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FINAL REPORT  
TWO-YEAR FEEDING STUDY IN RATS  
BY  
E. ROSS HART, PH.D.

LITTON BIONETICS, INC.  
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27 August 1976

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SPONSOR: Office of Naval Research

DATE: August 27, 1976

MATERIAL: RDX

SUBJECT: FINAL REPORT  
Two-Year Feeding Study in Rats  
LBI Project No. 1400

SUMMARY

Incorporation of RDX in the diets of rats at levels of 1.0, 3.1, and 10 mg/kg over a two-year period did not lead to appearance of important evidence of toxicity.

SPONSOR: Office of Naval Research

DATE: August 27, 1976

MATERIAL: RDX

SUBJECT: FINAL REPORT  
Two-Year Feeding Study in Rats  
LBI Project No. 1400

1. OBJECTIVE

The objective of this chronic feeding study was to evaluate the toxicity and pharmacologic effect of RDX when administered to male and female rats over their lifetime in an attempt to simulate the exposure that may be experienced by man when substances may be ingested for prolonged periods.

2. MATERIAL

The test material, labelled RDX, was received from the Office of Naval Research in September 1973, and was assigned BRL No. 726A. The material as received was a coarse white granular mixture moistened with alcohol. Additional quantities of the test material were received on January 15, 1974, May 16, 1974, October 2, 1974, and June 2, 1975, and were assigned BRL numbers 726B, 726C, 726D, and 726E, respectively.

3. EXPERIMENTAL DESIGN

A. Animals

The study was carried out in rats of the Charles River Sprague-Dawley strain with body weights averaging 98.5 grams for males and 87.9 grams for females at initiation.

B. Animal Groups

The rats were randomly assigned to the following groups:

<u>Group No.</u>	<u>No. of Animals</u>		<u>Daily Dosage</u> mg/kg
	<u>Male</u>	<u>Female</u>	
1	100	100	Zero - Control
2	100	100	Low - 1.0
3	100	100	Intermediate - 3.1
4	100	100	High - 10

### 3. EXPERIMENTAL DESIGN (Continued)

#### C. Diet Preparation

To minimize the explosive hazard of the dry RDX alone, a supply of the fine granular material was provided. It was supplied in preweighed, 5 gm portions packaged in plastic snap-top containers and wetted with 30% ethanol in water. A premix of RDX in ground rat chow was prepared in sufficient concentration and quantity to completely use one 5 gm portion. This premix was then used to prepare, on a weight/weight basis, the appropriate diet for each group.

#### D. Housing

Twenty-five (25) rats of each sex of each control or treatment group were housed individually in wire bottom cages. The others were housed in groups of three by sex in solid bottom plastic cages with sawdust bedding.

#### E. Observations

For those rats housed individually, body weights and food consumption were recorded weekly for the first 26 weeks, biweekly for the next 26 weeks, and every 4 weeks thereafter. Daily mortality checks were made on all rats regardless of housing, as were weekly records of appearance, behavior, and signs of toxic or pharmacologic effects.

#### F. Clinical Laboratory Measurements

The following clinical studies were performed on 10 male and 10 female animals from the control and each test group:

Hematology at 13, 26, 52, and 104 weeks, including:

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	reticulocyte count

Blood Chemistry at 52 and 104 weeks, including:

fasting blood sugar	serum potassium	serum alkaline phosphatase
blood urea nitrogen	serum chloride	serum glutamic-oxaloacetic transaminase
total serum protein	serum glutamic-pyruvic transaminase	serum glutamic-oxaloacetic transaminase
total serum bilirubin	methemoglobin	
serum sodium		

3. EXPERIMENTAL DESIGN (Continued)F. Clinical Laboratory Measurements

Urinalysis, using pooled samples per group at 13, 26, 52 and 104 weeks, including:

pH	bilirubin
specific gravity	microscopic examination of sediment
glucose	urine glutamic-oxaloacetic transaminase
ketones	

G. Interval Necropsies

At 52 weeks, 10 male and 10 female animals from the control and each test group were killed and gross necropsies performed. These animals were selected at random from the groups which were group housed. Those organs to be taken at termination (see below) were preserved in buffered 10% formalin. Organ weights were recorded for liver, kidneys, thyroids and adrenals.

H. Termination

The study was terminated at 104 weeks and all surviving rats were necropsied.

I. Organ Weights

The weights of the following organs were recorded for each rat:

thyroids (after fixation)	kidneys
heart	adrenals (after fixation)
liver	testes with epididymis
spleen	

J. Tissue Preservation

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

brain	spleen	testes with epididymis
pituitary	kidneys	seminal vesicles
thoracic spinal	adrenals	ovary
cord	stomach	uterus
eye	pancreas	skin
thyroids	small intestine	rib junction
lung	large intestine	bone marrow
heart	mesenteric lymph	nerve with muscle
liver	node	any unusual lesions
	urinary bladder	

### 3. EXPERIMENTAL DESIGN (Continued)

#### K. Histopathologic Examination

The following tissues from all animals from the control and the high level test group were examined microscopically after the interval and terminal sacrifices:

pituitary	adrenals	urinary bladder
thyroids	stomach	testes
heart	pancreas	ovary
liver	small intestine	bone marrow
spleen	large intestine	any unusual lesions
kidneys	mesenteric lymph node	

The target organs from the animals in the intermediate and the low level test groups were examined microscopically. Pathological examination was made of the organs of those animals that died during the course of the study in the control and the high level groups when autolysis did not make this impractical.

#### L. Statistical Analysis

The tabular presentations of numerical data in the Results Section include means and standard errors by group and sex. It is our standard policy to express means with the same degree of precision (i.e., number of decimal places) as the original data and to express standard error to two significant digits regardless of decimal places.

### 4. RESULTS

During the night preceding Day 76 of this study, there was a malfunction of the heating system in the building that resulted in excessive rises in temperature in animal rooms. A total of 59 rats assigned to this study were found dead. It seemed appropriate to deduct these from the "starting" population and report survival accordingly. On this basis survival was:

4. RESULTS (Continued)

	Males				Females			
	Control	Low	Med.	High	Control	Low	Med.	High
Initial Pop.	100	100	100	100	100	100	100	100
Deaths Due To								
Overheating	6	5	14	8	17	5	0	4
Deaths 1st. Yr.	1	3	3	4	0	1	5	2
Interim Kill	10	10	10	10	10	10	10	10
<b>SURVIVORS</b>								
12 Mo.	83	82	73	78	73	84	85	84
18 Mo.	77	77	70	75	70	80	83	78
19 Mo.	73	75	69	74	70	78	82	75
20 Mo.	68	72	66	70	68	75	81	69
21 Mo.	64	68	63	66	64	72	78	65
22 Mo.	60	66	63	63	62	67	70	62
23 Mo.	55	59	57	57	59	59	68	59
24 Mo.	50=60%	55=67%	51=70%	49=63%	53=73%	53=63%	61=72%	53=63%

It seems clear that the differences between groups are not important.

Body weights are presented as group means in Table 1. The few instances of statistically significant differences do not indicate important toxicity.

Food consumption measurements are similarly presented in Table 2. Again no important effects are seen.

Hematocytology results, as presented in Table 3, show a questionable tendency toward fluctuations in red cell counts, reticulocyte counts, cell volumes and hemoglobin values but no clear dose-effect trends occurred to result in a conclusion of compound effect.

The blood chemistry values presented in Table 4 show a few statistically significant differences particularly in electrolytes. However, these barely meet the criterion for significance and do not seem toxicologically important. Urinalysis results, presented in Table 5, all seem normal. Postmortem organ weights, presented as measured in Table 6 and as calculated percentage of terminal body weight in Table 7, indicate no important toxicity.

The gross necropsy findings are listed in Table 8. Again no important toxicity is noted.

A summary of the histopathology findings signed by the pathologist who examined the slides is attached together with a tabulation of the incidence of findings. Once again, no important toxicity is noted.

5. CONCLUSIONS

Incorporation of RDX in the diets of rats at levels of 1.0, 3.1 and 10 mg/kg over a two-year period did not lead to appearance of important evidence of toxicity.

Submitted by:



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## TABLES

TABLE 1 - BODY WEIGHTS

TABLE 2 - FOOD CONSUMPTION

TABLE 3 - HEMATOCYTOLOGY

TABLE 4 - BLOOD CHEMISTRY

TABLE 5 - URINALYSIS

TABLE 6 - ORGAN WEIGHTS

TABLE 7 - ORGAN WEIGHTS - BODY WEIGHTS

TABLE 8 - GROSS NECROPSY FINDINGS

TABLE 1  
 BODY WEIGHTS  
 (grams)

GROUP MEANS + STANDARD ERRORS  
 MALES

GROUP NO.	WEEK													
	0	1	2	3	4	5	6	7	8	9	10	11	12	13
<u>1 - CONTROL</u>														
MEAN	99.5	150.8	202.6	243.7	280.8	313.5	342.7	367.4	385.0	397.6	417.2	423.0	437.6	441.5
S.E.	2.9	3.7	4.3	5.2	6.4	6.5	7.3	6.9	8.4	9.1	8.8	9.1	9.2	9.7
<u>2 - LOW</u>														
MEAN	99.3	153.9	197.2	255.1	295.2	330.1	356.1	380.3	403.6	414.8	438.1	441.25	459.3	466.3
S.E.	1.7	2.2	3.6	3.8	4.5	5.4	7.1	6.6	6.7	6.8	7.7	7.8	8.3	9.3
<u>3 - MEDIUM</u>														
MEAN	94.7	147.2	194.7	245.9	288.9	321.6	354.8	377.4	397.3	415.3	432.4	438.6	456.5	457.3
S.E.	3.0	3.6	4.9	5.5	5.6	6.4	6.6	7.2	8.2	8.8	8.9	9.0	9.4	9.6
<u>4 - HIGH</u>														
MEAN	100.3	150.0	201.1	251.5	291.7	326.7	354.6	374.8	400.6	415.2	434.6	442.5	456.6	460.1
S.E.	2.6	3.3	4.1	5.0	5.6	5.8	7.2	8.7	7.4	7.5	7.9	8.1	9.0	7.6

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS + STANDARD ERRORS

MALES

GROUP NO.	WEEK													
	14	15	16	17	18	19	20	21	22	23	24	25	26	28
<u>1 - CONTROL</u>														
MEAN	458.2	459.4	473.4	479.0	482.7	503.4	501.6	507.9	517.1	522.0	526.5	525.9	517.5	541.2
S.E.	10	9.9	9.7	11	11	12	12	13	12	12	12	12	12	13
<u>2 - LOW</u>														
MEAN	471.6	484.7	495.7	497.0	499.0	501.2	514.2	517.1	523.9	528.0	534.8	537.2	537.1	553.4
S.E.	8.5	8.4	8.6	8.9	9.6	9.1	10	9.9	9.8	10	11	11	11	11
<u>3 - MEDIUM</u>														
MEAN	472.0	485.9	497.2	498.0	504.5	512.0	523.5	524.3	531.9	533.0	539.4	551.1	545.9	564.8
S.E.	10	10	13	12	12	12	13	12	12	12	12	12	12	12
<u>4 - HIGH</u>														
MEAN	471.9	482.3	492.1	502.7	508.9	514.5	523.8	526.5	530.3	527.3	533.8	543.3	538.6	555.6
S.E.	8.5	8.9	9.3	9.9	11	10	11	11	12	12	12	12	13	12

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

## GROUP MEANS + STANDARD ERRORS

GROUP NO.	WEEK												
	30	32	34	36	38	40	42	44	46	48	50	52	56
<u>1 - CONTROL</u>													
MEAN	555.8	569.8	569.9	572.7	586.8	597.5	597.5	601.7	608.7	606.8	611.3	621.9	616.1
S.E.	13	13	13	14	13	13	14	15	16	16	17	17	17
<u>2 - LOW</u>													
MEAN	560.3	584.4	570.2	579.9	592.1	604.7	611.9	610.6	619.0	618.5	617.3	625.6	625.3
S.E.	12	13	13	13	13	13	14	13	14	15	15	15	15
<u>3 - MEDIUM</u>													
MEAN	578.7	586.9	577.4	588.9	602.8	606.8	602.4	604.1	612.1	610.9	613.3	610.2	607.2
S.E.	13	12	14	14	14	15	15	16	15	16	15	15	17
<u>4 - HIGH</u>													
MEAN	568.5	584.6	575.6	589.7	599.9	599.6	597.2	609.1	624.8	616.1	618.8	610.2	614.0
S.E.	13	13	13	13	14	15	16	15	15	15	15	15	15

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS + STANDARD ERRORS

MALES

GROUP NO.	WEEK												
	60	64	68	72	76	80	84	88	92	94	96	100	104
<u>1 - CONTROL</u>													
MEAN	586.4	620.3	593.1	620.9	619.1	635.3	656.9	663.2	666.8	643.8	672.0	658.0	660.6
S.E.	17	19	17	17	15	17	16	19	18	23	19	18	21
<u>2 - LOW</u>													
MEAN	606.0	625.3	612.7	616.3	637.2	649.7	672.0	684.0	680.5	663.1	685.9	669.6	675.0
S.E.	15	16	13	16	15	17	18	19	21	28	23	25	28
<u>3 - MEDIUM</u>													
MEAN	596.6	599.8	547.9	607.2	624.5	620.6	649.1	659.4	662.8	663.4	666.3	648.5	643.0
S.E.	19	23	21	18	19	22	20	20	21	22	22	22	26
<u>4 - HIGH</u>													
MEAN	615.8	611.1	595.8	598.3	588.2	589.3	622.0	630.2	631.0	636.3	632.9	627.6	613.8
S.E.	15	14	13	14	17	19	18	18	21	19	20	22	32

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS + STANDARD ERRORS

FEMALES

GROUP NO.	WEEK													
	0	1	2	3	4	5	6	7	8	9	10	11	12	13
<u>1 - CONTROL</u>														
MEAN	90.2	131.3	155.2	174.0	195.2	210.2	227.0	327.5	244.8	246.1	256.1	262.5	259.7	264.8
S.E.	2.1	2.2	2.4	2.7	3.5	4.6	3.4	3.6	4.1	4.7	5.1	4.9	4.5	5.8
<u>2 - LOW</u>														
MEAN	87.1	128.1	154.7	170.1	189.0	204.3	216.2	228.0	236.1	241.1	248.0	251.0	254.8	257.7
S.E.	2.2	2.6	2.1	2.5	2.6	2.8	3.3	3.4	3.8	3.9	4.0	4.1	4.2	3.9
<u>3 - MEDIUM</u>														
MEAN	85.0	121.6	150.3	164.7	182.3	203.5	216.0	221.6	232.3	237.0	242.0	246.3	248.8	251.1
S.E.	2.3	2.6	2.8	3.7	3.3	3.1	3.3	4.1	3.8	3.5	3.5	3.9	4.0	3.9
<u>4 - HIGH</u>														
MEAN	89.4	124.2	151.4	173.8	193.3	203.4	217.5	231.1	238.2	245.2	253.1	252.1	260.0	260.8
A.W.	2.2	2.3	3.0	2.8	3.3	3.3	4.3	4.2	4.3	4.5	4.5	4.9	4.6	5.1

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

GROUP MEANS + STANDARD ERRORS

FEMALES

GROUP NO.	WEEK													
	14	15	16	17	18	19	20	21	22	23	24	25	26	28
<u>1 - CONTROL</u>														
MEAN	273.1	277.2	278.3	288.6	291.5	299.5	299.6	306.8	309.5	311.2	313.1	315.6	309.7	319.0
S.E.	5.3	5.1	5.5	5.6	5.7	5.9	6.2	6.3	6.6	6.5	6.7	7.1	7.3	7.6
<u>2 - LOW</u>														
MEAN	262.0	269.8	274.2	274.8	277.3	281.3	286.1	289.6	294.2	297.0	299.6	300.7	299.6	308.5
S.E.	4.9	5.0	4.8	4.6	4.9	4.7	5.2	5.4	5.4	5.6	5.3	5.3	5.7	6.3
<u>3 - MEDIUM</u>														
MEAN	256.2	264.7	268.7	270.0	273.8	277.2	280.6	280.7	283.1	285.5	287.7	292.6	291.9	298.4
S.E.	3.4	3.6	4.0	4.3	4.5	4.4	4.4	4.9	4.7	4.8	4.7	5.0	5.2	5.4
<u>4 - HIGH</u>														
MEAN	264.8	268.8	279.5	283.2	288.6	291.7	294.5	293.1	301.8	296.8	300.7	307.0	304.5	311.1
S.E.	5.4	5.1	5.1	5.4	5.5	5.5	5.5	5.8	6.1	6.2	6.0	6.4	6.5	6.5

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

## GROUP MEANS + STANDARD ERRORS

## FEMALES

GROUP NO.	WEEK												
	30	32	34	36	38	40	42	44	46	48	50	52	56
<u>1 - CONTROL</u>													
MEAN	325.1	335.4	337.5	337.3	343.8	351.8	355.5	356.1	360.1	363.4	367.7	373.7	376.7
S.E.	7.7	8.2	8.2	8.2	8.1	8.4	9.0	9.0	9.2	9.5	10	10	11
<u>2 - LOW</u>													
MEAN	316.4	323.3	321.7	322.4	326.9	331.8	334.8	333.5	339.8	342.1	345.0	349.7	350.7
S.E.	7.0	7.3	7.0	7.3	7.7	7.6	8.3	7.7	7.7	7.8	8.5	8.6	9.5
<u>3 - MEDIUM</u>													
MEAN	304.9	308.7	304.4	311.3	316.6	313.5	316.2	320.2	326.3	326.9	326.4	330.6	326.3*
S.E.	5.7	6.1	6.3	5.7	6.0	6.5	7.2	6.9	7.3	7.3	6.9	7.0	7.9
<u>4 - HIGH</u>													
MEAN	316.4	319.2	315.5	321.1	329.9	326.8	331.9	334.6	335.7	343.1	343.8	344.1	342.3*
S.E.	7.0	7.9	7.6	8.9	8.5	8.7	9.4	9.7	9.9	10	11	11	11

\*Significantly different from Control Group (P &lt; 0.05).

TABLE 1 (Continued)

BODY WEIGHTS  
(grams)

## GROUP MEANS ± STANDARD ERRORS

## FEMALES

GROUP NO.	WEEK												
	60	64	68	72	76	80	84	88	92	94	96	100	104
<u>1 - CONTROL</u>													
MEAN	360.6	376.4	352.8	378.3	386.8	391.3	421.0	430.6	433.4	440.4	452.8	455.7	450.2
S.E.	10	12	9.0	9.9	11	12	14	17	19	21	20	20	23
<u>2 - LOW</u>													
MEAN	329.6*	342.0	329.7	351.8	377.3	369.7	391.8	405.1	402.8	422.8	413.5	416.5	399.4
S.E.	8.9	8.4	12	13	16	8.7	9.8	14	12	17	13	12	14
<u>3 - MEDIUM</u>													
MEAN	315.8*	318.0*	319.7*	328.8*	337.7*	340.6*	361.2*	364.5*	375.3*	378.8*	374.3*	378.7*	368.5*
S.E.	8.3	7.3	6.9	6.3	6.7	8.7	9.9	11	11	12	13	14	17
<u>4 - HIGH</u>													
MEAN	334.9*	341.7	318.4*	344.9*	345.9	354.0*	372.9*	377.6*	385.0	398.6	404.8	397.5	408.2
S.E.	11	13	11	11	12	12	14	16	17	18	18	21	20

\*Significantly different from Control Group (P &lt; 0.05).

