201	206	275	262	245	269	223	279	203	183	219	187	239	223	236	169
65-091	F	344	303	347	305	368	318	314	360	327	350	315	292	335	263	296	300
500 ppm.:																	
65-078	M	250	231	270	285	339	336	283	342	276	299	325	246	364	314	305	278
65-079	M	299	215	219	222	267	274	233	311	228	223	248	216	240	295	243	177
65-087	M	420	361	417	432	399	424	418	403	302	376	385	149	450	477	395	295
65-092	F	220	181	231	200	205	221	225	231	189	206	229	134	190	214	207	215
65-094	F	336	339	401	394	384	353	353	457	331	372	315	261	348	353	309	341
65-095	F	181	210	225	320	260	244	241	299	254	294	274	205	290	275	257	282
2500 ppm.:																	
65-088	M	142	139	213	216	213	214	201	245	194	237	236	183	283	229	251	167
65-090	M	242	268	334	324	331	361	340	378	326	390	309	271	395	337	318	208
65-096	F	226	223	276	268	291	288	262	282	217	252	236	216	287	251	248	179
65-097	F	224	224	233	263	284	325	306	323	266	306	292	281	319	347	313	202
65-098	F	230	206	251	238	236	242	228	259	225	238	244	204	266	218	235	176
65-099	M	232	215	280	257	240	284	249	294	242	249	269	225	294	277	245	192

** Increased to 1000 ppm. in the 6th week of therapy.

** Increased to 5000 ppm. in the 6th week of therapy.

Ninety-Day Feeding Study in the Dog.

TABLE 3. Average Daily Compound Consumption, Mg./Kg./Day.

Animal No. & Group	Sex	Compound Administration Weeks												
		1	2	3	4	5	6	7	8	9	10	11	12	13
<u>100 ppm.:</u>														
65-072	M	4.7	5.2	5.4	4.6	4.7	3.2	3.3	3.5	2.9	4.4	3.1	3.5	2.4
65-074	M	4.5	4.4	4.9	4.4	4.5	3.6	3.4	3.4	2.8	3.3	3.1	3.0	2.2
65-076	M	4.6	4.1	4.2	4.5	4.4	3.5	3.7	3.5	3.1	3.4	3.2	2.7	3.0
65-077	F	5.1	4.6	4.7	4.2	3.9	3.5	3.5	3.6	3.0	3.5	3.2	2.7	3.0
65-085	F	4.6	4.0	4.2	3.6	4.4	3.0	2.8	3.2	2.5	3.3	3.0	3.1	2.3
65-091	F	4.4	4.7	3.9	4.0	4.2	3.7	3.7	3.2	3.0	3.4	2.6	2.8	3.0
<u>500 ppm.:</u>														
65-078	M	23.8	25.3	23.3	19.9	21.6	33.7	34.0	35.3	25.6	37.5	31.1	29.3	28.1
65-079	M	21.5	26.2	24.5	21.6	25.9	37.4	35.4	38.8	31.3	34.8	39.9	33.3	25.7
65-087	M	23.5	20.4	20.2	20.1	18.3	26.5	31.9	30.6	12.9	35.2	34.8	28.4	21.9
65-092	F	23.3	22.8	23.0	23.9	22.6	35.0	34.9	36.9	23.1	31.1	32.9	30.9	33.1
65-094	F	27.0	24.6	21.5	21.3	25.1	35.2	37.2	30.6	25.3	31.9	33.1	27.1	31.0
65-095	F	30.2	22.8	20.0	20.8	23.0	37.4	40.3	36.5	27.7	35.4	32.7	30.2	35.7
<u>2500 ppm.:</u>														
65-088	M	125.6	113.3	107.0	104.7	113.4	170.2	197.5	190.3	145.2	211.2	173.5	179.3	124.6
65-090	M	120.9	113.4	114.3	107.6	111.2	179.1	203.1	159.3	134.2	184.6	154.6	140.7	98.1
65-096	F	111.7	110.2	102.9	93.6	95.3	137.3	151.8	142.2	127.1	161.2	137.9	136.3	101.7
65-097	F	102.7	102.9	108.3	103.4	98.5	151.1	162.8	153.7	143.4	156.3	162.1	146.3	101.0
65-098	F	121.4	111.3	108.0	103.6	107.9	173.1	175.0	179.4	141.7	184.7	145.3	150.6	122.2
65-099	M	116.8	98.4	109.2	95.8	107.5	163.5	166.0	170.3	140.6	173.0	159.2	140.8	114.3

* Increased to 1000 ppm. in the 6th week of therapy.

** Increased to 5000 ppm. in the 6th week of therapy.

Ninety-Day Feeding Study in the Dog.

TABLE 4. Average Daily Water Intake (W.I.), ml.; Urine Output (U.O.), ml.; and Water Intake-to-Urine Output Ratio (W/U).

Time Interval	Control					
	Dog 65-038 F W.I. U.O. W/U	Dog 65-070 M W.I. U.O. W/U	Dog 65-081 F W.I. U.O. W/U	Dog 65-083 M W.I. U.O. W/U	Dog 65-086 M W.I. U.O. W/U	Dog 65-093 F W.I. U.O. W/U
Control Weeks						
1	520 190 2.7	895 128 7.0	610 90 6.8	915 468 2.0	640 139 4.6	365 110 3.3
2	498 234 2.1	801 168 4.8	603 121 5.0	1005 455 2.2	686 195 3.5	428 288 1.5
3	627 265 2.4	868 298 2.9	607 170 3.6	790 250 3.2	518 173 3.0	327 127 2.6
Compound Administration Weeks						
1	509 183 2.8	1425 435 3.3	690 109 6.3	1225 753 1.6	1025 380 2.7	350 208 1.7
9	553 198 2.8	1465 505 2.9	830 174 4.8	1248 578 2.2	1005 329 3.1	480 281 1.7
12	495 243 2.0	1213 426 2.8	723 238 3.0	1125 664 1.7	737 297 2.5	460 265 1.7

Ninety-Day Feeding Study in the Dog.

TABLE 4, Continued. Average Daily Water Intake (W.I.), mL.; Urine Output (U.O.), mL.; and Water Intake-to-Urine Output Ratio (W/U).

Time Interval	100 ppm.					
	Dog 65-072 M W.I. U.O. W/U	Dog 65-074 M W.I. U.O. W/U	Dog 65-076 M W.I. U.O. W/U	Dog 65-077 M W.I. U.O. W/U	Dog 65-085 F W.I. U.O. W/U	Dog 65-091 F W.I. U.O. W/U
Control Weeks						
1	580 70 8.3	635 239 2.7	860 213 4.0	660 128 5.2	645 290 2.2	648 173 3.7
2	490 109 4.5	850 295 2.9	808 286 2.8	585 210 2.8	684 319 2.1	773 161 4.8
3	587 130 4.5	900 340 2.6	867 307 2.8	747 233 3.2	807 297 2.7	470 210 2.2
Compound Administration Weeks						
1	850 286 3.0	1240 460 2.7	1135 343 3.3	773 300 2.6	790 389 2.0	738 176 4.2
9	1038 265 3.9	1488 361 4.1	1150 454 2.5	1280 433 3.0	1015 489 2.1	1060 316 3.4
12	853 319 2.7	1000 563 1.8	1258 390 3.2	975 465 2.1	770 430 1.8	750 259 2.9

Ninety-Day Feeding Study in the Dog.

TABLE 4, Continued. Average Daily Water Intake (W.I.), ml.; Urine Output (U.O.), ml.; and Water Intake-to-Urine Output Ratio (W/U).

Time Interval	500 ppm.*					
	Dog 65-078 M	Dog 65-079 M	Dog 65-087 M	Dog 65-092 F	Dog 65-094 F	Dog 65-095 F
	W.I. U.O. W/U	W.I. U.O. W/U	W.I. U.O. W/U	W.I. U.O. W/U	W.I. U.O. W/U	W.I. U.O. W/U
Control Weeks						
1	525 138 3.8	465 90 5.2	765 171 4.5	415 140 3.0	1455 354 4.1	840 120 7.0
2	555 159 3.5	498 108 4.6	1025 243 4.2	558 185 3.0	1378 553 2.5	434 255 1.7
3	647 155 4.2	487 145 3.4	593 180 3.3	460 233 2.0	1450 487 3.0	393 145 2.7
Compound Administration Weeks						
1	790 230 3.4	483 191 2.5	883 243 3.6	438 232 1.9	760 270 2.8	417 250 1.7
9	875 266 3.3	683 290 2.4	485 144 3.4	270 166 1.6	935 188 5.0	545 271 2.0
12	888 245 3.6	538 240 2.2	1100 403 2.7	380 258 1.5	918 349 2.6	485 217 2.2

* Increased to 1000 ppm. in the 6th week of therapy.

Ninety-Day Feeding Study in the Dog.

TABLE 4. Continued. Average Daily Water Intake (W.I.), ml.; Urine Output (U.O.), ml.; and Water Intake-to-Urine Output Ratio (W/U).

Time Interval	2500 ppm.*					
	Dog 65-088 M W.I. U.O. W/U	Dog 65-090 M W.I. U.O. W/U	Dog 65-096 F W.I. U.O. W/U	Dog 65-097 F W.I. U.O. W/U	Dog 65-098 F W.I. U.O. W/U	Dog 65-099 M W.I. U.O. W/U
Control Weeks						
1	480 205 2.3	545 139 3.9	570 103 5.5	505 198 2.6	365 95 3.8	463 149 3.1
2	549 240 2.3	574 195 2.9	573 173 3.3	488 228 2.1	448 156 2.9	558 214 2.6
3	607 263 2.3	587 193 3.0	593 130 4.6	573 273 2.1	580 157 3.7	580 195 3.0
Compound Administration Weeks						
1	750 430 1.7	704 185 3.8	645 115 5.6	690 414 1.7	513 203 2.5	613 183 3.3
9	785 389 2.0	867 249 3.5	720 188 3.8	780 320 2.4	745 191 3.9	605 268 2.3
12	605 329 1.8	843 280 3.0	648 175 3.7	650 343 1.9	535 225 2.4	387 210 1.8

* Increased to 5000 ppm. in the 6th week of therapy.

Ninety-Day Feeding Study in the Dog.