TABLE 2

FOOD CONSUMPTION  
(grams/day)

## GROUP MEANS + STANDARD ERRORS

## MALES

GROUP NO.	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
<u>1 - CONTROL</u>														
MEAN	18.5	22.2	25.5	29.2	29.0	28.2	26.9	26.7	29.0	26.6	25.7	25.6	22.6	26.3
S.E.	0.3	0.5	0.9	1.2	1.0	0.9	1.0	1.0	1.0	0.8	0.8	0.5	0.8	0.9
<u>2 - LOW</u>														
MEAN	18.8	21.1	25.5	28.0	28.2	30.5	26.9	27.3	28.7	27.2	27.1	26.0	22.8	25.8
S.E.	0.5	0.5	0.6	0.8	0.8	1.0	0.7	0.8	0.7	0.7	0.7	0.6	0.5	0.6
<u>3 - MEDIUM</u>														
MEAN	18.2	21.8	24.4	28.6	27.8	27.8	27.5	28.1	26.8	26.7	24.9	26.3	23.2	26.5
S.E.	0.4	0.5	0.7	0.6	0.6	0.6	0.5	0.6	0.5	0.6	0.5	0.5	0.4	0.5
<u>4 - HIGH</u>														
MEAN	19.0	22.3	25.1	29.5	28.5	29.9	27.0	28.1	29.9	28.7	28.9	27.8	24.7	26.6
S.E.	0.4	0.5	0.6	0.9	0.6	0.8	0.6	0.5	0.9	0.7	0.9	0.9	0.6	0.5

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

GROUP MEANS + STANDARD ERRORS

MALES

GROUP NO.	WEEK													
	15	16	17	18	19	20	21	22	23	24	25	26	28	
<u>1 - CONTROL</u>														
MEAN	27.7	28.1	25.6	24.9	25.5	26.0	25.1	25.0	23.7	25.5	22.8	23.4	27.6	
S.E.	0.5	0.9	0.8	0.7	0.7	0.9	0.7	0.5	0.6	0.6	0.5	0.7	0.5	
<u>2 - LOW</u>														
MEAN	27.7	29.5	26.5	25.6	25.2	26.1	25.9	25.3	24.9	25.7	24.5	24.9	27.6	
S.E.	0.7	1.0	0.7	0.5	0.6	1.0	0.8	0.7	0.8	0.6	0.8	0.7	0.9	
<u>3 - MEDIUM</u>														
MEAN	28.0	31.4	27.1	26.1	25.1	27.9	25.3	27.2	27.0	27.2	25.4	24.8	28.9	
S.E.	0.8	1.3	1.4	0.6	0.7	0.8	0.5	0.6	0.8	0.7	0.6	0.7	0.7	
<u>4 - HIGH</u>														
MEAN	26.6	27.6	27.9	28.2	26.6	27.4	24.5	26.5	25.3	26.5	24.8	25.2	27.9	
S.E.	0.6	0.8	0.9	0.8	0.5	1.2	0.6	0.7	0.7	0.6	0.8	0.8	0.8	

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

## GROUP MEANS ± STANDARD ERRORS

## MALES

GROUP NO.	WEEK												
	30	32	34	36	38	40	42	44	46	48	50	52	56
<u>1 - CONTROL</u>													
MEAN	25.1	25.3	23.4	22.1	21.7	20.8	20.0	22.2	22.6	22.6	23.4	23.3	22.8
S.E.	0.5	0.5	0.6	0.4	0.4	0.3	0.4	0.5	0.5	0.4	0.5	0.5	0.5
<u>2 - LOW</u>													
MEAN	26.6	25.7	25.3	22.3	21.8	22.1	21.0	23.6	21.5	22.8	21.9	22.6	22.7
S.E.	0.9	0.5	1.2	0.4	0.5	0.4	0.6	0.4	0.5	0.4	0.4	0.4	0.5
<u>3 - MEDIUM</u>													
MEAN	28.3	26.0	25.0	23.2	21.5	23.2	21.5	24.0	22.6	23.6	22.9	24.0	24.3
S.E.	0.9	0.9	1.1	0.5	0.5	0.5	0.8	0.7	0.7	0.9	0.4	0.6	0.7
<u>4 - HIGH</u>													
MEAN	26.0	27.8	23.7	22.4	22.2	22.9	21.8	23.9	23.0	23.0	23.1	23.1	24.2
S.E.	0.7	0.8	1.0	0.8	0.7	1.1	0.8	0.6	0.5	0.4	0.5	0.6	0.6

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

## GROUP MEANS + STANDARD ERRORS

## MALES

GROUP NO.	WEEK												
	60	64	68	72	76	80	84	88	92	94	96	100	104
<u>1 - CONTROL</u>													
MEAN	27.6	22.9	22.6	25.7	24.6	25.8	22.0	22.0	20.8	21.1	22.4	23.0	22.3
S.E.	0.9	0.5	0.6	0.5	0.5	1.1	0.7	0.5	0.4	0.4	0.5	0.4	0.6
<u>2 - LOW</u>													
MEAN	26.4	21.5	21.3	25.0	25.0	24.0	22.8	22.3	21.2	21.8	22.4	22.7	21.6
S.E.	0.6	0.7	0.5	0.5	0.4	0.6	0.6	0.6	0.6	0.7	0.9	0.9	1.1
<u>3 - MEDIUM</u>													
MEAN	25.7	20.1*	25.4*	25.4	24.5	23.4	27.0*	23.8*	23.0*	22.5	22.0	23.1	21.7
S.E.	0.7	0.7	0.6	0.6	0.7	0.7	2.2	0.6	0.6	0.8	0.8	0.7	1.1
<u>4 - HIGH</u>													
MEAN	24.2*	22.1	22.2	24.8	24.0	24.0	23.3	22.7	22.5*	21.1	22.1	23.5	20.2
S.E.	0.6	0.5	0.5	0.4	0.8	0.9	0.9	0.7	0.6	0.6	0.8	0.6	1.1

\*Significantly different from Control Group (P &lt; 0.05).

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

GROUP MEANS + STANDARD ERRORS

FEMALES

GROUP NO.	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
<u>1 - CONTROL</u>														
MEAN	17.3	20.5	20.9	23.5	23.7	21.0	19.8	22.1	24.4	21.1	21.5	19.5	17.0	20.6
S.E.	0.3	0.3	0.9	1.1	1.0	0.8	0.6	1.0	1.2	0.8	0.8	0.5	0.9	0.9
<u>2 - LOW</u>														
MEAN	16.3	17.8	21.4	23.0	23.6	23.6	21.4	23.1	23.5	23.0	22.5	18.9	17.2	21.5
S.E.	0.8	0.7	1.4	1.1	1.4	1.3	1.2	1.2	1.2	1.2	1.1	0.8	1.0	1.1
<u>3 - MEDIUM</u>														
MEAN	16.6	17.5	19.8	24.0	21.1	23.0	20.2	22.4	22.7	22.5	20.9	17.7	16.4	18.4
S.E.	0.5	0.7	1.1	1.3	1.1	1.3	0.8	1.2	1.4	1.1	1.3	0.8	0.7	1.0
<u>4 - HIGH</u>														
MEAN	16.0	17.8	21.0	25.0	24.1	24.9	23.2	24.2	25.1	23.0	23.5	21.0	18.3	20.7
S.E.	0.4	0.4	1.2	1.5	1.3	1.4	1.3	1.2	1.4	1.1	1.5	1.1	1.2	1.2

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

## GROUP MEANS ± STANDARD ERRORS

## FEMALES

GROUP NO.	WEEK													
	15	16	17	18	19	20	21	22	23	24	25	26	28	
<u>1 - CONTROL</u>														
MEAN	22.1	23.7	20.0	20.8	20.2	20.0	19.1	19.3	18.9	19.0	18.4	17.6	21.0	
S.E.	0.8	0.8	0.6	1.0	0.9	0.7	0.6	0.6	0.6	0.6	0.6	0.4	0.7	
<u>2 - LOW</u>														
MEAN	22.9	25.8	20.9	20.4	19.6	20.3	18.6	19.1	19.4	20.0	17.9	18.0	20.9	
S.E.	1.0	1.1	1.0	0.7	0.8	0.5	0.6	0.6	0.5	0.9	0.7	0.5	0.7	
<u>3 - MEDIUM</u>														
MEAN	20.6	22.9	21.5	20.9	20.5	20.6	18.1	20.2	19.3	20.2	19.0	18.3	20.1	
S.E.	0.8	1.0	1.2	1.3	1.1	0.8	0.7	1.0	0.6	1.0	0.8	0.7	0.6	
<u>4 - HIGH</u>														
MEAN	21.1	22.2	21.3	20.7	19.5	20.7	19.9	21.0	20.1	20.2	18.6	18.4	21.1	
S.E.	0.9	1.2	1.0	0.9	0.8	0.7	1.7	0.9	0.6	0.8	0.7	0.7	1.1	

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

GROUP MEANS + STANDARD ERRORS

FEMALES

GROUP NO.	WEEK												
	30	32	34	36	38	40	42	44	46	48	50	52	56
<u>1 - CONTROL</u>													
MEAN	19.0	18.6	17.3	15.7	15.9	15.4	16.0	16.2	17.4	18.5	17.9	17.9	18.2
S.E.	0.5	0.5	0.8	0.5	0.5	0.6	0.6	0.5	0.4	0.5	0.7	0.5	0.7
<u>2 - LOW</u>													
MEAN	20.7	18.3	18.2	16.1	15.8	15.4	16.0	16.6	17.2	18.6	17.4	17.9	17.6
S.E.	1.0	0.6	0.6	0.5	0.4	0.4	0.5	0.5	0.5	0.5	0.6	0.6	0.8
<u>3 - MEDIUM</u>													
MEAN	19.5	16.9	17.7	15.5	15.0	15.3	15.5	16.6	16.3	17.8	17.2	17.4	18.5
S.E.	0.7	0.5	1.0	0.4	0.3	0.6	0.4	0.4	0.5	1.0	0.8	0.5	0.8
<u>4 - HIGH</u>													
MEAN	20.1	19.7	18.0	17.1	16.6	15.7	16.3	17.3	16.5	17.0	17.2	17.9	18.3
S.E.	1.2	0.9	0.8	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.6

TABLE 2 (Continued)

FOOD CONSUMPTION  
(grams/day)

GROUP MEANS + STANDARD ERRORS

FEMALES

GROUP NO.	WEEK												
	60	64	68	72	76	80	84	88	92	94	96	100	104
<u>1 - CONTROL</u>													
MEAN	23.2	17.7	18.8	21.6	19.4	21.4	18.2	18.4	16.7	17.2	17.6	18.8	17.4
S.E.	0.7	0.6	0.7	0.7	0.5	0.9	0.4	0.5	0.6	0.6	0.6	0.6	0.5
<u>2 - LOW</u>													
MEAN	21.8	15.8*	15.4*	20.3	20.0	19.3	17.4	18.0	17.4	18.5	18.4	18.6	16.4
S.E.	0.7	0.6	0.6	0.6	0.7	0.8	0.6	0.6	0.6	0.8	0.6	0.6	0.9
<u>3 - MEDIUM</u>													
MEAN	20.8*	15.1*	15.6*	19.7*	19.2	19.0*	17.9	17.0	15.8	16.7	16.6	18.4	17.5
S.E.	0.7	0.6	0.6	0.4	0.5	0.7	0.6	0.6	0.5	0.6	0.6	1.0	0.8
<u>4 - HIGH</u>													
MEAN	20.6*	16.0	19.7	20.0	19.5	19.2	17.9	17.8	16.9	18.1	16.7	18.8	16.4
S.E.	0.9	0.7	0.9	0.8	0.6	0.7	0.8	0.9	0.9	0.8	0.7	0.7	0.7

\*Significantly different from Control Group (P &lt; 0.05).

TABLE 3  
HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>13-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	8.37	1.9	43.9	14.7	13.7	<1	20	79	<1	1
S.E.	0.29	0.30	0.92	0.29	1.1	-	3.0	3.2	-	-
<u>2 - LOW</u>										
MEAN	8.62	0.4**	47.5**	15.8**	14.7	0	11	88	<1	2
S.E.	0.16	0.10	0.56	0.18	0.47	0	2.0	1.9	-	0.37
<u>3 - MEDIUM</u>										
MEAN	8.59	2.1	43.8	14.7	15.2	0	25	73	1	1
S.E.	0.26	0.17	1.5	0.49	0.87	0	1.9	1.9	-	-
<u>4 - HIGH</u>										
MEAN	8.41	1.3	45.9	15.2	13.9	0	13	84	<1	2
S.E.	0.30	0.40	1.15	0.32	0.68	0	2.0	2.2	-	0.46

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.  
\*\*Significantly different from control group (p < 0.05).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	EO
<u>26-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	8.99	1.6	45.0	15.0	11.0	0	14	84	1	1
S.E. (N=9)	0.17	0.37	0.39	0.15	1.1		2.9	3.0	-	-
<u>2 - LOW</u>										
MEAN	9.31	3.0**	46.5**	15.4	12.7	0	23	74	1	2
S.E.	0.19	0.35	0.50	0.20	0.56		2.9	3.0	-	0.43
<u>3 - MEDIUM</u>										
MEAN	9.26	1.4	47.0**	15.2	13.8	0	19	80	1	1
S.E.	0.13	0.17	0.31	0.14	0.93		2.3	2.3	-	-
<u>4 - HIGH</u>										
MEAN	8.33**	1.9	45.4	15.1	12.9	<1	21	77	1	2
S.E.	0.21	0.26	0.53	0.17	0.65	-	2.5	2.5	-	0.63

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; EO - Eosinophils.

\*\*Significantly different from control group (p < 0.05).

Number of animals per group (N) is 10 except where otherwise noted.

TABLE 3 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS + STANDARD ERROR

## MALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>52-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	7.51	2.7	44.5	15.5	12.4	<1	22	76	1	1
S.E.	0.18	0.26	0.76	0.23	0.97	-	2.5	2.7	-	-
<u>2 - LOW</u>										
MEAN	7.41	2.4	44.0	15.1	12.6	0	18	81	<1	1
S.E.	0.24	0.30	0.68	0.24	0.58	-	3.2	3.3	-	-
<u>3 - MEDIUM</u>										
MEAN	7.30	2.9	43.5	15.1	14.2	0	19	79	1	1
S.E.	0.18	0.58	0.70	0.23	1.1	-	2.4	2.7	-	-
<u>4 - HIGH</u>										
MEAN	7.36	2.5	43.5	15.0	14.1	0	20	77	1	1
S.E.	0.31	0.31	1.2	0.48	0.68	-	2.2	2.3	-	-

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS ± STANDARD ERROR

MALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>104-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	7.68	0.2	42.5	13.9	10.2	0	32	65	2	2
S.E.	0.32	0.033	0.76	0.49	0.59	0.11	2.1	2.2	0.95	0.32
<u>2 - LOW</u>										
MEAN	7.91	0.7	41.3	14.3	8.9	0	28	70	-	2
S.E.	0.50	0.31	0.86	0.29	1.0	0	3.2	3.3	-	0.33
<u>3 - MEDIUM</u>										
MEAN	8.18	1.2**	43.5	14.5	8.0**	0	36	60	1	2
S.E.	0.22	0.23	0.76	0.30	0.70	0	4.9	4.9	0.38	0.48
<u>4 - HIGH</u>										
MEAN	7.55	1.9**	40.0**	13.9	6.7**	0	33	62	1	4
S.E.	0.24	0.31	0.84	0.29	0.34	0.11	3.0	2.9	0.47	0.82

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.  
 \*\*Significantly different from control group (p<0.05).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS + STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>13-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	7.29	1.1	39.6	13.6	10.4	0	16	82	1	1
S.E.	0.39	0.37	1.0	0.37	0.70		3.1	3.0		
<u>2 - LOW</u>										
MEAN	8.39**	0.1**	46.1**	15.8**	10.1	0	10	89	<1	1
S.E.	0.16	0.024	0.44	0.18	0.71		1.3	1.3		
<u>3 - MEDIUM</u>										
MEAN	8.55	2.2**	43.2	15.0	11.7	<1	14	84	1	1
S.E.	0.60	0.38	3.3	1.1	1.4	-	2.8	3.2	-	-
<u>4 - HIGH</u>										
MEAN	6.87	0.1**	43.5	14.6	13.6**	<1	11	87	<1	2
S.E.	0.30	0.023	1.7	0.58	0.46		2.0	2.1		0.45

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.  
 \*\*Significantly different from control group (p < 0.05).

TABLE 3 (Continued)

HEMATOCYTOLOGY

GROUP MEANS + STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>26-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	7.63	3.4	42.5	14.3	9.5	0	10	88	<1	1
S.E.	0.19	1.1	0.43	0.14	0.87		1.3	1.7	-	-
<u>2 - LOW</u>										
MEAN	8.67**	2.6	45.5**	15.1**	8.1	0	15	83	1	1
S.E.	0.14	0.33	0.51	0.19	0.72		2.1	2.2	-	-
<u>3 - MEDIUM</u>										
MEAN	8.70**	1.3	45.0**	14.9	7.6	0	20	78	1	2
S.E.	0.18	0.13	0.62	0.27	1.25		4.1	4.3	-	0.56
<u>4 - HIGH</u>										
MEAN	7.90	2.4	46.0**	15.6**	10.3	0	14	84	1	2
S.E.	0.26	0.54	0.52	0.13	0.75		1.4	1.6	-	0.33

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.  
 \*\*Significantly different from control group (p < 0.05).

TABLE 3 (Continued)

## HEMATOCYTOLOGY

## GROUP MEANS ± STANDARD ERROR

## FEMALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC %	CELL VOL. %	HEMO- GLOBIN gm %	MBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>52-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	6.90	2.4	44.0	15.3	10.0	<1	21	77	<1	1
S.E.	0.20	0.36	0.68	0.17	0.91	-	3.2	3.4	-	-
<u>2 - LOW</u>										
MEAN	6.72	2.7	42.0**	14.7**	11.9	0	25	73	1	1
S.E.	0.24	0.31	0.68	0.22	0.84	-	4.1	4.3	-	-
<u>3 - MEDIUM</u>										
MEAN	7.12	2.5	43.0	15.3	12.0	0	20	78	1	1
S.E.	0.15	0.31	0.61	0.22	1.3	-	4.6	4.6	-	-
<u>4 - HIGH</u>										
MEAN	6.95	3.2	43.5	15.3	10.9	0	20	77	1	2
S.E.	0.24	0.54	0.58	0.26	0.93	-	2.9	3.4	-	0.57

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.

\*\*Significantly different from control group (p &lt; 0.05).

TABLE 3 (Continued)

HEMATOCYTOLOGY  
GROUP MEANS + STANDARD ERROR

FEMALES

GROUP NO.	RBC/mm <sup>3</sup> (x 10 <sup>6</sup> )	RETIC. %	CELL VOL. %	HEMO- GLOBIN gm %	WBC/mm <sup>3</sup> (x 10 <sup>3</sup> )	DIFFERENTIAL (%)*				
						Ban	Seg	Ly	Mo	Eo
<u>104-WEEKS</u>										
<u>1 - CONTROL</u>										
MEAN	6.75	0.5	39.0	13.4	8.1	0	33	65	0.4	2
S.E.	0.20	0.11	0.77	0.32	0.76	0	4.3	4.2	0.22	0.37
<u>2 - LOW</u>										
MEAN	5.79	1.4**	37.8	13.2	8.5	0	39	58	0	2
S.E.	0.71	0.29	0.64	0.22	0.76	0	2.6	3.0	0.15	0.59
<u>3 - MEDIUM</u>										
MEAN	7.20	0.3	39.5	13.6	5.5**	0	34	64	1	1
S.E.	0.21	0.11	1.0	0.37	0.71	0	3.5	3.4	0.37	0.22
<u>4 - HIGH</u>										
MEAN	6.89	0.6	38.5	13.1	7.1	0	43	54	1	2
S.E.	0.12	0.23	0.45	0.18	0.50	0	2.3	2.4	0.28	0.53

\*Ban - Bands; Seg - Segmented Neutrophils; Ly - Lymphocytes; Mo - Monocytes; Eo - Eosinophils.  
\*\*Significantly different from control group (p<0.05).

TABLE 4  
BLOOD CHEMISTRY  
GROUP MEANS + STANDARD ERROR

GROUP NO.	GLU- COSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILI- RUBIN mg %	TOTAL PROTEIN gm %	MET- HGB. % Sat.	MALES	
												52-WEEKS	
<u>1 - CONTROL</u>													
MEAN	146	12.4	145	5.7	101	15.1	164	19.9	0.20	6.5	3.7		
S.E.	4.0	0.46	0.56	0.07	0.69	0.70	17	1.5	0.047	0.11	1.4		
<u>2 - LOW</u>													
MEAN	155	12.7	144	5.9	102	17.9	180	25.8*	0.09*	6.7	5.3		
S.E.	6.7	0.53	0.83	0.25	0.86	2.7	10	2.3	0.018	0.12	1.3		
<u>3 - MEDIUM</u>													
MEAN	137	14.7	145	5.9	101	18.1	183	23.0	0.12	6.5	8.5*		
S.E.	5.7	1.8	0.77	0.24	0.69	3.0	7.6	1.4	0.039	0.15	1.8		
<u>4 - HIGH</u>													
MEAN	137	12.2	145	5.9	101	17.4	168	19.0	0.12	6.6	2.2		
S.E.	3.1	0.60	0.81	0.20	0.72	1.1	13	1.0	0.026	0.15	0.85		

\*Significantly different from control group ( $p < 0.05$ ).

TABLE 4 (Continued)

## BLOOD CHEMISTRY

GROUP MEANS  $\pm$  STANDARD ERROR

## MALES

GROUP NO.	GLU- COSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILI- RUBIN mg %	TOTAL PROTEIN gm %	MET- HGB. % Sat.
<u>1 - CONTROL</u>											
MEAN	165	19	145	5.2	107	13.4	189	31	0.3	6.0	3.4
S.E.	8.7	2.2	0.49	0.12	0.59	2.1	28	5.1	0.057	0.11	0.77
<u>2 - LOW</u>											
MEAN	135	18	148**	5.7	107	11.3	247	34	0.3	6.1	6.4**
S.E.	13	2.4	0.86	0.33	0.87	1.8	22	4.4	0.038	0.12	0.18
<u>3 - MEDIUM</u>											
MEAN	141	17	150**	6.6**	110**	9.4	325**	61**	0.4	6.4**	2.2
S.E.	11	1.7	0.73	0.20	0.47	0.52	21	11	0.038	0.17	0.83
<u>4 - HIGH</u>											
MEAN	153	18	149**	6.4**	111**	9.4	161	38	0.5**	5.8	4.2
S.E.	7.9	2.5	0.66	0.46	0.77	0.53	14	4.2	0.06	0.15	1.3

\*Determinations made on different rats.

\*\*Significantly different from control group (p&lt;0.05).