TABLE 5. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-038, Female Dosage: Control	Control Periods			Compound Administration Months		
	1	2	3	1 1*	2	3
Hematology:						
Total Erythrocytes (x10 ⁶ /cmm.)	6.02	5.85	5.27	5.76	7.16	5.71
Hemoglobin, gm./100 ml.	15.2	13.3	13.2	14.1	17.5	15.9
Hematocrit, %	43	42	40	44	51	48
Sedimentation Rate, mm./hr.	0	2	2	1	0	0
Total Leucocytes, (x10 ³ /cmm.)	13.73	11.91	12.22	12.85	11.25	10.84
Differential Count:						
Neutrophils, %	51	57	61	47 42	46	44
Seg., %	49	57	60	47 41	46	41
Non-Seg., %	2	0	1	0 1	0	3
Lymphocytes, %	46	37	38	48 51	46	48
Eosinophils, %	1	3	0	1 2	6	2
Monocytes, %	2	3	1	4 5	2	6
Basophils, %	0	0	0	0 0	0	0
Appearance of Erythrocytes	No	No	No	SH	No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	98	110	108	99	104	100
Protein, gm./100 ml.	6.51	6.11	5.58	5.59	5.90	5.48
Albumin, gm./100 ml.	2.90	2.53	2.33	2.42	2.86	3.06
Albumin-to-Globulin Ratio	0.80	0.71	0.72	0.76	0.94	1.26
Urea Nitrogen, mg./100 ml.	11.5	15.0	15.5	14.2	14.0	11.2
Alkaline Phosphatase, units	11	6	8	5	5	6
Cholesterol, mg./100 ml.	196	212	211	200	178	184
Prothrombin Time, sec.	8	7	7	8	7	8
SGOT units/ml. ¹	15	18	16	16	15	14
SGPT units/ml. ²	15	15	17	18	15	11
Urinalysis:						
Volume, ml.	160	155	290	160	55	190
Color	S=C	S=C	LS-cl	S=C	S-cl	S=C
pH	7.3	7.3	7.2	7.1	7.2	7.3
Specific Gravity	1.052	1.042	1.042	1.022	1.035	1.031
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes	2-3					occ
Amorphous Urates	F				F	
Epithelial Cells	4-5		1-3	1-2	occ	occ
Erythrocytes						occ
Triple Phosphates	M	M	F	M	L	M
Ammonium Urates	F	M		F	M	
Bacteria	F	F	M	F	L	F

Code: S - Straw N - Negative E - Loaded * Repeat Determinations
 LS - Light Straw No - Normal F - Few ¹ Serum Glutamic Oxalacetic
 cl - Cloudy SH - Slight Hypochromia M - Many Transaminase
 C - Clear occ - Occasional ² Serum Glutamic Pyruvic
 Transaminase

██████████: Ninety-Day Feeding Study in the Dog.

TABLE 6. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-070, Male Dosage: Control	Control Periods			Compound Administration Months		
	1	2	3	1	2	3
<u>Hematology:</u>						
Total Erythrocytes ($\times 10^6$ /cmm.)	5.41	5.15	4.08	5.52	6.66	6.21
Hemoglobin, gm./100 ml.	12.1	10.7	11.3	13.4	15.6	16.2
Hematocrit, %	38	34	37	41	47	50
Sedimentation Rate, mm./hr.	5	5	1	2	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	17.42	14.10	13.43	15.10	11.75	12.52
<u>Differential Count:</u>						
Neutrophils, %	49	56	64	53	48	52
Seg., %	49	55	64	53	48	51
Non-Seg., %	0	1	0	0	0	1
Lymphocytes, %	49	42	33	44	43	41
Eosinophils, %	1	1	3	1	4	6
Monocytes, %	1	1	0	2	4	1
Basophils, %	0	0	0	0	1	0
Appearance of Erythrocytes	No	H	SH	No	SH	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	130 ^a	126	132	114	107	107
Protein, gm./100 ml.	5.95	5.76	4.92	5.13	5.41	5.50
Albumin, gm./100 ml.	2.60	2.38	2.18	2.45	2.71	2.64
Albumin-to-Globulin Ratio	0.78	0.70	0.80	0.92	1.00	0.92
Urea Nitrogen, mg./100 ml.	12.0	15.3	11.8	15.2	12.5	13.1
Alkaline Phosphatase, units	19	18	19	10	11	10
Cholesterol, mg./100 ml.	176	186	140	175	195	198
Prothrombin Time, sec.	8	8	8	8	7	8
SGOT units/ml. ¹	22	20	18	17	20	15
SGPT units/ml. ²	19	11	14	14	14	13
<u>Urinalysis:</u>						
Volume, ml.	80	105	150	455	480	225
Color	S-cl	S-cl	S-cl	LS-cl	LS-cl	S-cl
pH	6.0	6.2	6.8	6.1	6.2	6.8
Specific Gravity	1.060	1.062	1.046	1.026	1.014	1.032
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	3-4				occ	occ
Amorphous Urates	F					
Epithelial Cells	L	5-6		1-2	2-3	1-2
Triple Phosphates	M	M	F	F	occ	F
Calcium Oxalate			F			
Ammonium Urates	L		F	F	M	F
Bacteria	F	F	M	M	M	M

Code: S - Straw N - Negative L - Loaded a - Repeat 141

LS - Light Straw NO - Normal F - Few

cl - Cloudy SH - Slight Hypochromia M - Many

H - Hypochromia occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase

²Serum Glutamic Pyruvic Transaminase

Dog No. 65-081, Female	Control Periods			Compound Administration Months		
	1	2	3 3*	1 1*	2	3

<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	125	127	136	131 ^a	121	114
Protein, gm./100 ml.	5.91	5.85	5.00	5.05	5.75	5.65
Albumin, gm./100 ml	2.58	2.45	2.29	2.73	3.01	2.98
Albumin-to-Globulin Ratio	0.78	0.72	0.85	1.17	1.09	1.11
Urea Nitrogen, mg./100 ml.	10.3	13.8	10.8	11.6	12.8	13.0
Alkaline Phosphatase, units	17	18	19	10	12	12
Cholesterol, mg./100 ml.	161	162	153	149	175	167
Prothrombin Time, sec.	8	8	8	8	7	7
SGOT units/ml. ¹	19	22	30	18	23	18
SGPT units/ml. ²	19	19	18	1	19	11

	60	105	195	180	135	330
Volume, ml.						
Color	S-cl	S-cl	S-cl	S-cl	S-cl	LS-cl
pH	6.4	6.2	6.5	6.8	7.2	6.8
Specific Gravity	1.062	1.048	1.035	1.030	1.026	1.022
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N

Leucocytes	4-5	3-5			F	
Amorphous Urates	F		F	F		L
Epithelial Cells	F		occ	2-3	occ	
Triple Phosphates	L	M		F		F
Ammonium Urates	M	F	F	F	F	F
Bacteria	M	F	M	M	F	M

- ¹Serum Glutamic Oxalacetic Transaminase
- ²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 8. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-083, Male	Control Periods			Compound Administration Months		
Dosage: Control	1	2	3 3*	1	2	3
Hematology:						
Total Erythrocytes ($\times 10^6$ /cmm.)	4.51	4.67	3.62	5.13	6.41	6.26
Hemoglobin, gm./100 ml.	11.3	10.6	10.1	12.5	14.8	15.3
Hematocrit, %	35	34	35	40	44	47
Sedimentation Rate, mm./hr.	2	2	6	1	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	14.93	16.56	24.36 ^a	15.12	14.11	12.27
Differential Count:						
Neutrophils, %	63	63	86 83	62	49	45
Seg., %	62	60	85 81	61	49	43
Non-Seg., %	1	3	1 2	1	0	2
Lymphocytes, %	35	32	14 16	36	44	50
Eosinophils, %	0	0	0 0	0	3	0
Monocytes, %	2	5	0 1	2	4	5
Basophils, %	0	0	0 0	0	0	0
Appearance of Erythrocytes	No	SH	SH	No	No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	127	136	127	124	105	100
Protein, gm./100 ml.	5.95	5.93	5.35	5.13	5.49	5.40
Albumin, gm./100 ml.	2.80	2.58	2.45	2.69	2.85	2.90
Albumin-to-Globulin Ratio	0.89	0.77	0.85	1.16	1.06	1.16
Urea Nitrogen, mg./100 ml.	14.8	15.2	14.8	16.6	15.0	18.8
Alkaline Phosphatase, units	14	15	16	9	11	9
Cholesterol, mg./100 ml.	116	138	122	123	142	157
Prothrombin Time, sec.	8	8	8	9	7	8
SGOT units/ml. ¹	22	24	19	15	13	9
SGPT units/ml. ²	18	26 ^b	19	17	14	8
Urinalysis:						
Volume, ml.	300	220	375	410	525	330
Color	LS-cl	LS-cl	LS-cl	LS-cl	LS-cl	LS-cl
pH	6.8	6.5	6.8	7.5	6.0	6.5
Specific Gravity	1.018	1.012	1.019	1.013	1.016	1.012
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes			2-3			occ-3
Amorphous Urates	F	F				
Epithelial Cells	F	occ			F	2-5
Triple Phosphates	F		F	L	F	
Ammonium Urates	M			F	M	
Bacteria	L	L	F	M	M	F
Code: LS - Light Straw	N - Negative		L - Loaded		a - Repeat 23.39	
cl - Cloudy	No - Normal		F - Few		b - Repeat 26	
	SH - Slight Hypochromia		M - Many			
			occ - Occasional			
			¹ Serum Glutamic Oxalacetic Transaminase			
			² Serum Glutamic Pyruvic Transaminase			

Ninety-Day Feeding Study in the Dog.

TABLE 9. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-086, Male Dosage: Control	Control Periods			Compound Administration Months		
	1	2	3 3*	1 1*	2	3
<u>Hematology:</u>						
Total Erythrocytes (x10 ⁶ /cmm.)	4.81	4.40	3.70	5.18	6.13	6.09
Hemoglobin, gm./100 ml.	11.0	10.1	9.6	12.8	14.0	15.3
Hematocrit, %	35	32	31	40	43	45
Sedimentation Rate, mm./hr.	2	1	1	1	1	0
Total Leucocytes, (x10 ³ /cmm.)	13.79	12.20	13.57	17.48	10.92	9.11
<u>Differential Count:</u>						
Neutrophils, %	61	51	60	24 32	47	55
Seg., %	60	49	59	24 32	47	52
Non-Seg., %	1	2	1	0 0	0	3
Lymphocytes, %	30	42	35	70 64	51	37
Eosinophils, %	2	0	2	2 1	1	1
Monocytes, %	7	7	2	4 3	1	7
Basophils, %	0	0	1	0 0	0	0
Appearance of Erythrocytes	No	MH	No	MH	No	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	126 ^a	107	104	111	100	102
Protein, gm./100 ml.	5.58	5.41	4.75	4.73	4.96	5.04
Albumin, gm./100 ml.	1.96	2.09	2.09	2.45	2.50	2.70
Albumin-to-Globulin Ratio	0.54	0.63	0.76	1.07	1.02	1.15
Urea Nitrogen, mg./100 ml.	14.8	16.8	12.3	10.7	9.4	10.7
Alkaline Phosphatase, units	16	15	15	9	11	7
Cholesterol, mg./100 ml.	196	174	142	181	203	200
Prothrombin Time, sec.	7	8	7	8	7	8
SGOT units/ml. ¹	18	21	28 25	13	10	13
SGPT units/ml. ²	16	17	10	11	8	13
<u>Urinalysis:</u>						
Volume, ml.	125	165	130	290	130	230
Color	S-cl	LS-cl	S-cl	LS-cl	S-cl	S-cl
pH	6.3	6.8	6.8	7.2	7.0	7.3
Specific Gravity	1.044	1.018	1.060	1.016	1.016	1.022
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	2+ ^b	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	4-6	8-10	3-4	1-2	8-10	1-3
Amorphous Urates		F		F		
Epithelial Cells	F				F	occ
Erythrocytes						R
Triple Phosphates	F	F	L	M	occ	F
Ammonium Urates	M			F	L	
Bacteria	L	M	M	M	L	F