TABLE 4 (Continued)

## BLOOD CHEMISTRY

## GROUP MEANS + STANDARD ERROR

## FEMALES

GROUP NO.	GLU- COSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILI- RUBIN mg %	TOTAL PROTEIN gm %	MET- HGB. % Sat.	52-WEEKS	
<u>1 - CONTROL</u>													
MEAN	157	13.3	143	5.0	97	8.7	112	20.5	0.20	7.0	4.0		
S.E.	3.2	0.47	0.70	0.18	0.87	0.54	8.2	1.3	0.057	0.10	1.2		
<u>2 - LOW</u>													
MEAN	147	12.4	144	4.8	98	8.8	145*	22.9	0.13	6.9	6.5		
S.E.	4.7	0.68	0.89	0.15	0.77	0.71	7.5	1.8	0.021	0.060	1.9		
<u>3 - MEDIUM</u>													
MEAN	147	11.9	144	5.1	99	11.4	138*	21.2	0.16	7.0	8.5*		
S.E. (N=9)	4.1	0.69	0.38	0.28	0.93	1.3	10	1.8	0.037	0.17	1.8		
<u>4 - HIGH</u>													
MEAN	136*	12.7	144	5.0	100*	7.8	143	23.5	0.08	6.8	2.2		
S.E. (N=6)	4.3	0.39	0.83	0.15	0.99	0.55	19	3.0	0.017	0.16	1.04		

\*Significantly different from control group ( $p < 0.05$ ).  
Number of animals per group (N) is 10 except where otherwise noted.

TABLE 4 (Continued)

BLOOD CHEMISTRY											
GROUP MEANS + STANDARD ERROR											
FEMALES											
104-WEEKS											
GROUP NO.	GLU- COSE mg %	BUN mg %	Na mEq/L	K mEq/L	Cl mEq/L	ALK. PHOS. I.U.	SGOT I.U.	SGPT I.U.	TOTAL BILI- RUBIN mg %	TOTAL PROTEIN gm %	MET- HGB. % Sat.
<u>1 - CONTROL</u>											
MEAN	136	16	143	4.7	104	6.9	231	38	0.3	7.0	3.1
S.E.	9.0	1.4	0.60	0.16	1.3	0.24	29	6.5	0.048	0.12	0.98
<u>2 - LOW</u>											
MEAN	136	18	147**	5.6**	106	7.1	217	25	0.5**	6.8	2.7
S.E.	7.1	2.0	0.71	0.34	1.3	0.72	16	3.4	0.066	0.22	0.71
<u>3 - MEDIUM</u>											
MEAN	139	14	148**	5.1	109**	5.9**	242	36	0.4	6.8	3.9
S.E.	4.4	0.82	0.67	0.17	1.1	0.29	21	4.1	0.054	0.16	1.1
<u>4 - HIGH</u>											
MEAN	139	17	148**	4.6	109**	6.9	212	30	0.4	7.4**	-
S.E.	5.8	1.2	0.42	0.20	1.4	0.28	27	4.9	0.060	0.14	-

\*Determinations made on different rats.

\*\*Significantly different from control group (p<0.05).

TABLE 5  
URINALYSIS  
KEY TO ABBREVIATIONS AND SYMBOLS

Color:	Y = Yellow Str = Straw Bei = Beige Crm = Cream YBr = Yellow Brown Br = Brown
Appearance:	Cldy = Cloudy S1 Cldy = Slightly Cloudy
Albumin:	0 = Negative + = Trace 1+ = 30 mg 2+ = 100 mg 3+ = 300 mg 4+ = 1000 mg or greater
Other:	- or 0 = None seen or Negative + = Trace, Rare, Occasional 1+ = Slight, Small, Little 2+ = Moderate, Frequent 3+ = Severe, Heavy, Large, Many 4+ = Maximal
WBC:	cl = With clumps
Epithelial Cells:	sq = Squamous
Casts:	fgr = Finely Granular cgr = Coarsely Granular WBC = White Blood Count (Leukocyte) hy = Hyaline P = Pus
Crystals:	U.A. = Uric Acid T.P. = Triple Phosphate CA.OX = Calcium Oxalate LEU = Leucine SU = Sulfa
Other:	Yst = Yeast Mu = Mucous Threads Sp = Sperm

TABLE 5

## URINALYSIS - POOLED SAMPLES

13-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	PH	GLU- COSE	KE- TONES	BILI- RUBIN	UGOT	RBC	MICROSCOPIC EXAMINATION/HPF*				CRYSTALS**		
									WBC	EPITH	BACT	AMORPH	U.A.	T.P.	
1 - CONTROL	M	1.027	6.0	0	0	0	52	2-3	6-8	±	2+	1+	+	-	-
1 - CONTROL	F	1.027	7.0	0	0	0	34	0-1	10-12	-	2+	1+	-	+	-
2 - LOW	M	1.049	6.0	0+	1+	0	82	15-20	12-14 cl	+	-	3+	-	-	-
2 - LOW	F	1.026	6.0	0	0	0	24	-	8-10	-	+	1+	-	-	-
3 - MEDIUM	M	1.019	7.0	0	0	0	40	10-25	1-5	0-3	2+	1+	-	+	-
3 - MEDIUM	F	1.015	7.0	0	0	0	15	+	-	0-2	1+	1+	-	-	-
4 - HIGH	M	1.042	6.0	0	0	0	58	+	1-3	0-2	-	1+	-	-	3-10
4 - HIGH	F	1.013	7.0	0	0	0	17	-	0-2	0-1	2+	2+	-	-	0-2

\*Microscopic (Per High Power Field).

\*\*Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

+Positive for non-glucose reducing substances.

TABLE 5 (Continued)  
 URINALYSIS - POOLED SAMPLES  
 26-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	pH	GLU- COSE	KE- TONES	BILI- RUBIN	UGOT	RBC	MICROSCOPIC EXAMINATION/HPF*				CRYSTALS**		
									MBC	EPITH	BACT	AMORPH	U.A.	T.P.	
1 - CONTROL	M	1.015	7.0	0	0	0	15	-	2-4	-	+	1+	+	+	2+
1 - CONTROL	F	1.015	6.5	0	0	0	8	-	1-3	+	+	1+	-	-	-
2 - LOW	M	1.016	7.0	0	0	0	7	8-10	1-4	-	+	1+	+	+	+
2 - LOW	F	1.020	6.5	0	0	0	8	-	1-3	-	+	1+	+	-	-
3 - MEDIUM	M	1.024	7.0	0	0	0	10	4-6	0-2	-	+	1+	+	-	-
3 - MEDIUM	F	1.016	7.0	0	0	0	37	-	2-5	+	+	-	+	+	+
4 - HIGH	M	1.033	6.5	0	0	0	8	2-4	0-2	-	1+	1+	2+	-	-
4 - HIGH	F	1.021	6.0	0	0	0	32	-	1-3	+	1+	1+	+	+	-

\*Microscopic (Per High Power Field).

\*\*Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

TABLE 5 (Continued)

## URINALYSIS - POOLED SAMPLES

52-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	PH	GLU- COSE	KE- TONES	BILI- RUBIN	UGOT	RBC	WBC	MICROSCOPIC EXAMINATION/HPF*				CRYSTALS**		
										EPITH	BACT	AMDRPH	U.A.	I.P.		
1 - CONTROL	M	1.023	7.0	0	0	0	23	-	0-2	-	3+	2+	-	1+		
1 - CONTROL	F	1.013	7.0	0	0	0	15	-	0-2	-	3+	1+	-	1+		
2 - LOW	M	1.015	7.0	0	0	0	16	-	0-2	-	3+	1+	-	-		
2 - LOW	F	1.014	7.5	0	0	0	32	1-4	-	sq +	3+	1+	-	1+		
3 - MEDIUM	M	1.027	7.0	0	0	0	44	-	0-2	+	1+	1+	-	3+		
3 - MEDIUM	F	1.018	7.0	0	0	0	38	-	0-1	-	1+	1+	-	+		
4 - HIGH	M	1.040	7.0	0	0	0	22	1-8	0-2	+	1+	1+	-	3+		
4 - HIGH	F	1.020	7.0	0	0	0	33	2-6	0-1	+	1+	1+	-	3+		

\*Microscopic (Per High Power Field).

\*\*Crystals: U.A. - Uric Acid; I.P. - Triple Phosphate.

TABLE 5 (Continued)

URINALYSIS - POOLED SAMPLES  
104-WEEKS

GROUP NO. & DOSE LEVEL	SEX	SPEC. GRAV.	PH	GLU. COSE	KE- TONES	BILI- RUBIN	UGOT	RBC	WBC	MICROSCOPIC EXAMINATION/HPF*				CRYSTALS**	
										EPITH	BACT	AMORPH	U.A.	T.P.	
1 - CONTROL	M	1.018	7.0	3+	0	0	26	2-5	0-1	-	2+	2+	-	-	1+
1 - CONTROL	F	1.016	6.5	0	0	0	30	±	0-2	-	2+	2+	1+	-	-
2 - LOW	M	1.022	8.0	0	0	0	20	18-20	±	-	1+	1+	-	-	-
2 - LOW	F	1.015	6.0	0	0	0	13	12-16	4-6	-	3+	2+	1+	-	-
3 - MEDIUM	M	1.013	7.0	0	0	0	8	21-26	8-10	2-6	2+	1+	-	-	-
3 - MEDIUM	F	1.013	6.0	0	0	0	5	20-25	2-4	1-3	2+	1+	1+	-	-
4 - HIGH	M	1.019	8.0	0	0	0	22	1-3	0-1	1-2	2+	2+	-	-	3+
4 - HIGH	F	1.016	8.0	0	0	0	70	-	1-4	2-3	2+	2+	-	-	3+

\*Microscopic (Per High Power Field).

\*\*Crystals: U.A. - Uric Acid; T.P. - Triple Phosphate.

TABLE 6  
ORGAN WEIGHTS  
(grams)

52-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4772	658.0	0.0230	1.4020	14.7000	0.7200	4.0960	0.0510	5.6100
4775	670.0	0.0240	1.6830	14.8150	0.8840	3.8060	0.0700	6.0360
4781	529.0	0.0260	1.5230	13.0030	0.6740	3.5150	0.0510	3.8890
4784	712.0	0.0270	1.7930	14.1500	1.2080	3.5710	0.0610	6.2490
4787	627.0	0.0280	1.5570	13.5000	0.7640	3.2130	0.0510	6.3200
4790	574.0	0.0260	1.4600	13.1890	0.8360	3.2160	0.0660	4.5850
4793	604.0	0.0300	1.5730	14.6400	0.8040	4.2060	0.0500	5.1940
4796	645.0	0.0320	1.7750	17.6680	1.1070	3.7990	0.0690	5.6050
4799	589.0	0.0270	1.7410	16.0570	0.6520	4.1820	0.0580	4.4240
4802	655.0	0.0320	1.8570	17.7230	1.1050	4.3370	0.0640	6.1670
N	10	10	10	10	10	10	10	10
MEAN	626.7	0.0275	1.6456	14.9511	0.8814	3.7941	0.0591	5.4079
S.D.	53.1	0.0031	0.1506	1.7018	0.2060	0.4090	0.0080	0.8556
S.E.	16.8	0.0010	0.0476	0.5381	0.0651	0.1293	0.0025	0.2706

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

## 52-WEEK SACRIFICE - MALES

## GROUP 2 - LOW

ANIMAL NUMBER	RUDDY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4922	602.0	0.0160	1.7000	13.8490	0.7410	3.9390	0.0450	5.1020
4928	724.0	0.0300	2.1510	14.1460	0.9610	4.0950	0.0560	5.6380
4931	692.0	0.0350	1.7940	12.0280	0.8940	4.0280	0.0570	5.4170
4934	774.0	0.0320	2.0280	16.9190	1.0380	4.1650	0.0470	5.7270
4937	675.0	0.0350	1.7800	16.9180	0.7630	3.9030	0.0560	5.3320
4941	682.0	0.0270	1.7850	16.0460	0.9550	3.9670	0.0660	5.6210
4955	504.0	0.0260	1.3730	10.9000	0.6150	3.2420	0.0560	4.0630
4964	605.0	0.0260	2.1210	16.2890	0.8430	3.6350	0.0570	4.3760
4970	577.0	0.0310	1.4500	12.6470	0.7280	3.3810	0.0300	5.2000
4980	480.0	0.0280	1.4000	10.7440	0.5000	2.9000	0.0610	2.7600
N	10	10	10	10	10	10	10	10
MEAN	631.9	0.0288	1.7592	15.4480	0.7868	3.7255	0.0531	4.9236
S.D.	94.1	0.0051	0.2876	3.2486	0.1891	0.4215	0.0161	0.9358
S.E.	29.8	0.0016	0.0909	1.0273	0.0590	0.1333	0.0032	0.2959

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TABLE 6 (Continued)  
 ORGAN WEIGHTS  
 (grams)  
 52-WEEK SACRIFICE - MALES  
 GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5079	564.0	0.0250	1.4640	12.6550	0.7310	3.1210	0.0580	5.5320
5080	505.0	0.0330	1.3000	16.0300	0.8950	5.1300	0.0680	4.1000
5090	585.0	0.0340	1.5400	12.3300	0.6770	4.0230	0.0710	4.4550
5093	562.0	0.0310	1.4300	13.4410	0.9200	3.2950	0.0690	4.8920
5096	692.0	0.0240	2.0630	15.8450	0.7470	3.9390	0.0610	5.0640
5099	640.0	0.0380	1.7160	16.1410	0.8390	3.5000	0.0630	5.0750
5102	514.0	0.0300	1.5900	11.6490	0.6500	3.4190	0.0330	3.8710
5114	560.0	0.0380	1.9220	14.0320	0.8220	3.6230	0.0680	4.6440
5120	574.0	0.0280	1.6240	13.1420	0.7180	3.1830	0.0560	2.7710
5139	533.0	0.0290	1.8790	15.0690	1.2040	3.3070	0.0650	4.7350
N	10	10	10	10	10	10	10	10
MEAN	572.9	0.0320	1.6538	14.0312	0.8203	3.6540	0.0612	4.5139
S.D.	56.6	0.0046	0.2609	1.6491	0.1521	0.5992	0.0111	0.7809
S.E.	17.9	0.0015	0.0760	0.5215	0.0513	0.1895	0.0035	0.2469

TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

52-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5222	685.0	0.0330	1.7350	21.1400	1.1340	4.4850	0.0570	5.7110
5225	647.0	0.0350	1.6100	15.7470	0.7300	3.3330	0.0480	4.9210
5228	474.0	0.0240	1.3320	11.0520	0.6320	2.7860	0.0500	4.4550
5231	551.0	0.0260	1.4250	12.7240	0.6720	3.0240	0.0560	5.0990
5252	545.0	0.0270	1.8420	15.4220	0.8950	3.8810	0.0630	5.0300
5254	554.0	0.0300	1.8310	13.9490	0.7430	4.3700	0.0520	4.6080
5264	464.0	0.0240	1.4150	10.6470	0.5340	2.6470	0.0430	4.5320
5267	666.0	0.0310	1.7090	20.1650	1.0850	5.2120	0.0620	5.4840
5270	609.0	0.0270	1.7300	14.5910	0.8160	3.6450	0.0500	5.1110
5282	530.0	0.0280	1.4350	13.5460	0.6750	3.1440	0.0530	5.6030
N	10	10	10	10	10	10	10	10
MEAN	576.9	0.0285	1.6127	14.8983	0.8016	3.6527	0.0534	5.0554
S.D.	70.2	0.0037	0.1333	3.4059	0.1820	0.8306	0.0062	0.4437
S.E.	24.1	0.0012	0.0611	1.0960	0.0575	0.2627	0.0020	0.1403

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)  
104-WEEK SACRIFICE - MALES  
GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4522	736.2	0.0120	1.9000	17.8390	0.7960	4.9420	0.2070	6.2210
4523	682.0	0.0190	1.9780	15.7660	0.8600	3.9920	0.0300	7.1090
4525	618.8	0.0580	1.5580	13.9560	0.8040	3.3960	0.0620	5.5000
4526	455.9	0.0220	1.5470	17.0010	0.9620	5.9170	0.0880	5.1870
4527	646.3	0.0310	1.6190	12.2070	0.8400	3.5450	0.0450	2.8580
4529	631.8	0.0100	1.8140	23.5910	1.1040	4.4120	0.0420	4.3350
4530	631.1	0.0200	2.1860	14.2960	0.6940	3.6570	0.0470	5.9180
4531	796.6	0.0260	2.7510	16.8400	1.3740	4.6920	0.0630	6.9350
4533	633.0	0.0460	1.6100	16.7910	0.8780	4.2380	0.0710	5.7390
4535	602.1	0.0330	1.4140	18.1520	2.6120	3.4390	0.0730	4.3950
N	10	10	10	10	10	10	10	10
MEAN	643.4	0.0277	1.8377	16.6439	1.0924	4.2330	0.0728	5.4197
S.D.	89.1	0.0150	0.3974	3.0794	0.5676	0.7922	0.0502	1.2906
S.E.	28.2	0.0047	0.1257	0.9738	0.1795	0.2505	0.0159	0.4081

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

104-WEEK SACRIFICE - MALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4573	595.7	0.0320	1.5750	14.4650	0.9310	3.5190	0.0520	4.3910
4575	645.0	0.0380	1.7820	16.3230	0.6270	4.2540	0.0560	5.2630
4576	366.0	0.0370	1.4440	11.4030	0.6940	3.7530	0.1230	2.5930
4578	568.0	0.0370	1.3430	12.7080	0.9420	3.3760	0.0640	4.9380
4579	804.5	0.0440	1.9450	14.6600	1.5890	3.8400	0.0740	6.2670
4582	487.5	0.0260	1.2750	11.2830	0.8410	3.7960	0.0740	5.8870
4583	636.1	0.0340	1.3590	14.8580	0.8500	3.6920	0.0710	5.9930
4584	605.7	0.0280	2.6510	15.1510	0.7540	4.0880	0.0500	5.1920
4587	796.0	0.0470	1.7530	23.4490	1.1010	5.5180	0.0540	5.7440
4588	816.6	0.0410	2.1190	17.5380	1.3900	5.3020	0.1330	6.5560
N	10	10	10	10	10	10	10	10
MEAN	632.1	0.0364	1.7246	15.6838	0.9719	4.1138	0.0751	5.2844
S.D.	144.8	0.0067	0.4280	3.7853	0.3074	0.7292	0.0294	1.1465
S.F.	45.8	0.0021	0.1354	1.1970	0.0972	0.2306	0.0093	0.3625

TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

## 104-WEEK SACRIFICE - MALES

## GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4623	627.6	0.0310	1.5350	16.9130	0.4520	3.8370	0.0710	5.2430
4625	609.7	0.0350	1.4180	15.7740	1.0510	3.5970	0.0600	4.9570
4626	772.5	0.0460	2.4310	18.9080	1.1690	5.0420	0.0720	6.4430
4627	721.4	0.0490	1.6460	17.8850	0.4390	4.1700	0.0670	6.4610
4630	653.7	0.0550	2.2220	15.9740	1.1380	4.2340	0.1020	5.7430
4632	532.3	0.0430	1.6740	14.8440	0.7480	3.5790	0.0640	5.9290
4633	500.4	0.0640	1.4950	12.5730	0.5760	3.7290	0.1130	3.9510
4634	557.1	0.0290	1.7120	13.1750	0.8470	3.7980	0.0700	5.8190
4635	591.8	0.0360	1.7080	17.3730	0.9630	3.7100	0.1320	5.8120
4636	542.8	0.0450	1.8570	13.5720	0.9620	3.8300	0.0540	4.8960
N	10	10	10	10	10	10	10	10
MEAN	610.9	0.0433	1.8094	15.6941	0.9145	3.9526	0.0805	5.5274
S.D.	86.1	0.0110	0.2974	2.1300	0.1809	0.4397	0.0259	0.7754
S.E.	27.2	0.0035	0.0942	0.6736	0.0572	0.1391	0.0082	0.2452

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

104-WEEK SACRIFICE - MALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4672	678.6	0.0280	2.1350	17.4610	0.9730	4.3650	0.0950	7.0080
4674	720.1	0.0140	1.6320	15.8640	1.0600	4.1350	0.0510	5.6380
4675	754.6	0.0180	1.6860	7.5860	0.7650	4.8700	0.0390	5.7690
4677	605.8	0.0060	1.3550	15.2110	1.1450	4.4100	0.0600	6.4240
4678	600.5	0.0260	1.5870	14.7720	1.0260	3.7430	0.0260	4.5010
4680	712.1	0.0430	1.7040	16.7370	0.7950	3.6890	0.0350	6.3790
4681	468.4	0.0190	1.7710	14.7080	1.5950	3.8710	0.0420	6.2080
4682	561.7	0.0090	2.0880	14.9350	0.7110	3.7440	0.0350	4.2720
4684	584.9	0.0120	1.7060	16.0470	0.9680	4.3690	0.0390	5.6000
4686	555.9	0.0320	1.8770	22.2380	1.4030	5.9820	0.0600	5.2430
N	10	10	10	10	10	10	10	10
MEAN	624.3	0.0207	1.7541	15.5559	1.0441	4.3198	0.0482	5.7042
S.D.	89.6	0.0115	0.2318	3.5803	0.2798	0.6975	0.0198	0.8601
S.E.	28.3	0.0036	0.0733	1.1322	0.0885	0.2206	0.0063	0.2720

TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

## 52-WEEK SACRIFICE - FEMALES

## GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4700	412.0	0.0200	1.1890	9.0620	0.4440	2.1710	0.0730	0.1020
4703	345.0	0.0250	1.2090	9.3260	0.6090	2.4640	0.0850	0.1050
4709	344.0	0.0270	1.2650	7.5250	0.5290	2.0810	0.0710	0.0920
4712	382.0	0.0250	1.1120	10.8100	0.7780	2.5960	0.0920	0.1050
4715	355.0	0.0230	1.1730	9.8880	0.5670	2.2890	0.0810	0.0990
4718	370.0	0.0280	1.2000	9.4190	0.5390	2.1370	0.0890	0.0980
4721	365.0	0.0220	1.0950	9.3810	0.5590	2.1280	0.0730	0.0860
4724	440.0	0.0260	1.3350	11.4000	0.6200	2.3630	0.0820	0.1200
4727	285.0	0.0230	0.9900	6.8200	0.3900	1.8680	0.0640	0.0730
4730	390.0	0.0260	1.1020	8.5420	0.5740	2.1450	0.0710	0.0660
N	10	10	10	10	10	10	10	10
MEAN	366.8	0.0245	1.1670	9.2472	0.5609	2.2242	0.0781	0.0948
S.D.	42.1	0.0025	0.0972	1.3580	0.1041	0.2088	0.0090	0.0159
S.E.	13.3	0.0009	0.0307	0.4294	0.0329	0.0660	0.0029	0.0050