Code: S - Straw N - Negative L - Loaded * - Repeat Determinations
 LS - Light Straw No - Normal F - Few a - Repeat 134
 cl - Cloudy MH - Marked Hypochromia M - Many b - Repeat 1+
 1+ - Trace-to-slight R - Rare
 2+ - Slight-to-moderate occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 10. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-093, Female Dosage: Control	Control Periods			Compound Administration Months		
	1	2	3 3 ²	1	2	3
<u>Hematology:</u>						
Total Erythrocytes (x10 ⁶ /cmm.)	5.97	4.93	3.77	5.76	6.84	5.94
Hemoglobin, gm./100 ml.	12.6	11.1	10.2	12.6	14.8	14.6
Hematocrit, %	40	33	30	40	46	44
Sedimentation Rate, mm./hr	0	1	14 16	2	0	0
Total Leucocytes, (x10 ³ /cmm.)	15.90	14.53	9.21	17.51	12.34	11.90
<u>Differential Count:</u>						
Neutrophils, %	61	57	53	67	58	67
Seg., %	60	56	53	67	58	66
Non-Seg., %	1	1	0	0	0	1
Lymphocytes, %	37	39	44	29	38	32
Eosinophils, %	1	1	1	1	4	1
Monocytes, %	1	3	2	3	0	0
Basophils, %	0	0	0	0	0	0
Appearance of Erythrocytes	No	SH	SH	SH	No	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	127	125	115	118	112	112
Protein, gm./100 ml.	5.63	5.53	5.38	5.05	5.08	5.11
Albumin, gm./100 ml.	1.89	2.01	2.00	2.08	2.48	2.60
Albumin-to-Globulin Ratio	0.51	0.57	0.59	0.70	0.95	1.04
Urea Nitrogen, mg./100 ml.	13.5	13.0	12.0	12.8	13.8	14.6
Alkaline Phosphatase, units	19	18	19	13	13	10
Cholesterol, mg./100 ml.	144	128	147	132	115	124
Prothrombin Time, sec.	7	7	7	7	7	8
SGOT units/ml. ¹	16	17	19	12	15	12
SGPT units/ml. ²	22	22	26	16	18	15
<u>Urinalysis:</u>						
Volume, ml.	50	130	90	80	105	280
Color	S-C	S-C	DS-cl	S-C	S-C	S-cl
pH	7.4	7.0	7.0	7.4	8.0 ^a	7.3
Specific Gravity	1.050	1.022	1.058	1.041	1.027	1.031
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	F	1-3	1-2		6-8	occ
Amorphous Urates		F				
Epithelial Cells		1-2	1-2	1-2	2-3	1-2
Erythrocytes						occ
Triple Phosphates	F	F	M	F	L	
Ammonium Urates	F				F	F
Bacteria	F	F	F	F	M	F

Code: S - Straw N - Negative L - Loaded * - Repeat Determinations
 DS - Dark Straw No - Normal F - Few a - Repeat 6.8
 cl - Cloudy SH - Slight Hypochromia M - Many
 occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Dog No. 65-072, Male

Code: S - Straw
DS - Dark
cl - Cloudy

No - Normal

SH - Slight Hypochromia

H = Hypochromia

F - Few

M - Many

occ - Occasional

a - Repeat N

¹Serum Glutamic Oxalacetic Transaminase

²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 12. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-074; Male Dosage: 100 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2	3
<u>Hematology:</u>						
Total Erythrocytes ($\times 10^6$ /cmm.)	5.32	4.38	4.06	5.68	6.47	5.75
Hemoglobin, gm./100 ml.	12.1	9.0	11.0	13.0	15.2	16.1
Hematocrit, %	36	28	33	41	46	48
Sedimentation Rate, mm./hr.	4	4	1	0	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	15.22	11.90	10.16	10.11	12.23	10.68
<u>Differential Count:</u>						
Neutrophils, %	61	49	64	51	43	39
Seg., %	61	49	64	51	42	37
Non-Seg., %	0	0	0	0	1	2
Lymphocytes, %	35	38	36	43	48	52
Eosinophils, %	3	8	0	3	1	4
Monocytes, %	1	5	0	3	8	5
Basophils, %	0	0	0	0	0	0
Appearance of Erythrocytes	No	MH	No	SH	SH	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	109	118	119	119	116	113
Protein, gm./100 ml.	5.65	5.58	5.00	4.92	5.53	5.65
Albumin, gm./100 ml.	2.16	2.24	2.00	2.23	2.38	2.90
Albumin-to-Globulin Ratio	0.62	0.67	0.67	0.83	0.76	1.06
Urea Nitrogen, mg./100 ml.	13.2	15.0	12.5	13.3	11.2	12.0
Alkaline Phosphatase, units	15	17	15	9	11	9
Cholesterol, mg./100 ml.	131	144	147	123	158	172
Prothrombin Time, sec.	8	8	8	8	6	8
SGOT units/ml. ¹	18	17	19	14	12	13
SGPT units/ml. ²	19	18	16	16	13	15
<u>Urinalysis:</u>						
Volume, ml.	95	180	300	270	285	460
Color	S-C	S-cl	S-cl	S-cl	S-cl	LS-cl
pH	6.6	7.0	6.5	6.4	6.6	7.1
Specific Gravity	1.030	1.033	1.030	1.022	1.016	1.011
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	1-2	5-7	2-4	2-3		
Amorphous Urates				L	F	
Epithelial Cells	F	occ	occ			occ
Triple Phosphates	occ	F	F	F	occ	R
Calcium Oxalate	F					
Ammonium Urates	F				F	F
Bacteria	F	M	M	F	M	M

Code: S - Straw N - Negative L - Loaded
 LS - Light Straw No - Normal F - Few
 C - Clear SH - Slight Hypochromia M - Many
 cl - Cloudy MH - Marked Hypochromia R - Rare

occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Company Sanitized. Does not contain TSCA CBI

Dog No.: 65-076, Male

1. Serum Glutamic Oxalacetic Transaminase
2. Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 14. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-077, Female Dosage: 100 ppm.	Control Periods						Compound Administration Months		
	1	1*	2	3	3*		1	2	3
<u>Hematology:</u>									
Total Erythrocytes (x10 ⁶ /cmm.)	5.13		4.69	3.95			5.31	6.60	6.21
Hemoglobin, mg./100 ml.	11.5		9.9	11.5			12.1	15.4	15.6
Hematocrit, %	36		31	33			38	46	48
Sedimentation Rate, mm./hr.	3		2	10	12		1	0	0
Total Leucocytes, (x10 ³ /cmm.)	11.0		11.88	16.81			12.81	10.10	12.48
<u>Differential Count:</u>									
Neutrophils, %	40	41	54	43	47		61	52	65
Seg., %	38	40	53	42	46		61	52	63
Non-Seg., %	2	1	1	1	1		0	0	2
Lymphocytes, %	58	54	38	52	50		32	41	27
Eosinophils, %	0	2	2	2	1		3	1	5
Monocytes, %	2	3	6	3	2		4	6	3
Basophils, %	0	0	0	0	0		0	0	0
Appearance of Erythrocytes	No		H	No			MH	No	No
<u>Plasma Biochemistry:</u>									
Glucose, mg./100 ml.	118		121	125			128 ^a	126 ^b	96
Protein, gm./100 ml.	5.63		5.56	5.48			4.99	5.45	5.20
Albumin, gm./100 ml.	2.58		2.55	2.09			2.62	2.88	2.8
Albumin-to-Globulin Ratio	0.85		0.85	0.62			1.10	1.12	1.27
Urea Nitrogen, mg./100 ml.	11.5		10.5	14.5			12.9	13.0	12.6
Alkaline Phosphatase, units	20		21	18			12	15	11
Cholesterol, mg./100 ml.	155		153	188			142	182	169
Prothrombin Time, sec.	8		8	8			8	7	8
SGOT units/ml. ¹	26		23	18			16	16	13
SGPT units/ml. ²	16		17	12			14	11	13
<u>Urinalysis:</u>									
Volume, ml.	105		140	255			260	240	180
Color	S-cl		S-cl	S-cl			LS-cl	S-C	S-cl
pH	6.5		7.3	7.3			6.8	7.0	7.0
Specific Gravity	1.043		1.022	1.025			1.020	1.023	1.023
Albumin	N		N	N			N	N	N
Bilirubin	N		N	N			N	N	N
Glucose	N		N	N			N	N	N
Occult Blood	N		N	N			N	N	N
<u>Microscopic:</u>									
Leucocytes	3-4						1-2		occ
Amorphous Urates							F		
Epithelial Cells	F			1-2			3-4	F	1-3
Triple Phosphates	L		F	F			F	F	occ
Ammonium Urates	M		F					F	
Bacteria	L		M	F			F	M	M

Code: S - Straw N - Negative L - Loaded a - Repeat 128
 LS - Light Straw No - Normal F - Few b - Repeat 121
 C - Clear MH - Marked Hypochromia M - Many
 cl - Cloudy H - Hypochromia occ - Occasional
¹Serum Glutamic Oxalacetic Transaminase
²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 15. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-085, Female		Control Periods			Compound Administration Months		
Dosage: 100 ppm.		1	2	3	1	2	3
<u>Hematology:</u>							
Total Erythrocytes (x10 ⁶ /cmm.)	6.17	5.19	4.44	5.58	6.94	6.65	
Hemoglobin, gm./100 ml.	14.1	12.1	12.1	14.9	17.7	18.0	
Hematocrit, %	44	38	39	47	54	51	
Sedimentation Rate, mm./hr.	1	1	1	0	0	0	
Total Leucocytes, (x10 ³ /cmm.)	16.47	17.52	13.96	14.45	9.66	10.74	
<u>Differential Count:</u>							
Neutrophils, %	49	48	51	53	54	46	
Seg., %	47	47	51	53	53	46	
Non-Seg., %	2	1	0	0	1	0	
Lymphocytes, %	44	44	47	39	40	44	
Ebsinophils, %	2	4	2	3	2	4	
Monocytes, %	5	4	0	5	4	6	
Basophils, %	0	0	0	0	0	0	
Appearance of Erythrocytes	No	H	No	H	No	No	
<u>Plasma Biochemistry:</u>							
Glucose, mg./100 ml.	142 ^a	121	119	122	106	106	
Protein, gm./100 ml.	5.58	6.08	5.59	5.39	5.69	5.82	
Albumin, gm./100 ml.	2.16	2.20	2.39	2.60	2.82	3.14	
Albumin-to-Globulin Ratio	0.53	0.57	0.75	0.92	0.98	1.17	
Urea Nitrogen, mg./100 ml.	9.8	13.4	11.8	11.0	11.7	12.1	
Alkaline Phosphatase, units	15	15	13	8	11	8	
Cholesterol, mg./100 ml.	159	132	148	128	141	161	
Prothrombin Time, sec.	8	8	8	8	8	9	
SGOT units/ml. ¹	20	22	19	15	16	11	
SGPT units/ml. ²	25	19	19	14	17	9	
<u>Urinalysis:</u>							
Volume, ml.	140	135	325	335	165	200	
Color	S-cl	LS-cl	LS-cl	LS-cl	S-cl	S-cl	
pH	7.0	7.0	6.9	6.8	7.0	6.8	
Specific Gravity	1.023	1.019	1.027	1.011	1.015	1.018	
Albumin	N	N	N	N	N	N	
Bilirubin	N	N	N	N	N	N	
Glucose	N	N	N	N	N	N	
Occult Blood	N	N	N	N	N	N	
<u>Microscopic:</u>							
Leucocytes	6-8	4-5					
Amorphous Urates	F		F	F			
Epithelial Cells		F		2-3	F		
Erythrocytes						occ	
Triple Phosphates	F	F	F		M		
Ammonium Urates	M			F	L		
Bacteria	L	F	M	M	L	M	
Code:	S - Straw	N - Negative	L - Loaded	a - Repeat 148			
	LS - Light Straw	No - Normal	F - Few				
	C - Clear	H - Hypochromia	M - Many				
	cl - Cloudy	occ - Occasional					