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4847	308.0	0.0240	1.0970	9.1330	0.4900	1.9580	0.0790	0.0910
4850	365.0	0.0290	1.1850	8.9720	0.5950	2.3850	0.0910	0.0890
4853	311.0	0.0260	1.1130	7.5680	0.5710	2.2780	0.0750	0.0700
4856	335.0	0.0300	1.1230	10.1680	0.4050	2.1750	0.0800	0.0850
4859	405.0	0.0330	1.2350	9.2440	0.5800	2.7080	0.0850	0.1200
4862	268.0	0.0320	0.9420	8.0140	0.3490	2.0090	0.0780	0.1000
4865	420.0	0.0320	1.0400	10.9300	0.5400	2.6060	0.0750	0.1030
4868	482.0	0.0340	1.1580	12.4240	0.6340	2.6360	0.0870	0.0840
4871	394.0	0.0290	1.0400	9.1420	0.4330	2.0520	0.0770	0.1040
4878	310.0	0.0360	1.1590	8.4790	0.7320	2.1720	0.0850	0.1800
Mean	366.4	0.0305	1.1092	9.4054	0.5409	2.2979	0.0812	0.1026
S.D.	65.6	0.0037	0.0845	1.4362	0.1208	0.2740	0.0055	0.0304
S.E.	20.7	0.0012	0.0267	0.4542	0.0382	0.0867	0.0017	0.0096

TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

## 52-WEEK SACRIFICE - FEMALES

## GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5003	346.0	0.0290	1.0910	8.8670	0.5230	2.2270	0.0700	0.0980
5006	337.0	0.0240	1.0740	9.0900	0.5110	2.4580	0.0770	0.1080
5015	315.0	0.0310	1.2220	10.4180	0.6610	2.6890	0.0910	0.1120
5018	359.0	0.0310	1.2240	10.5530	0.5560	2.5660	0.0960	0.1530
5022	390.0	0.0360	1.0060	9.5600	0.5270	2.2980	0.0830	0.1500
5025	448.0	0.0300	1.0160	17.2710	0.4310	2.2960	0.1040	0.1940
5039	302.0	0.0310	1.0190	9.0610	0.5300	2.0870	0.0740	0.1080
5054	288.0	0.0280	1.0040	7.7040	0.4220	2.2120	0.0750	0.0990
5060	509.0	0.0300	1.3490	10.7900	0.9780	2.3730	0.0850	0.1240
5067	282.0	0.0270	1.1110	6.8880	0.5150	2.2310	0.0810	0.1070
N	10	10	10	10	10	10	10	10
MEAN	357.6	0.0304	1.1135	10.0222	0.5554	2.3434	0.0836	0.1253
S.D.	73.2	0.0026	0.1175	2.5299	0.1592	0.1814	0.0107	0.0310
S.E.	23.1	0.0068	0.0365	0.8949	0.0503	0.0574	0.0034	0.0098

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

52-WEEK SACRIFICE - FEMALES

GROUP 4 - HIGH

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5150	345.0	0.0250	1.0770	8.6170	0.5280	2.4780	0.0900	0.1600
5153	363.0	0.0230	1.1370	9.5950	0.6110	2.0450	0.0910	0.1660
5156	288.0	0.0190	0.4450	8.3000	0.5560	2.3740	0.0680	0.0890
5159	364.0	0.0250	1.0230	8.9070	0.5630	1.9710	0.0650	0.1030
5162	326.0	0.0250	1.1250	10.2970	0.5120	2.3190	0.0700	0.0810
5165	318.0	0.0250	0.9980	9.9780	0.4830	2.2190	0.0710	0.0890
5168	309.0	0.0200	1.0020	7.4810	0.5320	2.5210	0.0640	0.1010
5171	414.0	0.0370	1.5110	11.5110	0.5900	2.8390	0.0760	0.1600
5174	396.0	0.0250	1.1550	9.5520	0.6060	2.1390	0.0640	0.1500
5177	329.0	0.0280	1.0470	9.0290	0.5950	2.2550	0.0720	0.0650
N	10	10	10	10	10	10	10	10
MEAN	345.2	0.0252	1.1001	9.2250	0.5676	2.3160	0.0731	0.1164
S.D.	39.4	0.0049	0.1655	1.1165	0.0547	0.2543	0.0099	0.0383
S.E.	12.4	0.0016	0.0523	0.3531	0.0173	0.0804	0.0031	0.0121

TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 1 - CONTROL

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRE'LS	OVARIES
4497	292.9	0.0210	0.8860	8.8980	0.5680	2.4510	0.1400	0.1420
4498	366.0	0.0	1.2050	7.8960	0.6510	2.0830	0.0950	0.0
4499	308.3	0.0350	1.4610	12.4510	0.4610	3.3920	0.4790	0.1240
4500	412.1	0.0160	1.1690	9.3890	0.4380	2.0120	0.0410	0.0920
4501	360.3	0.0210	1.3040	9.2000	0.5510	2.6610	0.1190	0.1250
4502	680.4	0.0	1.4340	12.7980	0.8130	2.6960	0.0660	0.0780
4503	486.0	0.0280	1.1250	10.8370	0.3360	2.3200	0.0910	0.1280
4504	363.3	0.0160	0.8510	8.9540	0.3120	2.3660	0.0540	0.0880
4505	388.8	0.0060	1.0070	8.9270	0.3700	2.1960	0.0600	8.0760
4508	526.8	0.0570	1.3360	14.4950	0.4710	3.4130	0.0770	0.0920
N	10	8	10	10	10	10	10	9
MEAN	418.5	0.0250	1.1779	10.3845	0.4971	2.5590	0.1222	0.4939
S.D.	116.9	0.0155	0.2138	2.1644	0.1539	0.4962	0.1290	2.6559
S.E.	37.0	0.0055	0.0676	0.6845	0.0487	0.1569	0.0408	0.8853

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 2 - LOW

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4548	367.1	0.0260	1.0150	10.3230	0.6160	3.0650	0.1330	0.6000
4549	426.2	0.0400	1.4270	12.4720	0.5660	3.5160	0.0750	0.0490
4550	419.0	0.0340	1.5820	11.7310	0.5850	2.9470	0.0620	0.0730
4551	406.0	0.0560	1.6270	14.2900	0.8780	3.8850	0.2830	0.1280
4552	349.9	0.0370	1.0340	12.6430	0.7920	3.5790	0.1280	0.0280
4553	426.1	0.0340	1.1580	10.9570	0.5440	2.6200	0.0890	0.0640
4554	313.9	0.0290	1.4600	9.4000	0.6010	2.7400	0.0980	0.0500
4556	308.0	0.0310	1.4930	9.2720	0.6910	2.3820	0.1470	0.0560
4557	336.8	0.0420	1.4090	10.6210	2.0990	1.8790	0.0940	0.0500
4558	344.0	0.0600	1.0540	9.3300	0.5040	2.6870	0.1440	0.0550
N	10	10	10	10	10	10	10	10
MEAN	369.9	0.0389	1.3259	11.1039	0.7876	2.9300	0.1253	0.1213
S.D.	46.0	0.0112	0.2365	1.6685	0.4751	0.6047	0.0627	0.1911
S.E.	14.6	0.0035	0.0748	0.5276	0.1502	0.1912	0.0198	0.0604

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)

104-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	BODY WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4598	450.0	0.0370	1.0410	9.9920	0.6540	2.5660	0.0810	0.0440
4599	371.2	0.0300	1.2280	9.5070	0.5150	2.5960	0.0690	0.0800
4600	346.5	0.0350	0.9530	9.7560	0.7090	2.6620	0.1930	0.0590
4602	294.8	0.0230	1.3000	7.4280	0.4210	2.2970	0.0600	0.0340
4603	348.8	0.0310	1.0170	8.5790	0.3530	2.0580	0.1200	0.0500
4605	320.0	0.0340	1.0920	8.8990	0.4270	2.4900	0.0850	0.0620
4606	406.2	0.0370	1.3250	9.7260	0.5270	2.3250	0.0630	0.1060
4609	339.2	0.0380	0.7250	7.1820	0.4830	2.0940	0.4630	0.0880
4611	464.5	0.0300	2.0940	12.0610	0.6920	3.4730	1.2570	0.0670
4612	331.3	0.0280	1.3530	9.0970	0.6110	1.9210	0.0860	0.0650
N	10	10	10	10	10	10	10	10
MEAN	367.2	0.0323	1.2128	9.2227	0.5392	2.4482	0.2477	0.0655
S.D.	55.9	0.0048	0.3658	1.3819	0.1228	0.4381	0.3751	0.0214
S.E.	17.7	0.0015	0.1157	0.4370	0.0388	0.1385	0.1186	0.0068

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TABLE 6 (Continued)

ORGAN WEIGHTS  
(grams)  
104-WEEK SACRIFICE - FEMALES  
GROUP 4 - HIGH

ANIMAL NUMBER	REAR WEIGHT	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4647	328.1	0.0070	1.2600	8.2630	0.5330	1.9590	0.0520	0.0880
4648	398.4	0.0150	1.4140	11.0770	0.5820	2.6220	0.0670	0.1090
4650	369.1	0.0120	0.9390	8.5610	0.5160	2.1900	0.0660	0.1120
4651	302.4	0.0230	1.0400	8.9150	0.5160	2.3550	0.1080	0.1280
4652	321.8	0.0350	1.3290	10.9720	1.8360	2.9070	0.3470	0.1000
4653	502.5	0.0100	1.9710	13.9740	0.8560	3.2680	0.0620	0.0
4654	404.3	0.0180	1.4950	9.4450	0.3370	2.2460	0.0	0.1370
4655	360.2	0.0160	1.0040	8.0620	0.4210	2.0470	0.0530	0.0930
4657	348.6	0.0280	1.5770	16.0360	0.7790	5.8100	0.1260	0.1200
4658	297.2	0.0350	1.4560	9.1170	0.4270	2.1850	0.0780	0.1300
N	10	10	10	10	10	10	9	9
MEAN	363.3	0.0199	1.3485	10.4422	0.6803	2.7589	0.1066	0.1130
S.D.	61.1	0.0100	0.3103	2.6559	0.4360	1.1467	0.0936	0.0171
S.E.	19.3	0.0032	0.0981	0.8399	0.1379	0.3626	0.0312	0.0057

TABLE 7

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

52-WEEK SACRIFICE - MALES

GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4772	0.0035	0.2131	2.2432	0.1094	0.6225	0.0078	0.8526
4775	0.0036	0.2521	2.2112	0.1319	0.5681	0.0104	0.9009
4781	0.0049	0.3023	2.4592	0.1274	0.6645	0.0096	0.7352
4784	0.0038	0.2525	1.9874	0.1697	0.5015	0.0086	0.8777
4787	0.0045	0.2483	2.1531	0.1219	0.5124	0.0081	1.0080
4790	0.0045	0.2544	2.2977	0.1456	0.5503	0.0115	0.7988
4793	0.0049	0.2595	2.4079	0.1322	0.6918	0.0082	0.8543
4795	0.0050	0.2752	2.7392	0.1809	0.5990	0.0107	0.8690
4799	0.0046	0.2956	2.7261	0.1107	0.7100	0.0098	0.7511
4802	0.0049	0.2835	2.7058	0.1687	0.6621	0.0098	0.9415
N	10	10	10	10	10	10	10
M.F.	0.0044	0.2636	2.3941	0.1398	0.6082	0.0095	0.8589
S.D.	0.0006	0.0262	0.2525	0.0254	0.0734	0.0012	0.0829
S.E.	0.0002	0.0083	0.0830	0.0080	0.0232	0.0004	0.0262

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 52-WEEK SACRIFICE - MALES  
 GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4922	0.0030	0.2224	2.3005	0.1231	0.6543	0.0075	0.8475
4928	0.0041	0.2985	2.0445	0.1327	0.5056	0.0077	0.7787
4931	0.0051	0.2592	2.7997	0.1277	0.5221	0.0082	0.7828
4934	0.0041	0.2020	2.4443	0.1341	0.5381	0.0061	0.7399
4937	0.0052	0.2637	2.5064	0.1130	0.5762	0.0083	0.7899
4941	0.0040	0.2617	2.3228	0.1400	0.5817	0.0097	0.8242
4955	0.0051	0.2703	2.1457	0.1211	0.6382	0.0110	0.7998
4966	0.0043	0.3506	2.0924	0.1460	0.6008	0.0094	0.7233
4970	0.0054	0.2513	2.1919	0.0915	0.5860	0.0052	0.9012
4980	0.0058	0.2917	2.2383	0.1042	0.6042	0.0127	0.5750
N	10	10	10	10	10	10	10
MEAN	0.0046	0.2791	2.4206	0.1233	0.5729	0.0086	0.7762
S.D.	0.0004	0.0293	0.2100	0.0167	0.0338	0.0022	0.0872
S.E.	0.0003	0.0093	0.0663	0.0053	0.0107	0.0007	0.0276

TABLE 7 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

## 52-WEEK SACRIFICE - MALES

## GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5079	0.0051	0.2603	2.2399	0.1296	0.5534	0.0103	0.9809
5080	0.0065	0.2574	3.1743	0.1772	1.0158	0.0135	0.8119
5090	0.0058	0.2643	2.1077	0.1157	0.6877	0.0121	0.7615
5093	0.0055	0.2544	2.3916	0.1637	0.5863	0.0123	0.8705
5096	0.0035	0.2581	2.2897	0.1079	0.5692	0.0088	0.7318
5099	0.0059	0.2681	2.5220	0.1311	0.5469	0.0098	0.7930
5102	0.0070	0.3093	2.2603	0.1265	0.6652	0.0064	0.7531
5114	0.0068	0.3432	2.5057	0.1468	0.6470	0.0121	0.8293
5120	0.0049	0.2829	2.2995	0.1251	0.5545	0.0098	0.4828
5139	0.0054	0.3525	2.8272	0.2259	0.6205	0.0122	0.8884
N	10	10	10	10	10	10	10
MEAN	0.0057	0.2891	2.4014	0.1450	0.6446	0.0107	0.7903
S.D.	0.0010	0.0359	0.3204	0.0355	0.1397	0.0021	0.1310
S.F.	0.0003	0.0113	0.1013	0.0112	0.0442	0.0007	0.0414

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 52-WEEK SACRIFICE - MALES  
 GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
5222	0.0048	0.2533	3.0061	0.1655	0.6547	0.0083	0.8337
5225	0.0054	0.2488	2.4338	0.1128	0.5151	0.0074	0.7606
5228	0.0051	0.2810	2.3316	0.1333	0.5876	0.0105	0.9399
5231	0.0047	0.2593	2.3093	0.1220	0.5488	0.0102	0.9254
5252	0.0045	0.3149	2.6352	0.1530	0.6634	0.0108	0.8598
5258	0.0054	0.3281	2.4998	0.1332	0.7432	0.0093	0.8258
5264	0.0052	0.3050	2.2446	0.1366	0.5705	0.0093	0.9767
5267	0.0047	0.2655	3.0278	0.1629	0.7826	0.0093	0.8234
5270	0.0044	0.2841	2.3759	0.1340	0.5945	0.0082	0.8392
5282	0.0053	0.2708	2.5558	0.1274	0.5932	0.0100	1.0572
N	10	10	10	10	10	10	10
MEAN	0.0050	0.2811	2.5571	0.1381	0.6298	0.0093	0.8842
S.D.	0.0004	0.0270	0.2854	0.0172	0.0918	0.0011	0.0887
S.E.	0.0001	0.0085	0.0403	0.0054	0.0290	0.0003	0.0281

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 104-WEEK SACRIFICE - MALES  
 GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4522	0.0016	0.2581	2.4731	0.1081	0.6713	0.0281	0.8450
4523	0.0028	0.2900	2.3117	0.1261	0.5853	0.0044	1.0424
4525	0.0094	0.2518	2.2553	0.1299	0.5484	0.0100	0.8888
4526	0.0048	0.3393	3.7291	0.2110	1.2979	0.0193	1.1377
4527	0.0048	0.2505	1.8888	0.1300	0.5640	0.0070	0.4422
4529	0.0016	0.2871	3.7339	0.1747	0.6983	0.0066	0.6861
4530	0.0032	0.3464	2.2653	0.1100	0.5795	0.0074	0.9377
4531	0.0033	0.3453	2.1140	0.1725	0.5890	0.0079	0.6706
4533	0.0073	0.2543	2.6526	0.1387	0.6695	0.0112	0.9066
4535	0.0055	0.2348	3.0148	0.4338	0.5712	0.0121	0.7299
N	10	10	10	10	10	10	10
MEAN	0.0044	0.2858	2.6389	0.1735	0.6775	0.0114	0.8487
S.D.	0.0025	0.0433	0.6504	0.0970	0.2241	0.0072	0.1944
S.E.	0.0008	0.0137	0.2057	0.0307	0.0709	0.0023	0.0615

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 104-WEEK SACRIFICE - MALES  
 GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4573	0.0054	0.2644	2.4282	0.1563	0.5907	0.0087	0.7371
4575	0.0059	0.2763	2.5307	0.0972	0.6595	0.0087	0.8191
4576	0.0101	0.3945	3.1156	0.1896	1.0254	0.0336	0.7085
4578	0.0065	0.2364	2.2373	0.1658	0.5944	0.0113	0.8694
4579	0.0055	0.2418	2.4438	0.1975	0.4773	0.0092	0.7790
4582	0.0053	0.2615	2.3145	0.1725	0.7787	0.0152	1.2076
4583	0.0053	0.2136	2.3358	0.1336	0.5804	0.0112	0.9421
4584	0.0046	0.4377	2.5014	0.1245	0.6749	0.0083	0.8572
4587	0.0059	0.2202	2.9459	0.1383	0.6932	0.0068	0.7216
4588	0.0050	0.2595	2.1477	0.1702	0.6493	0.0163	0.8028
N	10	10	10	10	10	10	10
MEAN	0.0060	0.2806	2.5001	0.1546	0.6724	0.0129	0.8444
S.D.	0.0015	0.0748	0.3058	0.0310	0.1477	0.0079	0.1468
S.E.	0.0005	0.0236	0.0967	0.0098	0.0467	0.0025	0.0464

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - MALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4623	0.0049	0.2446	2.6949	0.1358	0.6114	0.0113	0.8354
4625	0.0057	0.2982	2.5872	0.1724	0.5900	0.0098	0.8130
4626	0.0060	0.3147	2.4476	0.1513	0.6527	0.0093	0.8340
4627	0.0068	0.2282	2.4792	0.1163	0.5780	0.0093	0.8984
4630	0.0084	0.3399	2.4436	0.1741	0.6477	0.0156	0.8785
4632	0.0081	0.3145	2.7887	0.1405	0.6724	0.0120	1.1138
4633	0.0128	0.2988	2.5126	0.1151	0.7452	0.0226	0.7896
4634	0.0052	0.3073	2.3649	0.1520	0.6817	0.0126	1.0445
4635	0.0061	0.2886	2.9356	0.1627	0.6269	0.0223	0.9621
4636	0.0083	0.3421	2.5004	0.1772	0.7056	0.0099	0.9020
N	10	10	10	10	10	10	10
MEAN	0.0072	0.2977	2.5755	0.1497	0.6512	0.0135	0.9091
S.D.	0.0023	0.0368	0.1784	0.0227	0.0521	0.0051	0.1061
S.E.	0.0007	0.0116	0.0564	0.0072	0.0165	0.0016	0.0335

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 104-WEEK SACRIFICE - MALES  
 GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	TESTES
4672	0.0041	0.3146	2.5731	0.1434	0.6432	0.0140	1.0327
4674	0.0019	0.2266	2.2030	0.1472	0.5742	0.0071	0.7829
4675	0.0024	0.2234	1.0053	0.1014	0.6454	0.0052	0.7645
4677	0.0010	0.2237	2.5109	0.1890	0.7280	0.0099	1.0604
4678	0.0043	0.2643	2.4599	0.1709	0.6233	0.0043	0.7495
4680	0.0060	0.2393	2.3504	0.1116	0.5180	0.0049	0.8958
4681	0.0041	0.3781	3.1401	0.3405	0.8264	0.0090	1.3254
4682	0.0016	0.3717	2.6589	0.1266	0.6665	0.0062	0.7605
4684	0.0021	0.2917	2.7435	0.1655	0.7504	0.0067	0.9574
4686	0.0058	0.3377	4.0004	0.2524	1.0761	0.0108	0.9432
N	10	10	10	10	10	10	10
MEAN	0.0033	0.2871	2.5645	0.1748	0.7052	0.0078	0.9272
S.D.	0.0018	0.0608	0.7495	0.0724	0.1573	0.0031	0.1814
S.E.	0.0006	0.0192	0.2370	0.0229	0.0497	0.0010	0.0574