- 1 Serum Glutamic Oxalacetic Transaminase
- 2 Serum Glutamic Pyruvic Transaminase

Company Sanitized. Does not contain TSCA CBI

Ninety-Day Feeding Study in the Dog.

TABLE 16. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-091, Female Dosage: 100 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2 0*	3
Hematology:						
Total Erythrocytes ($\times 10^6/\text{cmm.}$)	5.78	4.86	4.26	5.81	6.13	5.60
Hemoglobin, gm./100 ml.	12.6	11.6	11.6	14.2	15.2	15.3
Hematocrit, %	40	36	38	43	46	48
Sedimentation Rate, mm./hr.	1	1	0	0	0	0
Total Leucocytes, ($\times 10^3/\text{cmm.}$)	10.20	12.39	11.83	11.39	10.18	10.96
Differential Count:						
Neutrophils, %	49	45	46	56	30 40	41
Seg., %	49	43	46	56	30 39	41
Non-Seg., %	0	2	0	0	0 1	0
Lymphocytes, %	42	45	48	36	63 52	53
Eosinophils, %	3	5	3	6	3 0	3
Monocytes, %	6	5	3	2	4 8	3
Basophils, %	0	0	0	0	0 0	0
Appearance of Erythrocytes	No	No	H	H	No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	112	106	115	119	108	109
Protein, gm./100 ml.	5.58	5.38	4.80	5.01	5.08	5.20
Albumin, gm./100 ml.	1.90	1.95	1.98	2.35	2.56	2.73
Albumin-to-Globulin Ratio	0.52	0.57	0.70	0.88	1.01	1.10
Urea Nitrogen, mg./100 ml.	12.7	17.3	12.4	11.4	12.3	13.0
Alkaline Phosphatase, units	28	25	24	12	19	16
Cholesterol, mg./100 ml.	160	138	149	143	155	149
Prothrombin Time, sec.	8	7	7	8	8	10
SGOT units/ml. ¹	23	22	16	16	19	15
SGPT units/ml. ²	14	18	18	12	8	6
Urinalysis:						
Volume, ml.	150	205	140	120	175	355
Color	S-cl	LS-cl	S-cl	S-cl	S-cl	S-cl
pH	6.1	6.5	6.9	6.1	6.8	7.0
Specific Gravity	1.058	1.021	1.043	1.032	1.023	1.022
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes			3-4	3-4		
Amorphous Urates		F		F	F	F
Epithelial Cells	F		occ			occ
Triple Phosphates	M	F	L	M	M	
Ammonium Urates	M	F	M		M	
Bacteria	M	L	L	F	L	F
Code: S - Straw N - Negative L - Loaded LS - Light Straw No - Normal F - Few cl - Cloudy H - Hypochromia M - Many occ - Occasional ¹ Serum Glutamic Oxalacetic Transaminase ² Serum Glutamic Pyruvic Transaminase						

Ninety-Day Feeding Study in the Dog.

TABLE 17. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-078, Male	Control Periods			Compound Administration Months		
	1	2 2*	3 3*	1	2 2*	3
Dosage: 500 ppm.						
Hematology:						
Total Erythrocytes ($\times 10^6/\text{cmm.}$)	4.66	3.63	3.41	4.65	5.69	5.49
Hemoglobin, gm./100 ml.	12.0	8.0	9.3	11.7	14.5	15.3
Hematocrit, %	38	25	31	36	43	46
Sedimentation Rate, mm./hr.	2	16 20	3	1	0	0
Total Leucocytes, ($\times 10^3/\text{cmm.}$)	10.95	22.50 ^a	11.66	7.59	9.98	11.61
Differential Count:						
Neutrophils, %	55	26 27	69	52	41	54
Seg., %	55	26 27	69	51	41	54
Non-Seg., %	0	0 0	0	1	0	0
Lymphocytes, %	40	70 68	30	39	51	41
Eosinophils, %	3	4 3	1	5	4	4
Monocytes, %	2	0 2	0	4	4	1
Basophils, %	0	0 0	0	0	0	0
Appearance of Erythrocytes	No	H	H	No	No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	138 ^b	146	134	118	117	113
Protein, gm./100 ml.	5.82	6.13	4.92	4.74	5.25	5.16
Albumin, gm./100 ml.	2.68	2.39	2.00	2.42	2.71	2.78
Albumin-to-Globulin Ratio	0.85	0.64	0.69	1.04	1.06	1.17
Urea Nitrogen, mg./100 ml.	11.5	10.4	9.9	11.5	11.5	11.1
Alkaline Phosphatase, units	22	21	25	13	17 16	15
Cholesterol, mg./100 ml.	129	169	132	154	180	203
Prothrombin Time, sec.	8	8	8	8	7	9
SGOT units/ml. ¹	20	26	22	19	20	15
SGPT units/ml. ²	18	13	10	17	10	15
Urinalysis:						
Volume, ml.	80	175	150	140	140	275
Color	S-cl	LS-cl	S-cl	S-cl	S-cl	S-cl
pH	6.7	6.8	7.3	6.5	7.3	6.7
Specific Gravity	1.045	1.026	1.051	1.033	1.025	1.025
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	tr ^c	1+ ^d
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes			occ			R
Amorphous Urates	F	F		F	F	
Epithelial Cells	F	F		3-4	F	
Triple Phosphates	M	M	F	F	F	F
Ammonium Urates	M				M	
Bacteria	M	M	M	M	M	M
Code: S - Straw N - Negative L - Loaded a - Repeat 22.65 LS - Light Straw No - Normal F - Few b - Repeat 140 cl - Cloudy H - Hypochromia M - Many c - Repeat 1+ tr - Trace R - Rare d - Repeat 2+ 1+ - Trace-to- occ - Occasional * - Repeat Determinations slight 1Serum Glutamic Oxalacetic Transaminase 2+ - Slight-to- 2Serum Glutamic Pyruvic Transaminase moderate						

██████: Ninety-Day Feeding Study in the Dog.

TABLE 18. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-079, Male Dosage: 500 ppm.	Control Periods			Compound Administration Months		
	1 1*	2	3	1	2 2*	3
<u>Hematology:</u>						
Total Erythrocytes ($\times 10^6$ /cmm.)	4.72	4.21	4.00	5.15	5.70	5.49
Hemoglobin, gm./100 ml.	11.3	9.9	10.1	12.1	14.6	15.1
Hematocrit, %	35	33	34	38	44	46
Sedimentation Rate, mm./hr.	3	1	1	0	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	10.08	10.70	9.62	9.85	10.60	10.34
<u>Differential Count:</u>						
Neutrophils, %	42 43	51	56	48	41 32	50
Seg., %	40 41	51	55	48	40 32	48
Non-Seg., %	2 2	0	1	0	1 0	2
Lymphocytes, %	53 55	42	41	46	49 59	47
Eosinophils, %	2 0	0	1	2	1 1	0
Monocytes, %	3 2	7	2	4	9 8	3
Basophils, %	0 0	0	0	0	0 0	0
Appearance of Erythrocytes	No	MH	H	SH	H	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	142 ^a	140	132	124	120	113
Protein, gm./100 ml.	6.03	6.00	5.00	4.98	5.38	5.31
Albumin, gm./100 ml.	2.60	2.61	2.29	2.60	2.80	2.95
Albumin-to-Globulin Ratio	0.76	0.77	0.85	1.09	1.08	1.25
Urea Nitrogen, mg./100 ml	16.3	14.9	9.9	13.3	14.8	12.0
Alkaline Phosphatase, units	21	24	23	12	16 16	12
Cholesterol, mg./100 ml.	161	149	147	135	166	169
Prothrombin Time, sec.	7	8	8	8	7	8
SGOT units/ml. ¹	34	20	22	18	16	13
SGPT units/ml. ²	26	25	19	19	12	15
<u>Urinalysis:</u>						
Volume, ml.	50	30	200	75	105	85
Color	S-cl	S-C	S-cl	S-cl	S-cl	DS-cl
pH	6.9	6.5	6.9	6.9	7.5	7.3
Specific Gravity	1.050	1.050	1.027	1.026	1.033	1.030
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	1+b	4+c
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	20-30	5-7	1-2			1-3
Amorphous Urates				F		
Epithelial Cells	3-4	F	occ	1-2	F	
Erythrocytes						occ
Triple Phosphates	L	M	F	M	L	M
Ammonium Urates	F			F	F	
Bacteria	F	M	M	M	L	L
Flagellates			R			
Code: S - Straw N - Negative L - Loaded a - Repeat 144 DS - Dark Straw No - Normal F - Few b - Repeat 1+ C - Clear SH - Slight Hypochromia M - Many c - Repeat 4+ cl - Cloudy H - Hypochromia R - Rare * - Repeat Determinations 1+ - Trace-to- occ - Occasional slight ¹ Serum Glutamic Oxalacetic Transaminase 4+ - Marked ² Serum Glutamic Pyruvic Transaminase						

Company Sanitized. Does not contain TSCA CRF

Ninety-Day Feeding Study in the Dog.

TABLE 19. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-087, Male Dosage: 500 ppm.	Control Periods				Compound Administration Months		
	1 1*	2	3 3*		1	2 2*	3
<u>Hematology:</u>							
Total Erythrocytes (x10 ⁶ /cmm.)	5.29	4.55	4.39		5.64	6.38	6.91
Hemoglobin, gm./100 ml.	12.5	11.0	11.2		13.0	15.1	16.2
Hematocrit, %	40	33	35		40	45	50
Sedimentation Rate, mm./hr.	10 11	5	0		0	11 8	0
Total Leucocytes, (x10 ³ /cmm.)	12.38	9.44	9.92		9.73	10.72	11.54
<u>Differential Count:</u>							
Neutrophils, %	56	46	39 35		35	57	42
Seg., %	55	45	39 34		35	55	41
Non-Seg., %	1	1	0 1		0	2	1
Lymphocytes, %	42	46	59 62		60	37	51
Eosinophils, %	0	4	1 2		2	0	0
Monocytes, %	2	4	1 1		3	6	7
Basophils, %	0	0	0 0		0	0	0
Appearance of Erythrocytes	No	H	H		No	H	No
<u>Plasma Biochemistry:</u>							
Glucose, mg./100 ml.	140 ^a	124	116		116	103	113
Protein, gm./100 ml.	6.37	6.13	5.14		5.30	6.05	6.25
Albumin, gm./100 ml.	2.30	2.32	2.55		2.90	2.72	3.38
Albumin-to-Globulin Ratio	0.57	0.61	0.98		1.20	0.82	1.22
Urea Nitrogen, mg./100 ml.	11.5	11.8	9.6		12.7	12.3	8.0
Alkaline Phosphatase, units	15	13	14		9	19 17	9
Cholesterol, mg./100 ml	159	171	125		125	250 ^b	214
Prothrombin Time, sec.	8	7	8		8	7	8
SGOT units/ml. ¹	13	15	16		14	15	9
SGPT units/ml. ²	10	18	11		14	10	8
<u>Urinalysis:</u>							
Volume, ml.	125	150	305		150	110	360
Color	S-cl	S-C	S-cl		S-cl	DS-cl	LS-cl
pH	6.3	6.1	6.2		6.2	6.0	6.6
Specific Gravity	1.044	1.031	1.038		1.049	1.058	1.015
Albumin	N	N	N		N	N	N
Bilirubin	N	N	N		N	2+ ^c	N
Glucose	N	N	N		N	N	N
Occult Blood	N	N	N		N	N	N
<u>Microscopic:</u>							
Leucocytes	70-80	3-4	10-12		3-5	8-10	
Amorphous Urates		M	F				
Epithelial Cells	F	1-2	1-3		1-2	8-10	0-3
Triple Phosphates	F				F		
Calcium Oxalate		F					
Ammonium Urates	M				F	M	M
Bacteria	L	M	M		F	F	M
Code: S - Straw N - Negative L - Loaded a - Repeat 150							
LS - Light Straw No - Normal F - Few b - Repeat 215							
DS - Dark Straw H - Hypochromia M - Many c - Repeat 2+							
cl - Cloudy 2+ - Slight-to-occ - Occasional * - Repeat Determinations							
moderate ¹ Serum Glutamic Oxalacetic Transaminase							
² Serum Glutamic Pyruvic Transaminase							

Ninety-Day Feeding Study in the Dog.

TABLE 20. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-092 Dosage: 500 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2	3
Hematology:						
Total Erythrocytes ($\times 10^6$ /cmm.)	5.40	4.76	4.09	5.44	6.38	5.78
Hemoglobin, gm./100 ml	12.2	10.8	10.6	13.2	14.6	15.1
Hematocrit, %	39	34	35	42	45	46
Sedimentation Rate, mm./hr.	0	1	1	0	2	0
Total Leucocytes, ($\times 10^3$ /cmm.)	14.71	11.74	11.04	10.69	12.12	21.88
Differential Count:						
Neutrophils, %	67	73	65	66	80	77
Seg., %	65	72	65	66	80	73
Non-Seg., %	2	1	0	0	0	4
Lymphocytes, %	27	22	33	31	16	20
Eosinophils, %	1	1	2	1	0	0
Monocytes, %	5	4	0	2	4	3
Basophils, %	0	0	0	0	0	0
Appearance of Erythrocytes	No	H	H	SH	No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	116	120	118	109	108	107
Protein, gm./100 ml.	5.82	5.48	4.95	4.99	5.86	5.45
Albumin, gm./100 ml.	1.91	1.95	2.13	2.52	2.64	2.83
Albumin-to-Globulin Ratio	0.49	0.55	0.76	1.02	0.82	1.08
Urea Nitrogen, mg./100 ml.	18.0	16.8	19.4	19.0	14.5	11.3
Alkaline Phosphatase, units	15	18	18	12	17 ^a	13
Cholesterol, mg./100 ml.	140	122	120	121	191	160
Prothrombin Time, sec.	8	8	8	9	6	8
SGOT units/ml. ¹	22	20	25	15	11	13
SGPT units/ml. ²	28	29	14	18	17	11
Urinalysis:						
Volume, ml.	130	145	190	245	105	310
Color	S-cl	LS-cl	S-cl	LS-cl	S-C	LS-cl
pH	7.1	6.8	7.4	6.5	7.5	7.0
Specific Gravity	1.039	1.020	1.034	1.013	1.026	1.018
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes	8-10	8-10	4-5		12-15	
Amorphous Urates			F	F		
Epithelial Cells	F			3-4	3-4	occ
Triple Phosphates	M	F	F		M	occ
Ammonium Urates	M	F	F		F	
Bacteria	F	M	M	M	F	F

Code: S - Straw N - Negative L - Loaded a - Repeat 18
 LS - Light Straw No - Normal F - Few
 C - Clear SH - Slight Hypochromia M - Many
 cl - Cloudy H - Hypochromia occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase
²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 21. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-094, Female Dosage: 500 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2 2*	3
Hematology:						
Total Erythrocytes ($\times 10^6$ /cmm.)	4.96	4.99	4.14	4.84	6.01	5.10
Hemoglobin, gm./100 ml.	11.6	11.6	10.6	12.4	14.9	15.1
Hematocrit, %	37	36	34	38	46	46
Sedimentation Rate, mm./hr.	1	4	4	3	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	18.16	17.17	16.30	13.67	12.60	13.88
Differential Count:						
Neutrophils, %	48	49	55	58	41 29	53
Seg., %	47	48	55	58	41 29	53
Non-Seg., %	1	1	0	0	0 0	0
Lymphocytes, %	48	40	37	38	56 68	45
Eosinophils, %	1	8	2	2	1 0	0
Monocytes, %	3	3	6	2	2 2	2
Basophils, %	0	0	0	0	0 0	0
Appearance of Erythrocytes	No	SH	H	SH	H	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	108	114	122	114	118	113
Protein, gm./100 ml.	5.43	5.80	5.40	5.20	5.78	5.36
Albumin, gm./100 ml.	1.91	2.05	2.12	2.33	2.68	2.70
Albumin-to-Globulin Ratio	0.54	0.55	0.65	0.81	0.87	1.01
Urea Nitrogen, mg./100 ml.	10.1	11.8	10.3	10.5	10.2	10.0
Alkaline Phosphatase, units	23	21	25	15	17 18	15
Cholesterol, mg./100 ml.	128	129	126	141	181	192
Prothrombin Time, sec.	7	8	8	8	6	8
SGOT units/ml. ¹	17	19	19	20	16	17
SGPT units/ml. ²	13	11	13	14	6	14
Urinalysis:						
Volume, ml.	395	500	490	200	110	345
Color	LS-cl	LS-cl	S-cl	S-cl	S-cl	S-cl
pH	7.2	6.0	7.0	6.0	6.8	6.8
Specific Gravity	1.028	1.015	1.020	1.035	1.031	1.026
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes			1-2	1-2		3-5
Amorphous Urates		F				
Epithelial Cells			occ		F	1-3
Triple Phosphates	F		F		M	
Ammonium Urates	L			F	M	
Bacteria	L	M	M	L	L	L
Flagellates		M				

Code: S - Straw N - Negative L - Loaded * - Repeat Determinations
 LS - Light Straw No - Normal F - Few
 cl - Cloudy SH - Slight Hypochromia M - Many
 H - Hypochromia occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 22. Results of Hematological, Biochemical and Urinalysis Studies.

TABLE 22. Results of Hematological, Biochemical and Urinalysis Studies.							
Dog No. 65-095, Female Dosage: 500 ppm.	Control Periods			Compound Administration Months			
	1	1*	2	3	1	2	3
<u>Hematology:</u>							
Total Erythrocytes (x10 ⁶ /cmm.)	5.19		4.34	4.22	5.19	6.18	5.46
Hemoglobin, gm./100 ml.	11.6		11.9	10.4	12.4	14.9	15.0
Hematocrit, %	35		35	34	38	45	45
Sedimentation Rate, mm./hr.	1		1	2	0	0	0
Total Leucocytes, (x10 ³ /cmm.)	10.71		12.48	12.51	10.23	10.78	9.91
<u>Differential Count:</u>							
Neutrophils, %	28	30	63	37	50	50	51
Seg., %	25	30	62	37	50	50	49
Non-Seg., %	3	0	3	0	0	0	2
Lymphocytes, %	67	65	35	60	47	49	44
Eosinophils, %	1	2	0	1	2	1	2
Monocytes, %	4	3	2	2	1	0	3
Basophils, %	0	0	0	0	0	0	0
Appearance of Erythrocytes	No		SH	H	H	H	No
<u>Plasma Biochemistry:</u>							
Glucose, mg./100 ml.	108		122	121	110	107	103
Protein, gm./100 ml.	5.51		5.36	5.01	5.15	5.61	5.60
Albumin, gm./100 ml.	1.90		2.11	1.99	2.52	2.79	3.09
Albumin-to-Globulin Ratio	0.53		0.65	0.66	0.95	0.99	1.23
Urea Nitrogen, mg./100 ml.	12.0		13.3	9.0	11.9	11.8	12.6
Alkaline Phosphatase, units	16		17	14	10	14	11
Cholesterol, mg./100 ml.	142		162	154	136	167	204
Prothrombin Time, sec.	9		8	8	8	7	9
SGOT units/ml. ¹	19		20	15	14	12	10
SGPT units/ml. ²	17		22	11	16	14	15
<u>Urinalysis:</u>							
Volume, ml.	180		130	180	160	130	255
Color	S-cl		S-cl	S-cl	S-cl	S-cl	S-cl
pH	7.1		7.3	6.1	6.7	8.0 ^a	7.2
Specific Gravity	1.044		1.016	1.036	1.025	1.022	1.026
Albumin	N		N	N	N	N	N
Bilirubin	N		N	N	N	N	N
Glucose	N		N	N	N	N	N
Occult Blood	N		N	N	N	N	N
<u>Microscopic:</u>							
Leucocytes	F		1-2		1-2		
Amorphous Urates				F			
Epithelial Cells	2-3		occ			occ	
Erythrocytes							occ
Triple Phosphates	F		F	L	F	M	F
Ammonium Urates	L		F		F	F	
Bacteria	L		M	F	F	M	M
Waxy Casts	4-6/LPF						