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 52-WEEK SACRIFICE - FEMALES  
 GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4700	0.0045	0.2886	2.1935	0.1074	0.5264	0.0177	0.0248
4703	0.0072	0.3504	2.7032	0.1765	0.7142	0.0246	0.0304
4704	0.0078	0.3577	2.1475	0.1530	0.6049	0.0206	0.0267
4712	0.0065	0.2911	2.8248	0.2037	0.6746	0.0241	0.0275
4715	0.0065	0.3304	2.7334	0.1597	0.6448	0.0228	0.0279
4718	0.0076	0.3243	2.5434	0.1457	0.5776	0.0241	0.0265
4721	0.0050	0.3000	2.5791	0.1532	0.5830	0.0200	0.0241
4724	0.0059	0.3034	2.5909	0.1409	0.5370	0.0166	0.0273
4727	0.0081	0.3474	2.3930	0.1368	0.6554	0.0225	0.0256
4730	0.0067	0.2826	2.2672	0.1472	0.5500	0.0182	0.0169
n	10	10	10	10	10	10	10
MEAN	0.0067	0.3186	2.5072	0.1525	0.6074	0.0213	0.0258
S.D.	0.0010	0.0247	0.2357	0.0252	0.0637	0.0026	0.0030
S.E.	0.0003	0.0034	0.0745	0.0040	0.0201	0.0008	0.0011

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TABLE 7 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

## 52-WEEK SACRIFICE - FEMALES

## GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4847	0.0078	0.3562	2.2053	0.1571	0.6357	0.0256	0.0295
4850	0.0079	0.3247	2.4526	0.1630	0.6534	0.0249	0.0244
4853	0.0084	0.3579	2.4334	0.2093	0.7325	0.0241	0.0225
4856	0.0090	0.3352	3.0352	0.1209	0.6493	0.0239	0.0254
4859	0.0081	0.3049	2.2825	0.1432	0.6686	0.0210	0.0296
4862	0.0119	0.3515	2.2903	0.1302	0.7496	0.0291	0.0373
4865	0.0076	0.2476	2.5024	0.1286	0.6205	0.0179	0.0245
4868	0.0071	0.2402	2.5776	0.1315	0.5469	0.0180	0.0174
4871	0.0073	0.2607	2.2712	0.1085	0.5143	0.0193	0.0261
4874	0.0116	0.3734	2.7152	0.2361	0.7006	0.0274	0.0581
N	10	10	10	10	10	10	10
MEAN	0.0087	0.3153	2.6350	0.1531	0.6471	0.0231	0.0295
S.D.	0.0017	0.0495	0.2841	0.0407	0.0743	0.0039	0.0113
S.E.	0.0005	0.0150	0.0898	0.0129	0.0235	0.0012	0.0036

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TABLE 7 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

## 52-WEEK SACRIFICE - FEMALES

## GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5003	0.0084	0.3153	2.5027	0.1512	0.6436	0.0202	0.0283
5006	0.0086	0.3187	2.6773	0.1516	0.7294	0.0228	0.0320
5015	0.0105	0.3874	3.3073	0.2698	0.8537	0.0289	0.0356
5018	0.0086	0.3409	2.5396	0.1549	0.7148	0.0267	0.0426
5022	0.0092	0.2575	2.4511	0.1351	0.5892	0.0213	0.0385
5025	0.0067	0.2268	3.0551	0.0962	0.5125	0.0232	0.0433
5039	0.0103	0.3440	3.0070	0.1755	0.6911	0.0245	0.0358
5054	0.0047	0.3486	2.6750	0.1465	0.7681	0.0260	0.0344
5060	0.0059	0.2650	2.1198	0.1421	0.4662	0.0167	0.0244
5067	0.0095	0.3940	2.4626	0.1826	0.7918	0.0287	0.0379
N	10	10	10	10	10	10	10
MEAN	0.0087	0.3199	2.8058	0.1596	0.6760	0.0239	0.0353
S.D.	0.0015	0.0553	0.4474	0.0322	0.1235	0.0039	0.0059
S.E.	0.0005	0.0175	0.1373	0.0102	0.0391	0.0012	0.0019

TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 52-WEEK SACRIFICE - FEMALES  
 GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
5150	0.0072	0.3122	2.4777	0.1530	0.7183	0.0261	0.0464
5153	0.0063	0.3132	2.6716	0.1683	0.5634	0.0251	0.0457
5156	0.0066	0.3076	2.4014	0.1431	0.8243	0.0236	0.0309
5159	0.0069	0.2810	2.4470	0.1821	0.5415	0.0179	0.0283
5162	0.0077	0.3451	3.1586	0.1571	0.7113	0.0215	0.0248
5165	0.0079	0.3138	2.7918	0.1519	0.6978	0.0223	0.0280
5168	0.0065	0.3243	2.4210	0.1722	0.8159	0.0207	0.0327
5171	0.0089	0.3050	2.7804	0.1425	0.6857	0.0184	0.0386
5174	0.0063	0.2917	2.4071	0.1530	0.5402	0.0162	0.0379
5177	0.0045	0.3304	2.7444	0.1809	0.6854	0.0219	0.0198
N	10	10	10	10	10	10	10
MEAN	0.0073	0.3184	2.6402	0.1654	0.6784	0.0214	0.0333
S.D.	0.0009	0.0244	0.2417	0.0164	0.1024	0.0032	0.0068
S.E.	0.0003	0.0077	0.0764	0.0052	0.0324	0.0010	0.0024

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TABLE 7 (Continued)

## ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

## 104-WEEK SACRIFICE - FEMALES

## GROUP 1 - CONTROL

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4497	0.0072	0.3025	3.0379	0.1939	0.8368	0.0478	0.0485
4498	0.0	0.3295	2.1574	0.1779	0.5691	0.0260	0.0
4499	0.0114	0.4739	4.0386	0.1495	1.1002	0.1554	0.0402
4500	0.0039	0.2837	2.2783	0.1063	0.4882	0.0099	0.0223
4501	0.0058	0.3619	2.5534	0.1529	0.7386	0.0330	0.0347
4502	0.0	0.2108	1.6810	0.1195	0.3962	0.0097	0.0115
4503	0.0058	0.2315	2.2298	0.0691	0.4774	0.0187	0.0263
4504	0.0044	0.2342	2.4646	0.0859	0.6513	0.0149	0.0242
4505	0.0015	0.2590	2.2960	0.0952	0.5648	0.0154	2.0772
4508	0.0108	0.2536	2.7515	0.0894	0.6479	0.0146	0.0175
N	8	10	10	10	10	10	9
MEAN	0.0063	0.2941	2.5689	0.1240	0.6470	0.0345	0.2558
S.D.	0.0034	0.0787	0.6093	0.0423	0.2054	0.0441	0.6831
S.F.	0.0012	0.0249	0.1927	0.0134	0.0649	0.0139	0.2277

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 104-WEEK SACRIFICE - FEMALES  
 GROUP 2 - LOW

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4548	0.0071	0.2765	2.8120	0.1678	0.8349	0.0362	0.1798
4549	0.0094	0.3348	2.9263	0.1328	0.8250	0.0176	0.0115
4550	0.0081	0.3776	2.7998	0.1396	0.7033	0.0148	0.0174
4551	0.0138	0.4007	3.5197	0.2163	0.9569	0.0697	0.0315
4552	0.0106	0.2955	3.6133	0.2264	1.0229	0.0366	0.0080
4553	0.0080	0.2718	2.5715	0.1277	0.6149	0.0209	0.0150
4554	0.0092	0.4651	2.9946	0.1915	0.8729	0.0312	0.0159
4556	0.0101	0.4847	3.0104	0.2244	0.7734	0.0477	0.0182
4557	0.0124	0.4159	3.1349	0.6195	0.5546	0.0277	0.0148
4558	0.0174	0.3064	2.7122	0.1465	0.7811	0.0419	0.0160
N	10	10	10	10	10	10	10
MEAN	0.0106	0.3629	3.0095	0.2192	0.7940	0.0344	0.0328
S.D.	0.0031	0.0775	0.3352	0.1458	0.1437	0.0163	0.0520
S.E.	0.0010	0.0245	0.1060	0.0461	0.0455	0.0052	0.0164

REPRODUCIBLE COPY

TABLE 7 (Continued)

ORGAN WEIGHT-BODY WEIGHT PERCENTAGES

104-WEEK SACRIFICE - FEMALES

GROUP 3 - MEDIUM

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4548	0.0062	0.2313	2.2204	0.1453	0.5702	0.0180	0.0098
4549	0.0081	0.3308	2.5612	0.1387	0.6994	0.0186	0.0216
4660	0.0101	0.2750	2.8156	0.2046	0.7683	0.0557	0.0170
4602	0.0078	0.4410	2.5197	0.1428	0.7792	0.0204	0.0115
4603	0.0089	0.2916	2.4596	0.1012	0.5900	0.0344	0.0143
4605	0.0106	0.3413	2.7809	0.1334	0.7781	0.0266	0.0194
4606	0.0091	0.3262	2.3944	0.1297	0.5724	0.0155	0.0261
4609	0.0112	0.2137	2.1173	0.1424	0.6173	0.1365	0.0259
4611	0.0065	0.4508	2.5966	0.1490	0.7477	0.2706	0.0144
4612	0.0085	0.4084	2.7458	0.1844	0.5798	0.0260	0.0196
N	10	10	10	10	10	10	10
MEAN	0.0089	0.3310	2.5211	0.1472	0.6702	0.0622	0.0180
S.D.	0.0014	0.0823	0.2322	0.0287	0.0925	0.0817	0.0056
S.E.	0.0005	0.0260	0.0734	0.0091	0.0292	0.0259	0.0018

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TABLE 7 (Continued)  
 ORGAN WEIGHT-BODY WEIGHT PERCENTAGES  
 104-WEEK SACRIFICE - FEMALES  
 GROUP 4 - HIGH

ANIMAL NUMBER	THYROID	HEART	LIVER	SPLEEN	KIDNEYS	ADRENALS	OVARIES
4647	0.0021	0.3840	2.5184	0.1625	0.5971	0.0158	0.0268
4648	0.0038	0.3549	2.7804	0.1461	0.6581	0.0168	0.0274
4650	0.0033	0.2544	2.3194	0.1398	0.5933	0.0179	0.0303
4651	0.0076	0.3439	2.9481	0.1706	0.7768	0.0357	0.0423
4652	0.0109	0.4130	3.4096	0.5705	0.9034	0.1078	0.0311
4653	0.0020	0.3922	2.7809	0.1703	0.6503	0.0123	0.0
4654	0.0045	0.3698	2.3361	0.0834	0.5555	0.0	0.0339
4655	0.0044	0.2787	2.2382	0.1169	0.5683	0.0147	0.0258
4657	0.0080	0.4524	4.6001	0.2235	1.6667	0.0361	0.0344
4658	0.0118	0.4899	3.0676	0.1437	0.7352	0.0262	0.0437
N	10	10	10	10	10	9	9
MEAN	0.0058	0.3733	2.8999	0.1927	0.7707	0.0315	0.0329
S.D.	0.0035	0.0716	0.7030	0.1377	0.3330	0.0300	0.0065
S.E.	0.0011	0.0227	0.2223	0.0435	0.1053	0.0100	0.0022

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 1 - Males

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4524			NGL
4528			Pit.-enlarged; lf. lung-dark red; thick stomach walls.
4532	Rt. kid., adrenal involved in mass.		Lungs-white spots; lf. kidney-pale; bloody fluid in scrotal sacs; red fluid in abd. cavity.
4534			NGL
4536			Lung-mottled; renal pelvis dilated; lf. kidney-red fluid, blister-like area; mes. lymph node, enlarged, dark; bladder-red fluid, distended.
4541			Brain-soft, red clot on surface; kidney-pelvis dilated.
4774			Lungs-dark red; mes. arteries-hard, tortuous.
4776			Testes, sem. ves.-atrophied; kidney-enlarged, pitted; pelvis-dilated; lungs-mottled.
4778*			Hind quarters-paralyzed; pit.-greatly enlarged, black.
4779			Brain-adhered to skull; soft, clear fluid around brain; skull-indented, rt. side; ribs, sternum-misshaped.
4780			Kidney, liver-enlarged; liver-nottled; lungs-lg. red spots; int.-dark red.
4783*			Eyes, nostrils-bloody crust; GI tract-gray mucous.
4786			Lungs-hem.; kidneys-pelvis dilated, contains red fluid; stomach-pylorus blocked by hair ball; bladder-thick blood-colored fluid with clot; sem. ves. dark red.
4791	Sm. t.m.-mesentery.		Pit.-enlarged; lungs-hem., mottled; thymus-enlarged; thoracic cavity-red fluid; liver, kidney, adrenal-enlarged; abd. cavity-red, watery fluid; testes, sem. ves.-atrophied.
4795	Lg. intestine-firm t.m.		Badly cannibalized.
4797			Rt. testicle-atrophied; nostrils, lungs-frothy discharge; liver-gran. appearance.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 1 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4798			GI tract-red mucous; lungs-bright in color.
4803			Pit.-enlarged, lt. color; lungs-lf. lobe dark spots; kidneys-pale; GI tract-yellow mucous.
4808	Sm.nodular mass-rt. pelvic region.		Lungs-dark red; liver-pale, kid.-enlarged.
4815			Thyrds-enlarged; lungs-dark red; liver-dark, enlarged; kidneys-mottled, enlarged; GI tract-red mucous; testes, sem. ves.-atrophied
4818			Pit.-enlarged, black; lungs-dark red, splotchy; rt. kidney-blister; stomach-impacted with food, hair; testes-small; mammary tissue-active.
4819			Pit.-greatly enlarged.
4820*	Mass attached rt. ear (70gm).		Spleen-greatly enlarged.
4823			Pit.-greatly enlarged; lungs-red fluid; kidneys-pale; testes, sem. ves.-atrophied; thoracic, abd. cavity-red fluid.
4824*			Pit.-greatly enlarged.
4825			Pit.-enlarged, pale; lungs-congested; thymus, liver, kidneys, spleen-extrem. lg.; renal pelvis-gone; stomach walls-thickened; GI tract-empty, hem., testes, sem. ves.-atrophied; lymph nodes-greatly enlarged; saliv. glands-greatly enlarged; all tissues, organs have greenish-yellow slim appearance.
4826*	Mass-rt. adrenal-adhered to liver/kidney.		Pit.-greatly enlarged; lungs-nodules; lf. adrenal-sm., testes, sem. ves.-small; paralysis.
4827	Lf. eye- sm. mass or abscess.		Stomach-walls thickened. mes. lymph nodes-enlarged.
4829	White mass along optic nerve.		Supra-orbital lymph node-abscessed leading into skull under brain; involving pit.; thick white pus under brain; Abscess-lung, lf. lobe-lung adhered to chest wall; abscess-rt. ventral pelvis; testes, sem. ves.-atrophied.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 1 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4832	Lg. t.m.-thoracic, lf. ventral (624gm).	Spleen-enlarged, round margins; stomach-impacted with hair, food, bedding; bladder-red fluid; rt. sem. ves.-atrophied.	
4836			Cannibalized.
4841	Hard mass-lumbar region.	Lungs-hem.; pelvis-dilated; one adrenal-enlarged.	
4843		Lungs, liver-pale; kidneys, adrenals-enlarged, gray.	
4845		Died 2/2/75	Necropsy Sheet missing

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 2 - Males

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4572	T.M.-rt. thoracic ventral (239gm).		Lungs-mottled; heart-enlarged; liver-enlarged, mottled, pale; spleen-enlarged, rounded margins; kidneys-enlarged, contain pus; pelvis-dilated; adrenals-enlarged; bladder-thick walls; sem. ves.-atrophied.
4574			Lungs-mottled.
4577*	T.M. or swelling-rt. side head.		Liver-pale; spleen-slightly enlarged.
4580			Spleen-small.
4581			Lf. hind foot-abscess.
4585			Brain-red fluid, lf. side; cervical lymphs-bright red, enlarged; lungs-hem., light areas; stomach walls-appear thick; mes.-dark, prominent; kidneys-pelvis dilated; liver-pinpoint yellow spots all lobes.
4586	Pancreas possibly involved in mass surrounding spleen.		Unclothed blood over brain; rt. lung-white nodules, adhered to diaphragm; pancreas-thickened; yellow, cloudy fluid-abd. cavity; spleen, cecum, stomach-adhered.
4591			Lung-bright red; kidneys-pale, blistered; dorsal aorta-thickened walls; prostate-abscessed.
4924			Lungs-hem.; spleen-slightly enlarged; kidneys-pitted.
4930	Lg. t.m.-head/neck.		Autolyzed.
4933	Med. size t.m.-abd. cavity, adhered to GI tract, testicular fat.		Lungs-dark red; spleen-enlarged.
4939			Pit.-greatly enlarged; lungs-mottled.
4942			Autolysis.
4943			Clear watery fluid in chest cavity; lungs-bright red; kidneys-pitted, pale, pelvis dilated; testes-atrophied.
4948			Lungs-white areas; liver-enlarged; kidneys-white area-pelvis; dark red fluid in scrotum.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 2 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4954			Thyroid-bright red; lungs-mottled, red fluid; Pyers' patches prom.; mes. lymph-dark; sal., cervical lymphs-enlarged, dark.
4956	Med. t.m.-rt. abd., ventral (60gm)		Pit.-greatly enlarged; lungs-splotchy.
4959	Sm. t.m.-head, neck, ventral (19gm).		Lungs, liver-pale; heart, spleen-enlarged; rt. ear thickened, ulcerated.
4960			Lungs-mottled; liver-mottled.
4962			NGL
4963			Rt. eye-protruding; liver, spleen, kidney-enlarged; kidney-pale; liver-rounded margins; mes. lymph node-enlarged.
4971	T.M.-lf. thoracic (38gm).		Pit.-enlarged, dark red; scrotal hernia; hermaphroditic, uterus, ovaries, penis; no testes; sem. ves.-small.
4972			Lung-congested; heart-rt. auricle dilated; kidneys-greatly enlarged, pelvis dilated, red; urine in bladder.
4975	T.M.-lf. pelvic ventral, med.(111gm).		Paralysis-hind quarters before death; kidneys-pitted; arenavals-speckled.
4982	Med. mass-mesentery (93gm); mass attached to lwr. rt. lobe-lung.		Lungs-bright colored; blood colored urine in bladder.
4984	Nodule on thoracic spinal column.		Red material on brain surface; thyroid-slightly enlarged; ung-rt. lobe dark red; liver-greatly enlarged, lobes thick, margins rounded; spleen-enlarged; kidneys-cortex wide, pitted, wide striated zone between cortex, medulla; cervical lymphs-dark red; free fluid-red in abd. cavity; adrenals-slightly enlarged.
4987			Pit.-greatly enlarged, dark; blood colored fluid in chest cavity; kidney-pelvis dilated.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 2 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4989			Lungs-congested; white object in bladder neck.
4994	T.M.-ulcerated, lf. axilla, small, (18gm).		Testes-pale; spleen-slightly thickened; liver-very pale, margins rounded; kidney-wide striated zone between medulla, cortex; brain, pit., thyroid-pale.
4995			Lung-hem.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 3 - Males

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4622			Lf. kidney-black; rt. kidney-pale; testes, sem. ves.-atrophied; external appearance-diarrhea.
4624*			Pit.-enlarged, dark; stomach-walls thickened; sem. ves.-small.
4628*	Lg. t.m.-lf. side head/neck.		Lungs-white spots; kidneys-cortex wide, pink striated zone; adrenal-1f. slightly enlarged; stomach-walls thick; animal had record of swelling of joints of rt. hind foot.
4629			Thyroid-enlarged; heart-enlarged; kidneys-enlarged, pale, pitted; adrenals-pale; testes-small.
4631			Lung-congested; kidneys-pelvis dilated; 1f. side premaxilla swollen; 1f. eye-discharge.
4637			Lung-rt. side dark red.
4639	Sm. t.m.-lf. abd. dorsal.		Red clot on brain; lungs-bright red; rt. maxillary abscess below rt. eye.
4641	Lg. t.m. (195gm) in abd. involving spleen, stomach, 1f. kidney, 1f. adrenal. Sm. t.m. (11gm) rt. head/neck.		Lungs-pale; liver-pale; spleen-slightly enlarged; red fluid in scrotal sacs.
4645	T.M.-chest, subcu. (72gm).		Heart-flaccid, slightly enlarged; liver-pale, margins rounded; spleen-enlarged; sem. ves.-slightly small.
5074	Sm. t.m. head/neck latero-ventral 1f. side.		Liver-mottled.
5083			Heart-enlarged; liver-dark.
5085			NGF
5086			Liver-enlarged; thymus-enlarged; spleen-enlarged.
5089			Lung-dark brown, white spots on surface; liver-portion dark green in color.
5098			Liver-pale, 2 dark spots central lobe; lung-mottled; brain-2 nodules under brain, possible blood clots.

TABLE 3

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 3 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
5100	Hard mass in abd. cavity.		Lung-mottled; liver-enlarged, pale; testes-blood colored fluid in scrotum.
5103			Pit.-enlarged, dark red; lung-hem.; sem. ves.-enlarged.
5104	Sm. t.m. head/neck ventral filled with watery fluid.		Liver-pale; spleen-enlarged.
5109			Pit.-enlarged, pale; lung-dark red.
5119	Med. t.m.-ventral head/neck region.		Lung-congested.
5125	Sm t.m.-rt. fore legs.		Lung-abscessed; heart-encysted.
5126	Mass-rt. median liver lobe.		Lung-hem. with some nodules; liver-black spots.
5128	N.P.		
5131			Pit.-enlarged; thyroid-enlarged; lung-mottled; kidney-enlarged.
5133*			Brain-brown areas on surface; lung-yellow areas; heart-small; spleen-small; kidney-cortex wide, slightly pitted, pelvis slightly dilated, wide striated zone between cortex, medulla. Lg. in proportion to body weight; mes. lymph node-dark red in color; testes-small, flaccid.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 4 - Males

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4673			Lungs-dark red.
4676	Possible t.m. involving lf. thyroid.		Thyroid-enlarged; lungs-dark red, splotchy; adrenals-speckled.
4679			Thymus, spleen, mes. lymph nodes, kidney-enlarged; lungs-mottled, red with yellow; pancreas-nodular, dark; thyroid-dark; liver-yellow patches; bladder-full, appears blocked; rt. kidney-yellow mat.; testicles-purple, small; heart-flaccid; brain-dark area on surface; pit.-light area on surface.
4683			Brain-dark red with clot; lungs-dark red.
4685			Autolysis.
4687*			Testes, sem. ves.-atrophied.
4688	Sm. t.m.-rt. side head (9gm).		Lungs-splotchy; adrenals-triangular shape.
4690			Submax. sal.-enlarged; spleen-enlarged; rt. kidney-white, wedged spot-cortex; adrenal-slightly enlarged.
4693			Brain-clot; lungs-congested; kidneys-blistered, enlarged; testes, sem. ves.-atrophied; both rear feet-abscessed.
4694	T.M.-rt. side head		Lung-dark, white spots; rt. kidney-misaligned; testes-atrophied.
4696			Lungs-hem.; spleen-enlarged.
5223			Lungs-congested; adrenals-enlarged; heart-dark.
5224			Cannibalized.
5229			Brain-pale; pit-enlarged; kidneys-pale; thyroid-enlarged; liver-pale, enlarged; spleen-enlarged; testes-small.
5234			Lung-mottled.
5235			Lung-mottled.
5237	GI tract-more or less a t.m.		Liver-pale, enlarged; adrenals-pale, enlarged.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUND

## Group 4 - Males (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
5246			Brain-blood clot; lung-hem.
5249	Ulcerated mass-lat. side of head		Lung-abscessed; spleen-enlarged; kidney-irregular in shape with white nodular protrusions on surface, white areas extend into medulla.
5250	Ulcerated mass-lf. side head, involving lf. eye.		Lf. lung-contains fleshy mass; rt. lung-spongy area; liver-mottled; heart-rt. auricle distorted; spleen-enlarged, urinary bladder contains red fluid.
5251	Lg, t.m.-dorsal abd.. lf. side.		Lung-pale; liver-pale; small intestine contains yellow mucous.
5256			Lung-pale, dark red areas; Pit.-enlarge dark with red spots; kidneys-enlarged.
5257*			Pit.-enlarged, indented into brain; lung-mottled; liver-mottled; spleen-small; kidney-ulcerated lesion-left.
5265			Brain-dark red; liver-dark; pit.-dark; lung-mottled, med. lobe appears greatly enlarged, red.
5268*			Pit.-enlarged; stomach-contains yellowish-white mucous.
5277			Lung-mottled; liver-enlarged; adrenals-enlarged.
5283			Lung-mottled, congested, yellow nodules, yellow material inside; kidney-renal pelvis dilated; mes. lymph node-enlarged.
5284*			Pit.-enlarged.
5285			Lung-hem., congested; liver-enlarged; kidney-pale, enlarged.
5287			Lung-dark red all lobes. pinpoint yellow areas; brain-covered with red fluid.
5288			Pit.-enlarged, dark; lung-congested.
5292			Advanced autolysis.
5295			Lung-red blotchy areas; testes-very small.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 1 - Females

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4506	Sm. mass (16g) rt. pelvic, ventral; mass involving stomach, spleen, kid., adrenals, pancreas, liver, diaphragm.		Lungs-splotchy; liver-white spots; lf. side abd. distended, coffee colored fluid in abd. cavity.
4507	Mass (6gm) lf. pelvic, ventral; mass (28gm) rt. pelvic, ventral; mass (17gm) rt. thigh, ventral.		Heart-enlarged, pale; lungs-pale, mottled; liver-pale; spleen-greatly enlarged, misshapen; pit.-dark spot.
4509*			Stomach-app. irritated; pit.-enlarged.
4514	Sm. t.m. lf. ventral pelvic.		Lungs-dark red; liver-pale; rt. eye-abscess.
4516*	T.M. rt. ventral thorax (64gm); t.m. lf. side head/neck (26gm).		Spleen-enlarged; lf. adrenal-enlarged; rt. adrenal-small.
4517	T.M. rt. ventral pelvis (411gm)		Adrenals-enlarged, speckled.
4520	T.M. on adrenal?		Pit.-enlarged; lungs-congested.
4717			Adrenals-speckled; lungs-mottled, slightly enlarged.
4722	Lg. hard mass in abd. cavity.		Pit., adrenals, spleen-enlarged; Kid.-enlarged, black, pelvis dilated.
4723			Ovaries-enlarged, fluid-filled; liver-enlarged, mottled; lungs-mottled.
4725			Lf. ovary-cystic; lungs-mottled; pit.-greatly enlarged.
4729			Wasted; pit.-enlarged, dark; adrenals-speckled.
4737	Salivaries-enlarged mass-like, dark solid.		Lungs-deep red; spleen-enlarged, dark; adrenals-enlarged.
4738	Sm. t.m.-rt. pelvic ventral.		Lungs-dark red; lf. eye-red, scarred.
4739			Pit.-greatly enlarged, black; lungs-dark red; liver-dark red with light areas.
4742	Lg. t.m. (310gm) rt. abd. ventral-ulcerated.		Lungs-mottled; liver-slight enlarged; adrenals-enlarged, speckled; green mucous in GI tract; rt. ovary-red cyst.
4744			Pit.-greatly enlarged.
4757	Sm. t.m.-lf. thoracic cavity.		Pit.-greatly enlarged; slightly enlarged mes. lymph node; lungs-hemorrhagic; congested GI tract.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 1 - Females (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4767			Pit.-greatly enlarged; adrenals-enlarged.
4769	Lg. t.m. (184gm) mammary, lf. pelvic ventral.		Active mammary tissue; lungs-congested; pit.-slightly enlarged.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 2 - Females

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4547	T.M.-rt. thorax (235gm).		Pit.-enlarged, red; lungs-pale with dark areas; liver-pale, pitted; spleen-enlarged; adrenals-enlarged, lf. speckled.
4555	Lg. mass-lwr. rt. part of body; sm. mass-upr. lf. part of body.		Pit.-enlarged, bloody filled; lung-red.
4559	T.M.-rt. ventral pelvis (306gm); t.m. head, neck, ventral (82gm).		Adrenals-appear enlarged.
4563*			Pit.-greatly enlarged.
4564	T.M.-lf. ventral pelvis (353gm).		Liver-indented by ribs; pancreas-thickened.
4568	T.M.-lf. cervical (18gm).		Lungs-orange.
4848*			Pit.-greatly enlarged; appears emaciated; diarrhea.
4852	Lg. mass (262gm)-pelvic.		Cannibalized.
4857	Lg. mass (nodular)involving heart/lungs.		Eyes-filmed; thyroid-enlarged; lf. renal pelvis-dilated; pancreas dark; mes. lymph-enlarged, dark; uterus-dark.
4858	Sm. mass-mammary, pelvic.		Pit.-enlarged, white spots; spleen clear nodule; esophagus-impacted with food, bedding; adrenals-enlarged, white spots.
4861	Lg. t.m.-head, neck,ventral, ulcerated (393gm).		Stomach-greatly distended; mes. lymph node-enlarged, black; lungs-mottled; lf. adrenal-enlarged; liver,spleen-black.
4864	Sm. mass-rt. thoracic; t.m. inguinal.		Lumbar fat-yellow; lungs-hem.; liver-dark with black spots.
4873	Lg. t.m.-rt. ventral abd. (554gm).		Decomposed.
4874			Heart-appears small; lungs-nodules on all lobes.
4881			Pit.-enlarged.
4883			Pit.-enlarged, blood filled; thyroid-grey; lungs-nodules.
4884			Brain-pale, soft; pit.-enlarged; liver-pale; spleen-enlarged; lf. adrenal-enlarged.
4889			Pit.-enlarged.
4892	Subcu. thoracic t.m. (66gm).		Lungs-mottled, nodular; rt. adrenal-enlarged.
4893	T.M.-cecum (med.).		Abd. cavity-clear fluid; spleen-enlarged; renal pelvis-dilated; adrenals-white speckles; lungs-congested.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 2 - Females (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4895			Pit.-enlarged; lungs-hem.; lf. ovary-cystic.
4899	Rt. adrenal, kidney-involved in mass.		Lungs-pale, nodular; liver-enlarged, blistered; spleen-enlarged, blistered; blood clot-like mass in lumbar fat.
4900			Pit.-enlarged, blood filled; lungs-mottled; liver-spotted; lf. adrenal-enlarged.
4901			Submax. gland-enlarged; lungs-pale, red fluid in chest cavity; lf. kidney-cystic, contains red fluid, blood clots; lf. adrenal-enlarged, adhered to kidney.
4904	T.M.-lf. side abd., med., ventral, ulcerated (78gm).		Pit.-enlarged greatly; adrenals- slightly enlarged.
4905	Sm. t.m.-ventral thorax.		Lungs-white nodules, congested; liver-lobes thickened, mottled; rt. uterine horn distended; pit., spleen-enlarged.
4908	Mammary mass-pelvic region.		Lungs-dark; lf. adrenal-enlarged.
4909			Pit.-greatly enlarged; lungs-congested; adrenals-speckled; lf. ovary-cystic.
4912	Rt. pelvic ventral-med.		Active mammary tissue; white nodule-rt. lobe of lung; lungs-mottled; lf. ovary-dark; lf. uterine horn-fluid filled; pit.-slightly enlarged.
4916	Med. t.m.-rt. abd., ventral, ulcerated (61gm).		Pit.-enlarged.
4920*	Sm. fatty nodule attached to sm. intestine.		Pit.-greatly enlarged; bloody fluid under brain; bleeding from orbital sinus; lungs-white nodules; liver-nutmeg; adrenals-dark, slightly enlarged, lf. slightly larger; red pinpoint areas-lining.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 3 - Females

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4597			Lung-black spots; possible accidental death-caught upper jaw in cage.
4601*			Pit.-greatly enlarged.
4604			Autolysis-advanced.
4610			Pit.-enlarged, dark; adrenals-enlarged, pale.
4613			Pit.-enlarged, dar red; lungs-dark red; active mammary tissue-inguinal.
4614*			Pit.-enlarged; active mammary glands.
4615			Accidental - no tissues.
4617			Pit.-enlarged, black; lungs-spotchy.
4997*			Pit.-enlarged, yellow and black areas; spleen-rough; kidneys-granular, enlarged, blistered, pale; adrenals-enlarged.
4999			Pit.-enlarged greatly; thyroid-enlarged.
5001*	Lg. t.m.-lf. side.		Heart-appears enlarged; liver-pale; spleen-pale, enlarged, margins rounded; stomach-contains red fluid; mes. lymph node-slightly enlarged.
5012			NGL
5014			Ext. vulva opening-closed; urinary bladder distended with blood colored urine; chest cavity, abd. cavity-clear red fluid; lungs-nodules; kidney-pelvis dilated; adrenals-enlarged.
5016			Pit.-greatly enlarged; liver-congested, mottled; adrenals-slightly enlarged, speckled; thickened rt. ear.
5021			Uterus-greatly distended with red fluid; mes. lymph node-dark.
5029*	T.M.-lf. pelvic, ventral (59gm).		Pit.-enlarged greatly; lungs-white nodules.
5031			Pit.-greatly enlarged; lungs-congested.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 3 - Females (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
5038	Lg. t.m.-lf. flank groin (524gm); dark objects lying near spine (sm.)		Rt. lung-mottled; liver-margins rounded, renal pelvis dilated; mes. lymph node-dark.
5042	Lg. t.m.-lf. abd. ventral (119gm).		Chest-cavity-clear red fluid; lungs-dark red; pancreas-sero-gelatinous fluid; ovary-cystic.
5043			Pit.-enlarged, black; lungs-hem; yellow mucous-GI tract.
5046			Pit.-enlarged, black spotted; lung-contains foam; aortic arch-thick, tough; kidney-pale, blistered; mes. lymph node-enlarged.
5048	Sm. t.m.-pelvic, ventral (4gm); both uterine horns-sm. masses (gravid appearance); rt. lobe liver-cyst-like mass *		Pit.-enlarged, dark; liver-grey, rt. lobe dark red.
5051	Lg. t.m. ventral rt. side, abd., (544gm).		Liver-enlarged, light pale; spleen-enlarged; kidneys-black marginal line at cortex, medullary areas; adrenals-enlarged.
5055	Pancreas-multinodular mass; liver-pale, several lobe mass; lf. ovary-mass.		Abd. cavity-filled with blood; stomach-enlarged; spleen-enlarged, pale; rt. ovary-cyst, large; kidneys-nodules; heart-nodules; lung-nodules; lf. adrenal-enlarged, dark; pit.-enlarged.
5056			Pit.-large, dark red; lungs-white splotches on surface, speckled with black spots; kidneys-pale, mottled; eyes-covered black crust.
5062	Mass-right pelvic.		Pit.-enlarged, spotted.
5063			Lung-one lobe white, other pale; liver-enlarged, mottled; kidney-pale, yellow inside; adrenals-lf. tumor; lg. intes.-nodule.
5064			Stomach-fluid filled; kidneys-pitted; liver-pale; lungs-yellow fluid; pit.-enlarged.
5070	Lg. mass-rt. pelvic.		Pit.-enlarged; liver-pale; spleen-enlarged; adrenals-enlarged.

\*sacrificed-moribund

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 4 - Females

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
4649	Dark mass on lung.		Chest cavity filled with blood.
4656	Lg. t.m. involving uterus body, cervix, vagina.		Pit.-enlarged; spleen-enlarged; stones in renal pelvis; adrenals-white speckles; bleeding from vulva.
4659			Pit.-enlarged; lungs-white spots, hem.
4660*			Pit.-enlarged; head-tilted.
4661*	Rt. pelvic ven.-t.m. (5gm); mammary mass-pelvis.		Pit.-enlarged; adrenal-enlarged, dark.
4662	Sm. mass-cervical ven. (6gm).		Pit.-enlarged; lungs-congested.
4665*	Sm. t.m.-lf. pelvic ven. (37gm).		Lungs-pale; liver-mottled; kidneys-mottled; submax. glands-enlarged.
4666			Pit.-light color; liver-mottled, margins rounded; spleen-enlarged; lf. kidney-pelvis dilated through medulla, contains yellow frothy material; adrenals-speckled; GI tract-adhesions.
4667	Sm. t.m.-ventral pelvic; t.m.-ventral, thoracic (6.5gm).		Lungs-dark splotches, brown; spleen-slightly enlarged; pit.-slightly enlarged.
4668			Pit.-enlarged; one ovary atrophied.
4669	T.M.-lf. side head (18gm).		Lungs-dark red.
4671			Pit.-enlarged; membranes-pale.
5149	Hard mass over left premaxillary.		Rt. uterus-enlarged, filled with red colored fluid.
5154			Pit.-enlarged, dark red; Adrenals-enlarged.
5157	Tissue mass ventral right side.		
5161			Cannibalized.
5163	Sm. t.m. right ventral pelvic region.		Lung-light colored; liver-pale; Adrenals-enlarged.
5169	Tissue mass left side axilla area ventral.		NGF
5173	Med. size mass abdominal cavity.		Lung-mottled; Pit.-enlarged; Spleen-enlarged.
5178	Sm. t.m. left thoracic region.		Lung-pale, abcess right lower lobe; liver-pale; spleen-enlarged; ovaries-cystic.

TABLE 8

ANIMALS FOUND DEAD OR SACRIFICED - MORIBUNDGroup 4 - Females (contd)

<u>Animal #</u>	<u>Tissue Masses</u>	<u>Gross Findings</u>	<u>Other</u>
5180			Cannibalized.
5183	Lg. t.m. left ventral cervical region. Sm. t.m. left thoracic region.		Lung-mottled; liver-pale.
5190	Lg. t.m. right abdominal region. Sm. t.m. left abdominal region. Rt. lobe of liver hard mass.		Lungs-mottled; liver-pale, enlarged, right lobe hard mass.
5192			Pit.-enlarged; lf. ovary-cystic.
5193			Pit.-enlarged; lung-congested; ovary-lf. encysted; lf. norm dark red in portions.
5198	Med. t.m.-lf. ventral pelvic region.		Liver-pale; pit.-enlarged.
5201			Liver-adhered to diaphragm, GI tract; rt. kidney-fused with liver; GI tract-fused ball-like mass; mes. lymph node-enlarged beads.
5203	Lg. t.m.-rt. ventral pelvic region (270gm).		Lungs-pale, white blotchy areas; adrenals-enlarged.
5204			Lung-congested; liver-pale; spleen-cannibalized.
5210			Adrenals-enlarged; cannibalized.
5212			Brain-pale, soft; rt. thyroid-pale, enlarged; lung-pale; liver-pale.
5216			Liver-mottled; ovaries-large, dark; thyroid-enlarged.
5218	Hard mass around rt. ovary (in capsules).		Pit.-enlarged, dark spot in center; lungs-mottled.

\*sacrificed-moribund

PATHOLOGY

## TWO-YEAR TOXICITY STUDY IN RATS

## LBI PROJECT #1400

Narrative Description

To facilitate review of microscopic findings, 4 sets of tables have been prepared on each experimental group of rats, including Male Controls, Male High Dose, Female Controls and Female High Dose groups.

The first set of tables is designated "Histological Findings" and lists abnormalities in each tissue that had been specified for microscopic examination from each rat examined. In addition, there is a listing of abnormalities found at necropsy in tissues other than those that had been specified for microscopic examination (unusual lesions).

The second set of tables is designated "Neoplasms" and gives a diagnostic classification of all neoplasms and preneoplastic alterations listed in the first set of tables.

The third set of tables is designated "Summary". The table referring to each experimental group consists of two parts, namely, "Summary - Histological Findings" and "Summary - Neoplasms". This set of tables provides information on the numbers of specific pathologic items in relation to the tissue count in the case of tissues that were specified for microscopic examination and in relation to the animal count in the case of lesions found at necropsy in tissues that had not been specified for microscopic examination. In selected instances, the tables also furnish information on the average numerical grade of lesion severity.

The fourth set of tables is designated "Incidence" and consists of two parts designated "Incidence - Non-neoplastic Abnormalities" and "Incidence - Neoplasms". The incidence of specific pathologic alterations and tumors are presented as a percentage of affected tissues or as a percentage of affected rats as appropriate.

A mortality table based on whether or not animals survived until the arbitrary date of sacrifice is also included.

There are two addenda to the tables. One is a tabulation of histological findings in animals in control and high dose groups that died from excessive heat on Day 76 of the study. The second is a tabulation of histological findings and neoplasms in animals that were examined after the main tables had been prepared. However, data in this addendum are included in summary and incidence tables.

Microscopic studies could not be reported on 10 animals because the tissues or animals were lost.

The following is a list by number and group assignment:

<u>Group 1 - Female</u> (Control)	<u>Group 4 - Male</u> (High Dose)	<u>Group 4 - Female</u> (High Dose)
4754	4679	4666
	5224	5157
	5234	5161
	5242	5180
	5245	

#### Comments on Diagnostic Terminology

- (1) Myocardial fibrosis: This designation indicates any stage of a sequence of changes beginning with necrosis of occasional individual myocardial fibers and followed by loss of the affected fiber with collapse of the fibrous stroma (apparent fibrosis) and/or proliferation of stroma (real fibrosis). A variety of descriptive designations (including focal myocarditis and focal myocardial necrosis) could be applied to appropriate stages of the process, but the single designation "myocardial fibrosis" was chosen to simplify the tabulation of lesions.
- (2) Hyaline globules in hepatic parenchymal cells: These "structures" varied in microscopic appearance from circumscribed eosinophilic cytoplasmic globules reminiscent of the eosinophilic globules described by Anderson et al.<sup>1</sup> in damaged rat livers to barely visible irregular hyaline areas that might be interpreted as collections of proteinaceous fluid within the cytoplasm of the affected hepatic cells. The degree of hepatic cell involvement was never more than slight, there was no evidence of associated hepatic cell damage, and the range of incidence (in test animals and controls) was not significant.
- (3) Increased hemosiderin - spleen: Rats with heavy deposition of hemosiderin in the splenic pulp were noticed early in the process of microscopic examination. Since all spleens had microscopically demonstrable hemosiderin in varying amounts, an evaluation of increased hemosiderin over any selected norm was entirely subjective. However, observations recorded (in the incidence tables) suggest that female rats were more prone to increased hemosiderin in the spleen than males without significant differences between test animals and controls.
- (4) Chronic inflammation - kidneys: This designation indicates the common "chronic nephritis" or "glomerulonephrosis" of rats. The term "chronic inflammation" has been specified for use in the carcinogenesis program and is used in this report in compliance with the prescribed nomenclature. The condition ranges in microscopic appearance from distention of renal corpuscles and associated tubules with proteinaceous fluid to eventual atrophy of glomeruli and tubules along with fibrosis.

<sup>1</sup>Anderson, P.J., Cohen, S. and Barka, T.: Hepatic Injury. Archives of Pathology, Vol. 71, pp. 101/89 - 107/95 (1961).