Code: S - Straw N - Negative L - Loaded a - Repeat 7.0
 cl - Cloudy No - Normal F - Few * - Repeat Determinations
 SH - Slight Hypochromia M - Many LPF - Low Powered Field
 H - Hypochromia occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 23. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-088, Male Dosage: 2500 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2	3
<u>Hematology:</u>						
Total Erythrocytes ($\times 10^6$ /cmm.)	5.32	4.70	4.25	5.68	6.16	6.35
Hemoglobin, gm./100 ml.	12.1	11.0	10.7	12.8	15.8	15.9
Hematocrit, %	38	35	35	39	49	49
Sedimentation Rate, mm./hr.	1	1	0	0	0	0
Total Leucocytes, ($\times 10^3$ /cmm.)	16.72	17.69	12.78	12.38	13.25	12.29
<u>Differential Count:</u>						
Neutrophils, %	57	65	55	52	51	51
Seg., %	56	63	55	52	51	50
Non-Seg., %	1	2	0	0	0	1
Lymphocytes, %	42	28	39	44	40	41
Eosinophils, %	1	1	1	1	1	5
Monocytes, %	0	6	5	3	8	3
Basophils, %	0	0	0	0	0	0
Appearance of Erythrocytes	No	MH	H	MH	No	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml	128a	119	108	111	104	103
Protein, gm./100 ml.	5.99	5.73	4.85	4.98	5.78	5.58
Albumin, gm./100 ml.	2.53	2.55	2.32	2.60	3.03	3.22
Albumin-to-Globulin Ratio	0.73	0.80	0.92	1.09	1.10	1.36
Urea Nitrogen, mg./100 ml.	10.1	12.5	13.5	11.4	12.8	12.0
Alkaline Phosphatase, units	14	16	14	12	17 ^b	16
Cholesterol, mg./100 ml.	109	119	100	109	185	187
Prothrombin Time, sec.	9	9	8	8	7	9
SGOT units/ml. ¹	17	18	15	14	9	12
SGPT units/ml. ²	29 ^c	31	18	19	16	19
<u>Urinalysis:</u>						
Volume, ml.	140	130	325	280	255	215
Color	S-cl	S-C	LS-cl	LS-cl	LS-cl	LS-cl
pH	6.8	7.5	6.5	6.5	6.4	6.7
Specific Gravity	1.025	1.016	1.016	1.011	1.016	1.021
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	55-65	2-3	1-2			
Amorphous Urates		F	F	F		
Epithelial Cells		occ	occ	occ		
Triple Phosphates	F	M		F	occ	
Ammonium Urates	M				M	M
Bacteria	M	F	F	M	L	L

Code: S - Straw N - Negative L - Loaded a - Repeat 139
 LS - Light Straw No - Normal F - Few b - Repeat 18
 C - Clear MH - Marked Hypochromia M - Many c - Repeat 29
 cl - Cloudy H - Hypochromia occ - Occasional

¹Serum Glutamic Oxalacetic Transaminase
²Serum Glutamic Pyruvic Transaminase

Ninety-Day Feeding Study in the Dog.

TABLE 24. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-090, Male Dosage: 2500 ppm.	Control Periods			Compound Administration Months		
	1	2	3	1	2	3
<u>Hematology:</u>						
Total Erythrocytes (x10 ⁶ /cmm.)	5.47	4.88	4.76	5.25	6.03	6.06
Hemoglobin, gm./100 ml.	13.0	11.5	11.6	12.5	14.3	14.8
Hematocrit, %	40	36	36	39	43	45
Sedimentation Rate, mm./hr.	1	1	0	0	1	0
Total Leucocytes, (x10 ³ /cmm.)	15.76	15.72	13.47	11.36	14.41	12.60
<u>Differential Count:</u>						
Neutrophils, %	59	73	61	55	52	53
Seg., %	59	72	60	54	52	52
Non-Seg., %	0	1	1	1	0	1
Lymphocytes, %	34	25	34	42	42	40
Eosinophils, %	3	0	0	2	5	1
Monocytes, %	3	2	5	1	1	6
Basophils, %	1	0	0	0	0	0
Appearance of Erythrocytes	No	MH	SH	H	No	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	138 ^a	133	132	124 ^b	121 ^c	120
Protein, gm./100 ml.	5.63	5.38	4.80	4.90	5.86	5.60
Albumin, gm./100 ml.	1.93	1.98	2.05	2.20	2.55	2.58
Albumin-to-Globulin Ratio	0.52	0.58	0.75	0.81	0.78	0.86
Urea Nitrogen, mg./100 ml.	15.0	15.8	12.9	13.5	13.4	8.7
Alkaline Phosphatase, units	21	23	24	18	28 ^d	33 ^e
Cholesterol, mg./100 ml.	163	146	140	195 ^f	208	284
Prothrombin Time, sec.	7	7	7	7	6	7
SGOT units/ml. ¹	19	19	18	17	13	13
SGPT units/ml. ²	16	20	14	16	5	20
<u>Urinalysis:</u>						
Volume, ml.	155	135	205	120	115	360
Color	S-cl	S-C	S-cl	S-cl	S-cl	S-cl
pH	6.8	7.2	7.1	6.8	6.2	7.0
Specific Gravity	1.036	1.034	1.045	1.033	1.029	1.028
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	F	1-2	2-4	1-2		3-5
Amorphous Urates		F		F		
Epithelial Cells	F	occ	occ	3-4		1-3
Erythrocytes						occ
Triple Phosphates	M	M	M	M	M	F
Calcium Oxalate	F					
Ammonium Urates	M				M	
Bacteria	M	F	M	M	M	M
Code: S - Straw N - Negative L - Loaded a - Repeat 146 e - Repeat 32 C - Clear No - Normal F - Few b - Repeat 126 f - Repeat 200 cl - Cloudy MH - Marked Hypochromia M - Many c - Repeat 118 g - Repeat 221 SH - Slight Hypochromia occ - Occasional d - Repeat 23 H - Hypochromia						
¹ Serum Glutamic Oxalacetic Transaminase ² Serum Glutamic Pyruvic Transaminase						

Ninety-Day Feeding Study in the Dog.

TABLE 25. Results of Hematological, Biochemical and Urinalysis Studies.

TABLE 23. RESULTS OF HEMATOLOGY, PLASMA BIOCHEMISTRY AND URINALYSIS, 257							
Dog No. 65-096, Female		Control Periods			Compound Administration Months		
Dosage: 2500 ppm.		1	2	3	1	2	3
<u>Hematology:</u>							
Total Erythrocytes (x10 ⁶ /cmm.)		5.58	4.55	3.98	5.26	6.03	5.94
Hemoglobin, gm./100 ml.		12.2	11.3	10.5	12.3	12.8	13.1
Hematocrit, %		39	34	34	39	40	41
Sedimentation Rate, mm./hr.		1	1	0	0	0	0
Total Leucocytes (x10 ³ /cmm.)		11.15	11.96	10.40	12.51	11.82	12.66
<u>Differential Count:</u>							
Neutrophils, %		55	68	63	43	49	51
Seg., %		54	67	63	43	49	48
Non-Seg., %		1	1	0	0	0	3
Lymphocytes, %		43	27	36	55	43	46
Eosinophils, %		0	2	1	0	0	2
Monocytes, %		2	3	0	2	8	1
Basophils, %		0	0	0	0	0	0
Appearance of Erythrocytes		No	H	H	H	H	No
<u>Plasma Biochemistry:</u>							
Glucose, mg./100 ml.		109	130 ^a	121	126 ^b	118	118
Protein, gm./100 ml.		5.78	5.68	4.95	5.39	6.31	5.90
Albumin, gm./100 ml.		2.12	2.10	2.32	2.69	2.95	3.13
Albumin-to-Globulin Ratio		0.58	0.59	0.88	1.00	0.88	1.13
Urea Nitrogen, mg./100 ml.		13.0 ^c	13.5	11.3	12.4	12.0	10.7
Alkaline Phosphatase, units		22	22	22	14 ^d	19 ^c	18
Cholesterol, mg./100 ml.		167	158	131	215 ^d	269 ^e	307 ^f
Prothrombin Time, sec.		7	7	8	7	6	8
SGOT units/ml. ¹		19	20	20	19	15	20
SGPT units/ml. ²		14	11	16	14	11	15
<u>Urinalysis:</u>							
Volume, ml.		110	205	150	125	200	135
Color		S-cl	LS-C	S-cl	S-C	S-cl	S-cl
pH		6.5	7.1	7.1	6.8	6.8	6.8
Specific Gravity		1.057	1.025	1.051	1.048	1.020	1.045
Albumin		N	N	N	N	N	N
Bilirubin		N	N	N	N	N	N
Glucose		N	N	N	N	N	N
Occult Blood		N	N	N	N	N	N
<u>Microscopic:</u>							
Leucocytes		F	6-8		25-30	3-4	occ
Epithelial Cells		F	1-3	1-2	3-4	occ	1-3
Erythrocytes							8-10
Triple Phosphates		F	M	M	F	F	
Ammonium Urates		M				M	
Bacteria		M	F	M	F	M	F
Waxy Casts		2-3/LPF					
Code:	S - Straw	N - Negative	L - Loaded	a - Repeat 141	d - Repeat 210		
	LS - Light Straw	No - Normal	F - Few	b - Repeat 121	e - Repeat 251		
	C - Clear	H - Hypochromia	M - Many	c - Repeat 19	f - Repeat 300		
	cl - Cloudy	occ - Occasional					

1 Serum Glutamic Oxalacetic Transaminase
2 Serum Glutamic Pyruvic Transaminase
LPF - Low Powered Field

Ninety-Day Feeding Study in the Dog.

TABLE 26. Results of Hematological, Biochemical and Urinalysis Studies.

[illegible]

Company Sanitized. Does not contain TSCA CB

Ninety-Day Feeding Study in the Dog.

TABLE 27. Results of Hematological, Biochemical and Urinalysis Studies.