- (5) Calcinosis - kidneys: This designation refers to focal hematoxylinophilic concretions (focal mineralization) beneath the epithelium of the renal pelvis and to a lesser extent in the basement membrane of tubules in the renal medulla.
- (6) Capillary ectasia - adrenals: This term refers to foci of capillary alteration in the adrenal cortex ranging from a marked dilation of adjacent capillaries to the development of intracapillary hematoma-like accumulations of blood to which the designation hematocyst might also be applied.
- (7) Focal lipidosis - adrenals: This term refers to focal areas in the adrenal cortex containing a noticeable increase of lipid material as compared with adjacent cortex. The affected cortical cells were enlarged and the cytoplasm characteristically contained medium and large droplets of lipid material manifest in routine histologic preparations as medium and large cytoplasmic vacuoles. Developing foci of lipidosis were manifest as foci of moderate cell hypertrophy in which slight to moderate increase of lipid material was apparent.

#### Summary

The following notations are made from a non-statistical review of the tabular data.

There was a higher percentage of intercurrent deaths (natural deaths and moribund sacrifices) among male controls than male high dose animals. In the case of female animals the relationship was reversed, namely a lower percentage of intercurrent deaths among female controls than high dose females. Conclusions or impressions on survival are not warranted on these data alone and without statistical analysis.

Male rats had a higher incidence of myocardial fibrosis than females without relation to the compound tested.

Female rats had a higher incidence of increased hemosiderin in the spleen without relation to the compound tested.

Female rats had a higher incidence of increased hemopoiesis in the spleen without apparent relation to the compound tested.

Male rats had a higher incidence of chronic inflammation of the kidneys than females without relation to the compound tested.

Female rats had a higher incidence of renal calcinosis than males without relation to the compound tested.

Female rats had a higher incidence of capillary ectasia (hematocysts) in the adrenal cortex than males without relation to the compound tested.

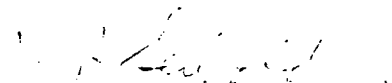
With regard to abnormalities affecting C-cells in the thyroids, the sum of C-cell hyperplasias and C-cell adenomas in each experimental group was within the same numerical and/or percentage range. Differences in the incidence of either hyperplasia or adenoma among groups of rats may thus reflect pathologic interpretation more than actual differences in the state of C-cells in the various groups.

Visual review of the tabulated data on neoplasms did not indicate any compound-related effect on the incidence or pattern of tumors among the different groups of animals.

### Conclusion

The degree and pattern of lesions and abnormalities seen in the organs of the control and test animals warrant a conclusion that they were unrelated to compound administration.

Submitted by:

  
\_\_\_\_\_  
H. R. Seibold, V.M.D.

KEY

- d = Died or was killed in extremis before termination of experiment.
- \* = Indicates presence of neoplasm (benign and/or malignant). So-called preneoplastic liver lesions are included.
- = No significant monospecific alterations were seen.
- + = Tissue alteration as specified.
- 1 = Minimal
- 2 = Slight
- 3 = Moderate
- 4 = Well marked
- 5 = Severe
- 0 = Tissue not examined.

## INCIDENCE - NON-NEOPLASTIC ABNORMALITIES

	Male		Female	
	Control	High Dose	Control	High Dose
<u>Pituitary</u>				
Abscess	2%		2%	
Cyst				2%
Massive necrosis	2%			
<u>Thyroid</u>				
C-cell hyperplasia	9%	2%	10%	6%
Follicular hyperplasia	1%			
<u>Heart</u>				
Myocardial fibrosis	20%	5%	5%	1%
Endocardial disease	1%	3%		
Bacterial endocarditis		3%		
<u>Liver</u>				
Hyaline globules	4%	6%	10%	5%
Fatty change	6%	3%	4%	2%
Passive congestion	2%	8%	1%	2%
Central necrosis	2%	5%	1%	6%
Reactive foci		1%		
Bile duct proliferation				1%
Increased hemosiderin				2%
Infarction				1%
Congenital cyst				1%
<u>Spleen</u>				
Increased hemosiderin	12%	8%	33%	35%
Increased hemopoiesis	1%	3%	9%	12%
Increased granulopoiesis				2%
Atrophy	4%	7%		
Reactive hyperplasia		4%		
Reticulosis	1%			
<u>Kidneys</u>				
Chronic inflammation	84%	78%	30%	23%
Calcinosis	1%	3%	25%	27%
Papillary necrosis	1%			
Metastatic abscesses		3%		
Suppurative pyelitis		1%	1%	2%
Interstitial nephritis				1%
<u>Adrenals</u>				
Capillary ectasia	5%	8%	64%	1%
Focal lipidosis	23%	21%	18%	20%
Cortical hemorrhage		1%		1%
Unilateral necrosis			1%	
Focal medullary hyperplasia			1%	

(continued)

INCIDENCE - NON-NEOPLASTIC ABNORMALITIES  
(Continued)

	Male		Female	
	Control	High Dose	Control	High Dose
<u>Pancreas</u>				
Focal acinar atrophy	7%	6%	4%	4%
Pancreatitis			1%	
<u>Stomach</u>				
Ulcer	3%	1%		
Chronic inflammation				1%
Mucosal atrophy	1%			
Mucosal calcification		10%	1%	
<u>Large Intestine</u>				
Nematodiasis	9%	4%	7%	2%
Impaction	2%			
Chronic colitis				2%
<u>Mesenteric Lymph Node</u>				
Hematoma	2%			
Fibrosis	2%			
Lymphadenitis		2%		
Lymphectasia			2%	
Reactive hyperplasia				3%
Increased pigmentation				5%
<u>Urinary Bladder</u>				
Urolith	2%			3%
Chronic ulcer			1%	
Cystitis	3%			3%
<u>Testes</u>				
Atrophy	11%	10%		
<u>Ovaries</u>				
Cyst			13%	15%
<u>Bone Marrow</u>				
Granulocytic hyperplasia	4%	12%		6%
Erythroid hyperplasia	3%		3%	1%
Decreased cellularity		2%		3%
Osteodystrophy	1%			
<u>Lungs</u>				
Alveolar histiocytosis	1%	3%	1%	6%
Bronchopneumonia	2%	1%		1%
Interstitial pneumonia		1%		
Murine pneumonia		1%		
Metastatic abscesses	1%			
Abscess				1%

(continued)

INCIDENCE - NON-NEOPLASTIC ABNORMALITIES  
(Continued)

	Male		Female	
	Control	High Dose	Control	High Dose
<u>Uterus</u>				
Hydrometra			1%	
Endometria polyp				2%
<u>Skeleton</u>				
Periostitis		1%		
<u>Multiple Distribution</u>				
Polyarteritis	5%	3%	1%	
Metastatic calcification	6%	4%		
Focal granulomatosis	1%			
Chronic abscesses	1%			
<u>Integument</u>				
Pyogenic granuloma	1%			
Abscess		1%		
<u>Mammary Gland</u>				
Cystic hyperplasia			1%	
Chronic mastitis			1%	
Galactocele				4%
<u>No Organ Specified</u>				
Pyemia		1%		
Chronic abscess				2%
Acute peritonitis				1%
Chronic peritonitis				1%
Fat necrosis				1%
Types of lesions	41	38	28	43

SUMMARY  
HISTOLOGICAL FINDINGS

Male - Control

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
<u>Pituitary</u>			
Neoplasms		19	51
Massive necrosis		1	51
Abscess		1	51
<u>Thyroids</u>			
Neoplasms		1	77
C-cell hyperplasia		7	77
Follicular hyperplasia		1	77
<u>Heart</u>			
Myocardial fibrosis	(2)	16	82
Endocardial disease		1	82
<u>Liver</u>			
Neoplasms		4	82
Hyaline globules	(2)	3	82
Fatty change	(3.2)	5	82
Passive congestion		2	82
Central necrosis		2	82
<u>Spleen</u>			
Increased hemosiderin		10	81
Increased hemopoiesis		1	81
Reticulosis		1	81
Atrophy		3	81
<u>Kidneys</u>			
Chronic inflammation	(3)	68	81
Calcinosis	(3)	1	81
Congenital cyst		1	81
Papillary necrosis		1	81
<u>Adrenals</u>			
Neoplasms		5	79
Capillary ectasia	(1.6)	4	79
Focal lipidosis	(1.4)	18	79
<u>Pancreas</u>			
Neoplasms		2	71
Focal acinar atrophy	(1)	5	71

(continued)

## SUMMARY

## HISTOLOGICAL FINDINGS

Male - Control (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
<u>Stomach</u>			
Ulcer		2	78
Mucosal atrophy		1	78
<u>Small Intestine</u>			
		0	75
<u>Large Intestine</u>			
Nematodiasis		5	55
Impaction		1	55
<u>Mesenteric Lymph Node</u>			
Hematoma		1	53
Fibrosis		1	53
<u>Urinary Bladder</u>			
Urolith		1	61
Cystitis	(3)	2	61
<u>Testes</u>			
Neoplasms		5	80
Atrophy		9	80
<u>Bone Marrow</u>			
Granulocytic hyperplasia		3	77
Erythroid hyperplasia		2	77
Osteodystrophy		1	77
		Incidence	Animal Count
<u>Lungs</u>			
Neoplasms		2	83
Alveolar histiocytosis		1	83
Bronchopneumonia		2	83
Metastatic abscesses		1	83
<u>Integument</u>			
Neoplasms		1	83
Pyogenic granuloma		1	83
<u>Multiple Distribution</u>			
Polyarteritis		4	83
Metastatic calcification		5	83
Focal granulomatosis		1	83
Chronic abscesses		1	83

(continued)

SUMMARY  
HISTOLOGICAL FINDINGS  
Male - Control (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Animal Count
<u>Mammary Gland</u> Neoplasms		1	83
<u>No Organ Specified</u> Neoplasms		6	83
<u>Soft Tissue</u> Neoplasms		3	83
<u>Parathyroid</u> Neoplasms		2	83

SUMMARY  
HISTOLOGICAL FINDINGS

Male - High Dose

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
<u>Pituitary</u>			
Neoplasms		9	36
<u>Thyroids</u>			
Neoplasms		5	66
C-cell hyperplasia		1	66
<u>Heart</u>			
Myocardial fibrosis	(1.5)	4	76
Endocardial disease		2	76
Bacterial endocarditis		2	76
<u>Liver</u>			
Neoplasms		5	77
Hyaline globules	(1.8)	5	77
Fatty change	(3.5)	2	77
Passive congestion		6	77
Central necrosis		4	77
Reactive foci		1	77
<u>Spleen</u>			
Increased hemosiderin		6	76
Increased hemopoiesis		2	76
Atrophy		5	76
Reactive hyperplasia		3	76
<u>Kidneys</u>			
Chronic inflammation	(2.7)	59	76
Calcinosis	(2)	2	76
Metastatic abscesses		2	76
Suppurative pyelitis		1	76
<u>Adrenals</u>			
Neoplasms		5	73
Capillary ectasia	(1.5)	6	73
Focal lipidosis	(1.3)	15	73
Cortical hemorrhage		1	73
Focal medullary hyperplasia		1	73
<u>Pancreas</u>			
Focal acinar atrophy	(1.8)	4	70
<u>Stomach</u>			
Neoplasms		1	74
Mucosal calcification		1	74
Ulcer		1	74

(continued)

## HISTOLOGICAL FINDINGS

Male - High Dose (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
<u>Small Intestine</u>		0	72
<u>Large Intestine</u>			
Nematodiosis		2	47
<u>Mesenteric Lymph Node</u>			
Lymphadenitis		1	52
<u>Urinary Bladder</u>		0	57
<u>Testes</u>			
Neoplasms		9	73
Atrophy		7	73
<u>Bone Marrow</u>			
Granulocytic hyperplasia		8	66
Decreased cellularity		1	66
		Incidence	Animal Count
<u>Lung</u>			
Tumors		1	77
Alveolar histiocytosis		2	77
Interstitial pneumonia		1	77
Murine pneumonia		1	77
Bronchopneumonia		1	77
<u>Integument</u>			
Neoplasms		3	77
Abscess		1	77
<u>Multiple Distribution</u>			
Polyarteritis		2	77
Metastatic calcification		3	77
<u>Skeleton</u>			
Periostitis		1	77
<u>No Organ Specified</u>			
Neoplasms		4	77
Pyemia		1	77
<u>Soft Tissue</u>			
Neoplasms		3	77
<u>Salivary Gland</u>			
Neoplasms		1	77
<u>Parathyroid</u>			
Neoplasms		1	77

SUMMARY  
HISTOLOGICAL FINDINGS  
Female - Control

	Average Numerical Grade of Lesion Severity	Incidence	Tissue Count
<u>Pituitary</u>			
Neoplasms		37	62
Abscess		1	62
<u>Thyroids</u>			
Neoplasms		1	67
C-cell hyperplasia		7	67
<u>Heart</u>			
Myocardial fibrosis	(1.5)	4	73
<u>Liver</u>			
Neoplasms		8	72
Hyaline globules	(2)	7	72
Fatty change	(3)	3	72
Passive congestion		1	72
Central necrosis		1	72
<u>Spleen</u>			
Increased hemosiderin		23	70
Increased hemopoiesis		6	70
<u>Kidneys</u>			
Chronic inflammation	(1.8)	22	73
Calcinosis	(1.6)	18	73
Suppurative pyelitis		1	73
<u>Adrenals</u>			
Neoplasms		1	73
Capillary ectasia	(2.7)	47	73
Focal lipidosis	(2)	13	73
Unilateral necrosis		1	73
<u>Pancreas</u>			
Neoplasms		1	69
Focal acinar atrophy	(1)	3	69
Pancreatitis		1	69
<u>Stomach</u>			
Mucosal calcification		1	71

(continued)

SUMMARY  
HISTOLOGICAL FINDINGS  
Female - Control (Continued)

	Average Numer- ical Grade of Lesion Severity	Incidence	Tissue Count
<u>Small Intestine</u>		0	68
<u>Large Intestine</u>			
Nematodiasis		4	58
<u>Mesenteric Lymph Node</u>			
Lymphectasia		1	43
<u>Urinary Bladder</u>			
Chronic ulcer		1	68
<u>Ovaries</u>			
Neoplasms		1	70
Cyst/s		9	70
<u>Bone Marrow</u>			
Erythroid hyperplasia		2	67
<u>Lung</u>			
Alveolar histiocytosis		1	73
		Incidence	Animal Count
<u>Mammary Gland</u>			
Neoplasms		25	73
Cystic hyperplasia		1	73
Chronic mastitis		1	73
<u>Uterus</u>			
Neoplasms		1	73
Hydrometra		1	73
<u>Multiple Distribution</u>			
Polyarteritis		1	73
<u>Integument</u>			
Neoplasm		2	73
<u>No Organ Specified</u>			
Neoplasm		6	73

SUMMARY  
HISTOLOGICAL FINDINGS

Female - High Dose

	Average Numer- ical Grade of Lesion Severity	Incidence	Tissue Count
<u>Pituitary</u>			
Neoplasms		37	65
Cyst		1	65
<u>Thyroids</u>			
Neoplasms		4	68
C-cell hyperplasia		4	68
<u>Heart</u>			
Myocardial fibrosis	(2)	1	81
<u>Liver</u>			
Preneoplastic alterations		3	81
Neoplasms		2	81
Hyaline globules	(2)	4	81
Fatty change	(4)	2	81
Passive congestion		2	81
Central necrosis		5	81
Bile duct proliferation	(2)	1	81
Increased hemosiderin		2	81
Infarction		1	81
Congenital cyst		1	81
<u>Spleen</u>			
Increased hemosiderin		28	81
Increased hemopoiesis		10	81
Increased granulopoiesis		2	81
<u>Kidneys</u>			
Chronic inflammation	(1.5)	19	82
Calcinosis	(2.1)	22	82
Suppurative pyelitis		2	82
Interstitial nephritis		1	82
Congenital cyst		2	82
<u>Adrenals</u>			
Capillary ectasia	(2.7)	49	80
Focal lipidosis	(2)	16	80
Cortical hemorrhage		1	80
<u>Pancreas</u>			
Focal acinar atrophy	(1.7)	3	73

(continued)

## SUMMARY

## HISTOLOGICAL FINDINGS

Female - High Dose (Continued)

	Average Numer- ical Grade of Lesion Severity	Incidence	Tissue Count
<u>Stomach</u>			
Neoplasms		1	78
Chronic inflammation		1	78
<u>Small Intestine</u>			
		0	73
<u>Large Intestine</u>			
Nematodiasis		1	57
Chronic colitis		1	57
<u>Mesenteric Lymph Node</u>			
Reactive hyperplasia		1	37
Increased pigmentation		2	37
<u>Urinary Bladder</u>			
Cystitis	(3)	2	70
Urolith		2	70
<u>Ovaries</u>			
Cysts		11	73
<u>Bone Marrow</u>			
Erythroid hyperplasia		1	70
Granulocytic hyperplasia		4	70
Decreased cellularity		2	70
		Incidence	Animal Count
<u>Lung</u>			
Alveolar histiocytosis		5	82
Bronchopneumonia		1	82
Abscess		1	82
<u>Mammary Gland</u>			
Neoplasms		31	82
Galactocele		3	82
<u>Uterus</u>			
Neoplasms		3	82
Endometrial polyp		2	82
<u>Thymus</u>			
Neoplasms		1	82

(continued)

## SUMMARY

## HISTOLOGICAL FINDINGS

Female - High Dose (Continued)

	Average Numerical Grade of Lesion Severity	Incidence	Animal Count
<u>No Organ Specified</u>			
Neoplasms		4	82
Chronic abscess		2	82
Acute peritonitis		1	82
Chronic peritonitis		1	82
Fat necrosis		1	82
<u>Integument</u>			
Neoplasms		2	82
<u>Soft Tissue</u>			
Neoplasms		1	82

## SUMMARY

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## NEOPLASMS

## Male - Control

	<u>Benign Tumors</u>		<u>Malignant Tumors</u>	
	Incidence	Tissue Count	Incidence	Tissue Count
<u>Pituitary</u>				
Adenoma	19	51		
<u>Thyroids</u>				
C-cell adenoma	1	77		
<u>Liver - Preneoplastic Alterations</u>				
Basophilic focus	1	82		
Eosinophilic focus	1	82		
Clear cell focus	1	82		
<u>Liver - Neoplasms</u>				
Hepatocellular carcinoma			1	82
<u>Adrenals</u>				
Cortical adenoma	1	79		
Pheochromocytoma	3	79		
Cortical carcinoma			1	79
<u>Pancreas</u>				
Islet cell adenoma	2	71		
<u>Testes</u>				
Interstitial cell tumor	5	80		
	Incidence	Animal Count	Incidence	Animal Count
<u>Mammary Gland</u>				
Adenocarcinoma			1	83
<u>Lung</u>				
Alveolar/bronchiolar adenoma	2	83		
<u>No Organ Specified</u>				
Malignant lymphoma			1	83
Multiple plasmacytoma			1	83
Myeloid leukemia			1	83
Carcinoma			1	83
Adenocarcinoma			1	83
Synovial sarcoma			1	83
<u>Soft Tissue</u>				
Fibroma	3	83		
<u>Integument</u>				
Squamous cell carcinoma			1	83
<u>Parathyroid</u>				
Adenoma	2	83		
<u>Total</u>	38		10	
(Less Preneoplastic Alterations)				

Comment: A total of 41/83 animals had one or more tumors.

SUMMARY  
NEOPLASMS  
Male - High Dose

	<u>Benign Tumors</u>		<u>Malignant Tumors</u>	
	Incidence	Tissue Count	Incidence	Tissue Count
<u>Pituitary</u>				
Adenoma	9	36		
<u>Thyroids</u>				
C-cell adenoma	5	66		
<u>Liver - Preneoplastic Alterations</u>				
Clear cell focus	1	77		
<u>Liver - Neoplasms</u>				
Neoplastic nodules	3	77		
Hepatocellular carcinoma			1	77
<u>Adrenals</u>				
Pheochromocytoma	5	73		
<u>Stomach</u>				
Squamous papilloma	1	74		
<u>Testes</u>				
Interstitial cell tumor	9	73		
	Incidence	Animal Count	Incidence	Animal Count
<u>Salivary Gland</u>				
Mixed tumor	1	77		
<u>Lung</u>				
Alveolar/bronchiolar adenoma	1	77		
<u>No Organ Specified</u>				
Sarcoma			2	77
Lymphosarcoma			1	77
Carcinoma			1	77
<u>Soft Tissue</u>				
Fibroma	3	77		
<u>Integument</u>				
Squamous cell carcinoma			3	77
<u>Parathyroid</u>				
Adenoma	1	77		
<u>Total</u>	38		8	
(Less Preneoplastic Alterations)				

Comment: A total of 38/77 animals had one or more tumors.

SUMMARY  
NEOPLASMS  
Female - Control

	<u>Benign Tumors</u>		<u>Malignant Tumors</u>	
	Incidence	Tissue Count	Incidence	Tissue Count
<u>Pituitary</u>				
Adenoma	34	62		
<u>Thyroids</u>				
C-cell adenoma	1	67		
<u>Liver - Preneoplastic Alterations</u>				
Clear cell focus	1	72		
Basophilic focus	5	72		
<u>Liver - Neoplasms</u>				
Neoplastic nodule	1	72		
Hepatocellular carcinoma			1	72
<u>Adrenals</u>				
Cortical adenoma	1	73		
<u>Pancreas</u>				
Islet cell adenoma	1	69		
<u>Ovaries</u>				
Sarcoma			1	70
	Incidence	Animal Count	Incidence	Animal Count
<u>Integument</u>				
Basal cell carcinoma			1	73
Fibrosarcoma			1	73
<u>Mammary Gland</u>				
Fibroadenoma	20	73		
Adenocarcinoma			6	73
<u>Uterus</u>				
Leiomyoma	1	73		
<u>No Organ Specified</u>				
Sarcoma			2	73
Lymphosarcoma			1	73
Reticulum cell sarcoma			1	73
Malignant lymphoma			1	73
Myeloid leukemia			1	73
Total	<u>59</u>		<u>16</u>	

Comment: A total of 52/73 animals had one or more tumors.