Dog No. 65-098, Female Dosage: 2500 ppm.	Control Periods			Compound Administration Months		
	1 1*	2	3	1	2 2*	3
Hematology:						
Total Erythrocytes ($\times 10^6/\text{cmm.}$)	5.20	4.86	4.49	5.27	6.36	5.70
Hemoglobin, gm./100 ml.	12.6	12.1	11.3	13.7	15.1	15.4
Hematocrit, %	40	37	38	43	45	47
Sedimentation Rate, mm./hr.	0	0	0	0	0	0
Total Leucocytes, ($\times 10^3/\text{cmm.}$)	15.10	13.91	15.31	13.41	11.45	12.61
Differential Count:						
Neutrophils, %	39 38	43	72	58	40 59	47
Seg., %	39 38	42	72	58	40 58	45
Non-Seg., %	0 0	1	0	0	0 1	2
Lymphocytes, %	52 53	40	25	41	49 36	44
Eosinophils, %	3 3	2	1	0	2 1	3
Monocytes, %	6 6	5	2	1	9 4	6
Basophils, %	0 0	0	0	0	0 0	0
Appearance of Erythrocytes	No	H	No	No	No No	No
Plasma Biochemistry:						
Glucose, mg./100 ml.	106	112	112	117	112	111
Protein, gm./100 ml.	5.82	5.63	4.95	5.15	5.70	5.70
Albumin, gm./100 ml.	2.40	2.24	2.38	2.60	2.94	3.09
Albumin-to-Globulin Ratio	0.70	0.66	0.93	1.02	1.06	1.18
Urea Nitrogen, mg./100 ml.	14.8	14.3	11.3	11.5	11.7	12.3
Alkaline Phosphatase, units	23	20	25	20	24 ^a	24
Cholesterol, mg./100 ml.	133	117	120	198 ^b	244 ^c	249
Prothrombin Time, sec.	8	8	8	8	6	8
SGOT units/ml. ¹	19	19	24	19	12	7
SGPT units/ml. ²	21	19	13	20	23 ^d	16
Urinalysis:						
Volume, ml.	80	155	205	135	120	255
Color	S-cl	S-cl	S-cl	S-cl	S-cl	S-C
pH	7.0	7.0	7.1	7.1	8.0 ^e	7.5
Specific Gravity	1.060	1.019	1.032	1.031	1.024	1.039
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
Microscopic:						
Leucocytes	F	6-8	1-2	1-2	3-4	
Epithelial Cells	F	1-2		2-3	occ	
Erythrocytes						occ
Triple Phosphates	F	M	F	F	M	
Ammonium Urates	M			F	F	F
Bacteria	M	F	F	F	L	F

Code: S - Straw N - Negative L - Loaded a - Repeat 22 e - Repeat 6.5
 C - Clear No - Normal F - Few b - Repeat 201
 cl - Cloudy H - Hypochromia M - Many c - Repeat 214
 occ - Occasional d - Repeat 28

¹Serum Glutamic Oxalacetic Transaminase²Serum Glutamic Pyruvic Transaminase

Dog No. 65-099, Male	Control Periods			Compound Administration Months		
	1	2 2*	3	1	2	3
Dosage: 2500 ppm.						

<u>Hematology:</u>						
Total Erythrocytes (x10 ⁶ /cmm.)	5.55	5.15	4.41	5.82	6.40	6.19
Hemoglobin, gm./100 ml.	12.8	12.1	11.3	13.7	14.9	15.3
Hematocrit, %	40	36	36	41	45	45
Sedimentation Rate, mm./hr.	1	0	0	0	0	0
Total Leucocytes, (x10 ³ /cmm.)	15.36	13.16	11.67	10.62	13.74	11.71
<u>Differential Count:</u>						
Neutrophils, %	60	72	64	60	59	68
Seg., %	58	68	64	60	57	68
Non-Seg., %	2	4	0	0	2	0
Lymphocytes, %	32	16	22	33	36	26
Eosinophils, %	5	8	11	3	2	0
Monocytes, %	3	4	3	4	3	6
Basophils, %	0	0	0	0	0	0
Appearance of Erythrocytes	No	MH	No	H	H	No
<u>Plasma Biochemistry:</u>						
Glucose, mg./100 ml.	119	134 ^a	120	128 ^b	121 ^c	118
Protein, gm./100 ml.	5.67	5.24	4.60	5.05	5.82	5.21
Albumin, gm./100 ml.	2.23	1.90	2.04	2.40	2.50	2.70
Albumin-to-Globulin Ratio	0.65	0.57	0.80	0.91	0.75	1.07
Urea Nitrogen, mg./100 ml.	13.0	12.6	10.5	9.8	8.2	11.5
Alkaline Phosphatase, units	17	20	17	15	28 ^d	33 ^e
Cholesterol, mg./100 ml.	182	150	120	170 ^f	233 ^g	270
Prothrombin Time, sec.	7	7	8	8	6	8
SGOT units/ml. ¹	23	19	18	12	11	11
SGPT units/ml. ²	16	15	22	17	13	18
<u>Urinalysis:</u>						
Volume, ml.	105	145	80	150	200	210
Color	S-C	LS-C	DS-cl	S-cl	S-cl	S-C
pH	6.8	7.0	6.1	6.9	7.3	7.4
Specific Gravity	1.057	1.017	1.060	1.028	1.025	1.036
Albumin	N	N	N	N	N	N
Bilirubin	N	N	N	N	N	N
Glucose	N	N	N	N	N	N
Occult Blood	N	N	N	N	N	N
<u>Microscopic:</u>						
Leucocytes	F			F		
Amorphous Urates		F	M			
Epithelial Cells	F	occ		1-2		occ
Triple Phosphates	F		F	F	M	M
Ammonium Urates	M	F		F	M	
Bacteria	M	F	F	M	L	F

Code: S - Straw	N - Negative	L - Loaded	a - Repeat 125	e - Repeat 30
LS - Light Straw	No - Normal	F - Few	b - Repeat 126	f - Repeat 179
DS - Dark Straw	MH - Marked Hypochromia	M - Many	c - Repeat 114	g - Repeat 209
C - Clear	H - Hypochromia	occ - Occasional	d - Repeat 24	
cl - Cloudy		1Serum Glutamic Oxalacetic Transaminase		
		2Serum Glutamic Pyruvic Transaminase		

[REDACTED] Ninety-Day Feeding Study in the Dog.

TABLE 28-A. Total Cholesterol Values, Mg. per 100 Ml. Plasma.

Dietary Level	Sex	Control Period			Compound Admin. Months		
		1	2	3	1	2	3
<u>Control:</u>							
65-038	F	196	212	211	200	178	184
65-070	M	176	186	140	175	195	198
65-081	F	161	162	153	149	175	167
65-083	M	116	138	122	123	142	157
65-086	M	196	174	142	181	203	200
65-093	F	144	128	147	132	115	124
<u>100 ppm.:</u>							
65-072	M	132	139	120	118	158	163
65-074	M	131	144	147	123	158	172
65-076	M	159	163	132	163	181	203
65-077	F	155	153	188	142	182	169
65-085	F	159	132	148	128	141	161
65-091	F	160	138	149	143	155	149
<u>500 ppm.:</u>							
65-078	M	129	169	132	154	180	203
65-079	M	161	149	147	135	166	169
65-087	M	159	171	125	125	215	214
65-092	F	140	122	120	121	191	160
65-094	F	128	129	126	141	181	192
65-095	F	142	162	154	136	167	204
<u>2500 ppm.:</u>							
65-088	M	109	119	100	109	185	187
65-090	M	163	146	140	195	208	284
65-096	F	167	158	131	215	269	307
65-097	F	129	133	147	175	233	274
65-098	F	133	117	120	198	244	249
65-099	M	182	150	120	170	233	270

Ninety-Day Feeding Study in the Dog.

TABLE 29. Necropsy Observations.

Animal Number	Sex	Organ	Comment
<u>Control:</u>			
65-070	M	small intestine ileocolic junction cecum, colon	Few hookworms present. Mild mucosal congestion. Few 2 to 3 mm. hemorrhages.
65-083	M	small intestine	Ascarid.
65-086	M	ileocolic junction cecum urinary bladder heart	Mild mucosal congestion. Several 2 to 3 mm. mucosal hemorrhages. Few petechial hemorrhages. Tricuspid valve, 2 mm. hematoma.
65-038	F	cecum	Few petechia in the mucosa.
65-081	F	ileocolic junction colon	Mild mucosal congestion. Several mucosal petechiae.
65-093	F	small intestine	Few petechial hemorrhages at the gastroduodenal junction, fecal material was present in the stomach.
<u>100 ppm.:</u>			
65-072	M	ileocolic junction urinary bladder	Mucosal congestion. Petechial hemorrhages at the neck.
65-074	M	small intestine ileocolic junction	Few hookworms present. Mild mucosal congestion.
65-076	M	urinary bladder	Area of hyperemia at neck.
65-077	F	small intestine	Areas of hyperemia at ileocolic orifice.
65-085	F	small intestine cecum, colon	3 mm. raised firm area in the duodenum; terminal portion of the ileum had mild mucosal hemorrhage at the ileocolic junction. Mild mucosal hemorrhage.
65-091	F	stomach ileocolic junction cecum, colon	Fecal material present in the stomach. Mild mucosal congestion. Several 2 mm. areas of hemorrhage in the mucosa.

Ninety-Day Feeding Study in the Dog.

TABLE 29, Continued. Necropsy Observations.

Animal Number	Sex	Organ	Comment
<u>1000 ppm.:</u>			
65-078	M	duodenum	Few petechial hemorrhages at pylorus.
		small intestine	Moderate mucosal congestion throughout the anterior half.
		ileocolic junction	Mild mucosal congestion.
65-079	M	small intestine	Several 1 to 2 mm. hemorrhages at the gastroduodenal junction.
		ileocolic junction	Mild mucosal congestion.
65-087	M	urinary bladder	Few petechial hemorrhages at the neck.
65-092	F	urinary bladder	Few petechial hemorrhages at the neck.
65-094	F	stomach	Many scattered gray raised areas less than 1 mm. in diameter in pyloric region.
		cecum	Few 2 mm. hemorrhages scattered in the mucosa.
65-095	F	stomach	Few petechial hemorrhages in the pyloric region.
		small intestine	Petechial hemorrhages at the gastroduodenal junction, several ascarids.
		ileocolic junction	Mild mucosal congestion.
		cecum	Few mucosal petechiae.
<u>5000 ppm.:</u>			
65-088	M	small intestine	Few mucosal petechiae scattered throughout the middle third of the intestine.
65-090	M	small intestine	Few 1 mm. hemorrhages at the gastroduodenal junction.
65-099	M	small intestine	Ascarid
		cecum	Few 1 to 2 mm. mucosal hemorrhages.
65-096	F	cecum	Several 2 mm. mucosal hemorrhages.
65-097	F	cecum	Several mucosal petechiae.
		small intestine	Several mucosal petechiae at the terminal portion of the ileum.
		urinary bladder	Several circumscribed dark areas with light centers approximately 1 mm. in diameter scattered throughout the mucosa.

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[REDACTED]: Ninety-Day Feeding Study in the Dog.

TABLE 29, Continued. Necropsy Observations.

Animal Number	Sex	Organ	Comment
<u>5000 ppm., Cont'd.:</u>			
65-098	F	heart	10 mm. white streak in the left ventricular wall.

Ninety-Day Feeding Study in the Dog.

TABLE 30. Actual (Grams) and Relative (% Body Weight) Organ Weights.

Group & Animal		Sex	Terminal Body Wt. Kg.	Spleen		Liver		Adrenals		Kidneys		Ovaries/ Testes	
				Wt.	%	Wt.	%	Wt.	%	Wt.	%	Wt.	%
<u>Control:</u>													
65-070		M	13.0	29.12	0.224	310.87	2.391	0.90	0.007	63.99	0.492	23.08	0.178
65-083		M	8.5	30.70	0.361	242.42	2.852	0.98	0.012	43.25	0.509	14.22	0.167
65-086		M	9.2	28.58	0.311	248.83	2.705	0.98	0.011	49.53	0.538	18.90	0.205
65-038		F	8.2	19.98	0.244	198.81	2.425	1.40	0.017	38.58	0.470	0.67	0.008
65-081		F	9.2	24.32	0.264	250.50	2.723	1.06	0.012	39.62	0.431	0.74	0.008
65-093		F	6.1	13.59	0.223	151.11	2.477	0.78	0.013	29.28	0.480	0.41	0.007
<u>100 ppm.:</u>													
65-072		M	8.7	25.87	0.297	238.89	2.746	0.82	0.009	55.60	0.639	19.78	0.227
65-074		M	10.8	32.31	0.299	285.70	2.645	1.23	0.011	58.12	0.538	13.86	0.128
65-076		M	11.9	25.39	0.213	325.52	2.735	1.02	0.009	50.68	0.426	17.71	0.149
65-077		F	9.4	29.18	0.310	241.79	2.572	1.11	0.012	43.93	0.467	0.55	0.006
65-085		F	7.2	25.31	0.352	177.56	2.466	1.21	0.017	33.08	0.459	0.62	0.009
65-091		F	9.9	23.40	0.236	210.70	2.128	1.16	0.012	52.61	0.531	0.58	0.006
<u>1000 ppm.:</u>													
65-078		M	9.9	23.70	0.239	281.62	2.845	1.00	0.010	61.60	0.622	14.95	0.151
65-079		M	6.9	18.11	0.262	210.71	3.054	0.84	0.012	44.15	0.640	10.10	0.146
65-087		M	13.5	41.42	0.307	443.25	3.283	1.98	0.015	71.48	0.529	21.78	0.161
65-092		F	6.5	18.18	0.280	209.89	3.229	0.98	0.015	29.50	0.454	0.66	0.010
65-094		F	11.0	28.50	0.259	320.71	2.916	1.12	0.010	59.81	0.544	0.71	0.006
65-095		F	7.9	18.73	0.237	228.27	2.889	1.18	0.015	38.31	0.491	0.90	0.011
<u>5000 ppm.:</u>													
55-088		M	6.7	19.79	0.295	301.90	4.506	0.84	0.013	34.61	0.517	9.71	0.145
55-090		M	10.6	19.67	0.186	479.03	4.519	1.41	0.013	55.24	0.521	19.00	0.179
55-099		M	8.4	17.88	0.213	396.70	4.723	0.93	0.011	46.71	0.556	12.76	0.152
55-096		F	8.8	21.99	0.250	339.91	3.863	1.02	0.012	52.03	0.591	0.60	0.007
55-097		F	10.0	24.09	0.241	426.29	4.263	1.00	0.010	53.12	0.531	0.72	0.007
55-098		F	7.2	16.50	0.229	327.31	4.546	0.60	0.008	39.72	0.552	0.54	0.008

<u>Thymus</u>		<u>Heart</u>		<u>Lung</u>		<u>Thyroid</u>		<u>Brain</u>		<u>Pituitary</u>	
<u>Wt.</u>	<u>%</u>	<u>Wt.</u>	<u>%</u>	<u>Wt.</u>	<u>%</u>	<u>Wt.</u>	<u>%</u>	<u>Wt.</u>	<u>%</u>	<u>Wt.</u>	<u>%</u>
38.20	0.294	115.72	0.890	115.40	0.888	1.37	0.011	84.27	0.648	0.069	0.0005
16.13	0.190	62.81	0.739	85.70	1.008	0.59	0.007	78.86	0.928	0.059	0.0007
22.71	0.247	76.21	0.828	90.44	0.983	0.93	0.010	82.02	0.892	0.072	0.0008
10.08	0.123	68.12	0.831	67.13	0.819	0.79	0.010	69.42	0.847	0.049	0.0006
15.53	0.169	77.50	0.842	74.62	0.811	0.73	0.008	83.24	0.905	0.065	0.0007
16.61	0.272	53.34	0.874	60.60	0.993	0.52	0.009	70.79	1.160	0.039	0.0006
21.59	0.248	80.53	0.926	87.30	1.003	0.72	0.008	78.35	0.901	0.072	0.0008
20.81	0.193	79.67	0.738	102.91	0.953	0.90	0.008	77.45	0.717	0.071	0.0007
21.01	0.177	84.59	0.711	102.98	0.865	0.82	0.007	92.08	0.774	0.071	0.0006
21.13	0.225	76.89	0.818	91.10	0.969	0.74	0.008	86.68	0.922	0.066	0.0007
18.00	0.250	55.00	0.764	72.12	1.002	0.86	0.012	68.21	0.947	0.064	0.0009
16.51	0.167	87.09	0.880	90.40	0.913	0.72	0.007	73.05	0.738	0.078	0.0008
20.29	0.205	72.22	0.729	75.96	0.767	0.73	0.007	87.77	0.887	0.060	0.0006
19.77	0.287	59.67	0.865	65.18	0.945	-	-	78.20	1.133	0.091	0.0013
37.81	0.280	89.63	0.664	119.10	0.882	1.35	0.010	84.98	0.629	0.031	0.0002
13.69	0.211	47.00	0.723	64.39	0.991	0.42	0.006	67.48	1.038	0.055	0.0008
20.10	0.183	81.71	0.743	95.25	0.866	0.88	0.008	78.13	0.710	0.086	0.0008
14.75	0.187	63.85	0.808	76.72	0.971	0.75	0.009	63.71	0.806	0.071	0.0009
16.55	0.247	44.20	0.660	60.50	0.903	0.53	0.008	70.70	1.055	0.052	0.0008
24.43	0.230	64.29	0.607	73.78	0.696	1.32	0.012	79.51	0.750	0.076	0.0007
24.51	0.292	58.48	0.696	70.01	0.833	0.58	0.007	80.91	0.963	0.059	0.0007
19.39	0.220	62.55	0.711	63.91	0.726	0.62	0.007	78.35	0.890	0.072	0.0008
24.90	0.249	75.79	0.758	69.43	0.694	0.83	0.008	73.31	0.733	0.077	0.0008
12.53	0.174	51.61	0.717	60.50	0.840	0.97	0.013	68.41	0.950	0.064	0.0009

██████: Ninety-Day Feeding Study in the Dog.

TABLE 31. Histopathologic Observations.

Animal No and Group	Sex	Tissue	Comment
<u>Control:</u>			
65-070	M	all tissues	No lesion.
65-083	M	all tissues	No lesion.
65-086	M	all tissues	No lesion.
65-038	F	skin	Folliculitis with lymphocyte and plasma cell infiltrate in corium.
		kidney	Moderate subacute pyelonephritis.
65-081	F	all tissues	No lesions.
65-093	F	kidney	Moderate subacute pyelonephritis.
<u>100 ppm. (Liver Only):</u>			
65-072	M		No lesion.
65-074	M		No lesion.
65-076	M		No lesion.
65-077	F		No lesion.
65-085	F		No lesion.
65-091	F		No lesion.
<u>1000 ppm. (Liver Only):</u>			
65-078	M		No lesion.
65-079	M		No lesion.
65-087	M		No lesion.
65-092	F		No lesion.
65-094	F		No lesion.
65-095	F		No lesion.

Company Seal: This does not contain (SCA CB)

Ninety-Day Feeding Study in the Dog.

TABLE 31, Continued. Histopathologic Observations.

Animal No. and Group	Sex	Tissue	Comment
<u>5000 ppm.:</u>			
65-088	M	liver	Hepatocytes appeared hypertrophied as compared to controls with less coarse granularity to their cytoplasm.
65-090	M	kidney liver	Moderate subacute pyelonephritis. Hepatocytes slightly hypertrophied with cytoplasm less coarsely granular than control.
65-099	M	liver	Hepatocytes slightly hypertrophied with less coarse granularity of cytoplasm than control.
65-096	F	all tissues	No lesion.
65-097	F	liver	Slight portal lymphocytic infiltrate.
65-098	F	heart	Small areas of calcification of myocardial fibers.
		liver	Hepatocytes hypertrophied as compared to controls with less coarse granularity of cytoplasm.

Company Sanitized. Does not contain TSCA CB1

██████████: Ninety-Day Feeding Study in the Dog.

TABLE 32. Summary of Incidence of Histopathologic Lesions.

Tissue and Lesion	Control		100 ppm.		1000 ppm.		5000 ppm.	
	Male	Female	Male	Female	Male	Female	Male	Female
brain - no lesion	3/3	3/3					3/3	3/3
spinal cord - no lesion	3/3	3/3					3/3	3/3
peripheral nerve - no lesion	3/3	3/3					3/3	3/3
eye - no lesion	3/3	3/3					3/3	3/3
pituitary - no lesion	3/3	3/3					3/3	3/3
thyroid - no lesion	3/3	3/3					3/3	3/3
parathyroid - no lesion	1/1	2/2					2/2	1/1
adrenal - no lesion	3/3	3/3					3/3	3/3
trachea - no lesion	3/3	3/3					3/3	3/3
lung - no lesion	3/3	3/3					3/3	3/3
heart - no lesion	3/3	3/3					3/3	2/3
- myocardial calcification								1/3
aorta - no lesion	3/3	2/2					3/3	3/3
spleen - no lesion	3/3	3/3					3/3	3/3
lymph node - no lesion	3/3	3/3					2/2	3/3
thymus - no lesion	3/3	3/3					3/3	3/3
bone marrow - no lesion	3/3	3/3					3/3	3/3
salivary gland - no lesion	3/3	3/3					3/3	3/3
esophagus - no lesion	3/3	3/3					3/3	3/3
stomach - no lesion	3/3	3/3					3/3	3/3
small intestine - no lesion	3/3	3/3					3/3	3/3
large intestine - no lesion	3/3	3/3					3/3	3/3
pancreas - no lesion	3/3	3/3					2/2	3/3

██████████

Company Sanitized. Does not contain TSCA CBI

██████████: Ninety-Day Feeding Study in the Dog.

TABLE 32, Continued. Summary of Incidence of Histopathologic Lesions.

Tissue and Lesion	Control		100 ppm.		1000 ppm.		5000 ppm.	
	Male	Female	Male	Female	Male	Female	Male	Female
liver - no lesion	3/3	3/3	3/3	3/3	3/3	3/3		1/3
- hepatocyte hypertrophy							3/3	1/3
- portal infiltrate								1/3
gall bladder - no lesion	3/3	3/3					3/3	3/3
kidney - no lesion	3/3	3/3					2/3	3/3
- subacute pyelonephritis				2/3			1/3	
urinary bladder - no lesion	3/3	3/3					3/3	3/3
testis or ovary - no lesion	3/3	3/3					3/3	3/3
prostate or uterus - no lesion	3/3	3/3					3/3	3/3
skeletal muscle - no lesion	3/3	3/3					3/3	2/2
skin - no lesion	3/3	2/3					3/3	3/3
- folliculitis				1/3				
bone - no lesion	3/3	3/3					3/3	3/3