## SUMMARY

## NEOPLASMS

Female - High Dose

	<u>Benign Tumors</u>		<u>Malignant Tumors</u>	
	Incidence	Tissue Count	Incidence	Tissue Count
<u>Pituitary</u>				
Adenoma	37	65		
<u>Thyroid</u>				
C-cell adenoma	4	68		
<u>Liver - Preneoplastic Alterations</u>				
Basophilic foci	3	81		
<u>Liver - Neoplasms</u>				
Neoplastic nodule	1	81		
Carcinoma			1	81
<u>Stomach</u>				
Squamous cell carcinoma			1	78
	Incidence	Animal Count	Incidence	Animal Count
<u>Integument</u>				
Fibroma	1	82		
Squamous cell carcinoma			1	82
<u>Uterus</u>				
Leiomyosarcoma			1	82
Adenocarcinoma			1	82
Carcinoma			1	82
<u>Mammary Gland</u>				
Adenoma	3	82		
Fibroadenoma	23	82		
Adenocarcinoma			7	82
<u>Thymus</u>				
Thymoma	1	82		
<u>No Organ Specified</u>				
Sarcoma			1	82
Myelosarcoma			1	82
Malignant lymphoma			1	82
Adenocarcinoma			2	82
<u>Soft Tissue</u>				
Sarcoma			1	82
<u>Total</u>				
(Less Preneoplastic Alterations)	70		19	

Comment: A total of 61/82 animals had one or more tumors.

## PROJECT #1400

## MORTALITY

	Heat Deaths	52 Week Sacrifice	Natural Death and Moribund Sacrifice	Working Number	Terminal Sacrifice
Male Control	6	10	34 (41%)	84	50 (59%)
Male High Dose	8	10	33 (40%)	82	49 (64%)
Female Control	17	10	20 (77%)	73	53 (73%)
Female High Dose	4	10	33 (38%)	86	53 (62%)

ADDENDUM TO TABLES

LBI PROJECT #1400

Histological Findings

Heat Deaths

Group No.	1 - Male - Control				4 - Male - High Dose							
Animal No.	4805	4812	4813	4816	4838	4840	5240	5241	5243	5244	5247	5248
<u>Pituitary</u>	0	-	0	-	-	0	-	0	0	-	0	0
<u>Thyroids</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Heart</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Liver</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Spleen</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Kidneys</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Calcinosis</u>												
<u>Adrenals</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Pancreas</u>	-	0	-	0	-	-	-	-	-	-	-	-
<u>Stomach</u>	-	-	-	-	-	-	-	0	-	-	-	-
<u>Small Intestine</u>	-	-	-	-	-	-	-	-	0	-	-	-
<u>Large Intestine</u>	-	-	-	0	-	-	-	-	-	-	-	-
<u>Mesenteric Lymph Node</u>	-	-	-	-	-	-	-	-	-	0	-	-
<u>Urinary Bladder</u>	-	-	0	0	-	-	-	-	0	-	-	-
<u>Ovaries/Testes</u>	-	-	-	-	-	-	-	-	-	-	-	-
<u>Bone Marrow</u>	-	-	-	-	-	-	-	-	-	-	-	-

(continued)

ADDENDUM TO TABLES

LBI PROJECT #1400

Histological Findings

Heat Deaths  
(continued)

Group No.	1 - Female - Control										4 - Female - High Dose									
	4697	4698	4699	4705	4706	4707	4751	4752	4753	4755	4756	4759	4762	4763	4766	4768	5184	5186	5187	5188
<u>Pituitary</u>	0	0	-	-	0	-	-	-	0	0	-	-	0	-	0	-	-	-	-	0
<u>Thyroids</u>	-	-	-	-	0	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Heart</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Liver</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Spleen</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Kidneys</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Calcinosis</u>	-	-	-	-	-	-	-	-	3	-	-	-	-	-	-	-	-	-	-	-
<u>Adrenals</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Pancreas</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Stomach</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Small Intestine</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Large Intestine</u>	-	-	-	-	0	-	0	-	-	-	-	-	-	-	-	0	-	-	-	-
<u>Mesenteric Lymph Node</u>	0	-	-	0	0	0	0	-	-	-	0	-	-	-	-	0	-	-	-	-
<u>Urinary Bladder</u>	-	0	-	-	0	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-
<u>Ovaries/Testes</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Bone Marrow</u>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

ADDENDUM TO TABLES

LBI PROJECT # 1400

Histological Findings and Neoplasms

Group No.	1 - Male Control	4 - Male High Dose	1 - Female Control	4 - Female High Dose
Animal No.	4524 4536 4779 4845	4257 5283	4/25	4659 5216
<u>Tissue Findings</u>				
<u>Pituitary Neoplasms (adenoma)</u>	0	*	+	0
<u>Thyroids</u>	0	-	-	-
<u>Heart</u>	-	-	-	-
<u>Liver</u>	-	-	-	-
<u>Fatty change</u>	-	3	3	-
<u>Passive congestion</u>	-	+	-	-
<u>Central necrosis</u>	-	1	-	-
<u>Spleen</u>	-	-	-	-
<u>Increased hemosiderin</u>	-	-	+	+
<u>Atrophy</u>	+	-	-	-
<u>Kidneys</u>	-	-	-	-
<u>Chronic inflammation</u>	-	1	-	-
<u>Adrenals</u>	-	-	-	-
<u>Capillary ectasia</u>	1	-	-	-
<u>Cortical hemorrhage</u>	-	-	-	+
<u>Pancreas</u>	0	0	-	-
<u>Stomach</u>	-	-	-	-
<u>Ulcer</u>	-	-	-	-
		+		

(continued)

APPENDUM TO TABLES

LBI PROJECT # 1400

Histological Findings and Neoplasms (Continued)

Group No.	1 - Male Control	4 - Male High Dose	1 - Female Control	4 - Female High Dose
Animal No.	4524 4536 4779 4845	4257 5283	4725	4659 5216
<u>Tissue Findings</u>				
<u>Small Intestine</u>	0	-	-	-
<u>Large Intestine</u>	-	-	-	-
<u>Mesenteric Lymph Node</u>	-	0	-	0
<u>Urinary Bladder</u>	0	0	-	0
<u>Cystitis</u>	3	-	-	0
<u>Testes</u>	-	-	-	N/A
<u>Atrophy</u>	-	+	-	N/A
<u>Ovaries</u>	N/A	N/A	N/A	N/A
<u>Cyst</u>	N/A	N/A	N/A	N/A
<u>Bone Marrow</u>	-	-	-	-
<u>Granulocytic hyperplasia</u>	-	-	-	-
<u>Osteodystrophy</u>	+	-	+	-
<u>Lungs</u>	-	-	-	-
<u>Bronchopneumonia</u>	-	+	-	-
<u>Multiple Distribution</u>	-	-	-	-
<u>Metastatic calcification</u>	+	-	-	-
<u>No Organ Specified</u>	-	-	-	-
<u>Neoplasm (malignant Lymphoma)</u>	-	-	-	*

## INCIDENCE - NEOPLASMS

	Male		Female	
	Control	High Dose	Control	High Dose
<u>Pituitary</u>				
Chromophobe adenoma	37%	25%	55%	57%
<u>Thyroids</u>				
C-cell adenoma	1%	8%	1%	6%
<u>Thymus</u>				
Thymoma	0	0	0	1%
<u>Parathyroid</u>				
Adenoma	3%	2%	0	0
<u>Liver - Preneoplastic Alterations</u>				
Basophilic focus	1%	0	7%	4%
Eosinophilic focus	1%	0	0	0
Clear cell focus	1%	1%	1%	0
<u>Liver</u>				
Neoplastic nodule	0	4%	1%	1%
Hepatocellular carcinoma	1%	1%	1%	0
Carcinoma	0	0	0	1%
<u>Adrenals</u>				
Cortical adenoma	1%	0	1%	0
Cortical carcinoma	1%	0	0	0
Pheochromocytoma	4%	7%	0	0
<u>Stomach</u>				
Squamous papilloma	0	1%	0	0
Squamous cell carcinoma	0	0	0	1%
<u>Pancreas</u>				
Islet cell adenoma	3%	0	1%	0
<u>Testes</u>				
Interstitial cell tumor	6%	12%	NA	NA
<u>Ovaries</u>				
Sarcoma	NA	NA	1%	0
<u>Salivary Gland</u>				
Mixed tumor	0	1%	0	0
<u>Mammary Gland</u>				
Adenoma	0	0	0	4%
Fibroadenoma	0	0	27%	28%
Adenocarcinoma	1%	0	8%	9%
<u>Lung</u>				
Alveolar/bronchiolar adenoma	2%	1%	0	0

(continued)

INCIDENCE - NEOPLASMS  
(continued)

	Male		Female	
	Control	High Dose	Control	High Dose
<u>Integument</u>				
Squamous cell carcinoma	1%	4%	0	1%
Basal cell carcinoma	0	0	1%	0
Fibrosarcoma	0	0	1%	0
Fibroma	0	0	0	1%
<u>Soft Tissue</u>				
Fibroma	4%	4%	0	0
Sarcoma	0	0	0	1%
<u>Uterus</u>				
Leiomyoma	NA	NA	1%	0
Leiomyosarcoma	NA	NA	0	1%
Adenocarcinoma	NA	NA	0	1%
Carcinoma	NA	NA	0	1%
<u>No Organ Specified</u>				
Sarcoma	0	3%	3%	1%
Lymphosarcoma	0	1%	1%	0
Reticulum cell sarcoma	0	0	1%	0
Myelosarcoma	0	0	0	1%
Synovial cell sarcoma	1%	0	0	0
Malignant lymphoma	1%	0	1%	1%
Myeloid leukemia	1%	0	1%	0
Multiple plasmacytoma	1%	0	0	0
Carcinoma	1%	1%	0	0
Adenocarcinoma	1%	0	0	2%

## SUMMARY OF INCIDENCE

Rats with one or more tumors	49%	49%	71%	74%
Tumors benign	79%	83%	79%	79%
Tumors malignant	21%	17%	21%	21%
Rats with one or more mammary tumors	1%		33%	38%
Mammary tumors benign	0%		77%	79%
Mammary tumors malignant	100%		23%	21%
Rats with malignant mammary tumors	1%		8%	9%
Number of rats with two types mammary tumor			2	2
Rats with mammary tumors having two types of tumor			8%	6%
Types of tumors	18	14	17	19
Benign tumors + rats	46%	49%	80%	85%
Malignant tumors + rats	12%	10%	22%	23%
Total tumors + rats	58%	60%	103%	109%

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	I - Male - Control																			
Animal No.	4522	4523	4525	4526	4527	4528	4529	4530	4531	4532	4533	4534	4535	4537	4538	4539	4540	4541	4542	4543
Tissue Findings																				
Pituitary	0	-	0	-	0	+	-	0	-	0	0	0	0	0	0	0	0	0	0	0
Neoplasms																				
Massive Necrosis																				
Abscess																				
Thyroids																				
Neoplasms																				
C-cell hyperplasia	+																			
Follicular hyperplasia																				
Heart																				
Myocardial fibrosis	-	1	-	-	-	-	-	-	-	-	-	-	-	-	2	1	-	-	-	-
Endocardial disease																				
Liver																				
Neoplasms	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hyaline globules																				
Fatty change																				
Passive congestion																				
Central necrosis																				
Spleen																				
Increased hemost- derin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-
Increased hemopoiesis																				
Reticulosis																				
Atrophy																				

TWO-YEAR TOXICITY STUDY IN RATS

LEI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4522	4523	4525	4526	4527	4528	4529	4530	4531	4532	4533	4534	4535	4537	4538	4539	4540	4541	4542	4543	
<u>Tissue Findings</u>																					
<u>Kidneys</u>																					
Chronic inflammation	0	3	2	4	2	2	4	4	3	5	3	3	1	4	3	3	1	2	3	3	3
Calcinosis										3											
Congenital cyst																					
Papillary necrosis																					
<u>Adrenals</u>																					
Neoplasms																					
Capillary ectasia	2			2			1														2
Focal lipidosis																					
<u>Pancreas</u>																					
Neoplasms																					
Focal acinar atrophy										1	1	1	1	0	0	0	0	0	0	1	1
<u>Stomach</u>																					
Ulcer																					
Mucosal atrophy																					
<u>Small Intestine</u>																					
Impaction																					
<u>Large Intestine</u>																					
Neumatiasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Impaction																					
<u>Resenteric Lymph Nodes</u>																					
Hematomas																					
Fibrosis																					

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
	4522	4523	4525	4526	4527	4528 <sup>d</sup>	4529	4530	4531	4532 <sup>d</sup>	4533	4534 <sup>d</sup>	4535	4537	4538	4539	4540	4541 <sup>d</sup>	4542	4543
Tissue Findings																				
Urinary Bladder	0	-	-	-	-	-	-	-	-	-	0	0	-	-	-	-	-	-	-	-
Urolith	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cystitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Testes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Atrophy	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-
Granulocytic hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Erythroid hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lungs																				
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Alveolar histiocytosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bronchopneumonia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Metastatic abscesses	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Integument																				
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pyogenic granuloma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Multiple Distribution	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polyarteritis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Metastatic calcification	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Focal granulomatosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic abscesses	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TWO-YEAR TOXICITY STUDY IN RATS  
 LBI PROJECT #1400  
 Histological Findings

Group No.	1 - Male - Control (Continued)																			
Animal No.	4522	4523	4525	4526	4527	4528	4529	4530	4531	4532	4533	4534	4535	4537	4538	4539	4540	4541	4542	4543

Tissue Findings

- Mammary Gland
- Neoplasms
- No Organ Specified
- Neoplasms
- Soft Tissue
- Neoplasms
- Parathyroid
- Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological findings

Group No. Animal No.	1 - Male - Control (Continued)																			
	4544	4545	4546	4773	4774	4776	4777	4778	4780	4782	4783	4785	4786	4788	4791	4792	4794	4795	4797	4798
Tissue Findings	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pituitary Neoplasms	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Massive necrosis	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abscess	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thyroids	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neoplasms	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C-cell hyperplasia	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Follicular hyperplasia	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Heart	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Myocardial fibrosis	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Endocardial disease	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Liver	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neoplasms	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hyaline globules	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fatty change	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Passive congestion	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Central necrosis	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Increased hemosiderin	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Increased hemipotesis	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reticulosis	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Atrophy	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

TWO-YEAR TOXICITY STUDY IN RATS

UBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
	4544	4545	4546	4773	4774	4776	4777	4778	4780	4782	4783	4785	4786	4788	4791	4792	4794	4795	4797	4798
Tissue Findings																				
Kidneys																				
Chronic inflammation	3	3	3	3	4	5	1	2	2	2	2	1	4	1	1	3	-	0	-	4
Calcinosis																				
Congenital cyst																				
Papillary necrosis																				
Adrenals																				
Neoplasms																				
Capillary ectasia	1	-	-	-	-	-	2	1	2	1	1	1	1	1	1	1	-	-	-	-
Focal lipidosis	-	-	-	-	-	0	-	0	-	-	-	0	-	-	-	-	-	-	-	-
Pancreas																				
Neoplasms																				
Focal acinar atrophy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	-	-
Stomach																				
Ulcer																				
Mucosal atrophy																				
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-
Large Intestine	0	0	-	0	-	-	0	-	-	0	-	-	-	-	-	-	-	-	0	-
Neumatoliasis																				
Impaction																				
Meenteric Lymph Nodes	0	-	0	-	-	1	0	-	-	0	-	-	-	-	-	-	-	-	0	0
Hematomata																				
Fibrosis																				



TWO-YEAR TOXICITY STUDY IN RATS

LRI PROJECT #14(M)

Histological Findings

Group No. I - Male - Control (Continued)

Animal No. 4544 4545 4546 4773 4774 4776 4777 4778 4780 4782 4783 4785 4786 4788 4791 4792 4794 4795 4797 4798

Tissue Findings

Mammary Gland

Neoplasms

No. Organ Specified

Neoplasms

Soft Tissue

Neoplasms

Parathyroid

Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
	4800	4801	4803 <sup>d</sup>	4804	4806	4807	4808 <sup>d</sup>	4809	4810	4811	4814	4815 <sup>d</sup>	4817	4818 <sup>d</sup>	4819 <sup>d</sup>	4820 <sup>d</sup>	4821	4822	4823 <sup>d</sup>	4824 <sup>d</sup>
Tissue Findings																				
Pituitary	0	-	+	-	0	-	*	-	*	*	-	*	-	*	*	0	-	-	*	*
Neoplasms																				
Massive necrosis																				
Abscess																				
Thyroids																				
Neoplasms																				
C-cell hyperplasia	+																			
Follicular hyperplasia																				
Heart																				
Myocardial fibrosis	2	-	-	-	3	-	2	-	-	-	-	2	-	-	-	-	-	-	-	3
Endocardial disease																				
Liver																				
Neoplasms																				
Hyaline globules																				
Fatty change	4																			
Passive congestion																				
Central necrosis																				
Spleen																				
Increased hemosiderin	-	+	+	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-	+	+
Increased hemopoiesis																				
Reticulosis																				
Atrophy																				

120-MONTH TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																				
Animal No.	4800	4801	4803	4804	4806	4807	4808	4809	4810	4811	4814	4815	4817	4818	4819	4820	4821	4822	4823	4824	
Tissue Findings																					
Kidneys																					
Chronic inflammation	4	4	4	3	2	-	4	4	1	3	2	5	4	3	4	-	3	4	3	2	-
Calcinosis																					
Congenital cyst																					
Papillary necrosis																					
Adrenals	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																					
Capillary ectasia																					
Focal lipodosis			1						2											1	
Pancreas																					
Neoplasms																					
Focal acinar atrophy																					
Stomach																					
Ulcer																					
Mucosal atrophy																					
Small intestine																					
Large intestine	0	0	-	-	-	0	0	0	-	-	-	-	0	-	-	-	-	-	-	0	-
Neutrophils																					
Impaction																					
Mesenteric Lymph Nodes	0	-	-	-	-	-	-	-	-	0	-	-	0	0	0	-	-	-	-	-	-
Hematomas																					
Fibrosis																					

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Male - Control (Continued)																			
	4800	4801	4803 <sup>d</sup>	4804	4806	4807	4808 <sup>d</sup>	4809	4810	4811	4814	4815 <sup>d</sup>	4817	4818 <sup>d</sup>	4819 <sup>d</sup>	4820 <sup>d</sup>	4821	4822	4823 <sup>d</sup>	4824 <sup>d</sup>
Tissue Findings																				
Urinary Bladder	0	-	-	0	0	-	-	-	-	0	-	-	-	-	-	-	-	-	-	0
Urolith																				
Cystitis																				
Testes																				
Neoplasms																				
Atrophy																				
Bone Marrow																				
Granulocytic hyperplasia																				
Erythroid hyperplasia																				
Lung																				
Neoplasms																				
Alveolar histiocytosis																				
Bronchopneumonia																				
Metastatic abscesses																				
Integument																				
Neoplasms																				
Pyogenic granuloma																				
Multiple Distribution																				
Polyarteritis																				
Metastatic calcification																				
Focal granulomatosis																				
Chronic abscesses																				

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	Animal No.	1 - Male - Contro: (Continued)
	4900 4801 4803 <sup>d</sup> 4804 4806 4807 4808 <sup>d</sup> 4809 4810 4811 4814 4815 <sup>d</sup> 4817 4818 <sup>d</sup> 4819 <sup>d</sup> 4820 <sup>d</sup> 4821 4822 4823 <sup>d</sup> 4824 <sup>d</sup>	

Tissue Findings

Mammary Gland  
Neoplasms

No Organ Specified  
Neoplasms

Soft Tissue  
Neoplasms

Parathyroid  
Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	I - Male - Control (Continued)																		
	4825 <sup>d</sup>	4826 <sup>d</sup>	4827 <sup>d</sup>	4828 <sup>d</sup>	4829 <sup>d</sup>	4830	4831	4832 <sup>d</sup>	4833	4834	4835	4836 <sup>d</sup>	4837	4839	4841 <sup>d</sup>	4842	4843 <sup>d</sup>	4844	4846
Tissue Findings	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pituitary	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neoplasms	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Massive necrosis	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abscess	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thyroids	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neoplasms	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C-cell hyperplasia	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Follicular hyperplasia	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Liver	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Myocardial fibrosis	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Endocardial disease	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Liver	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Neoplasms	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hyaline globules	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fatty change	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Passive congestion	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Central necrosis	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Increased hemosiderin	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Increased hemopoiesis	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reticulosis	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Atrophy	-	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	I - Male - Control (Continued)																		
Animal No.	4825 <sup>d</sup>	4826 <sup>d</sup>	4827 <sup>b</sup>	4828	4829 <sup>d</sup>	4830	4831	4832 <sup>d</sup>	4833	4834	4835	4836 <sup>d</sup>	4837	4839	4841 <sup>d</sup>	4842	4843 <sup>d</sup>	4844	4846
<u>Kidneys</u>	-	2	3	4	4	0	-	3	3	3	1	-	3	3	2	2	5	3	3
Chronic inflammation	-																		
Calcinosis	-																		
Congenital cyst	-								†										
Papillary necrosis	-																		
<u>Adrenals</u>	-																		
Neoplasms	-																		
Capillary ectasia	-									3				2					1
Focal lipidosis	-																		
<u>Pancreas</u>	-																		
Neoplasms	-																		
Focal acinar atrophy	-																		
<u>Stomach</u>	-																		
Ulcer	-																		
Mucosal atrophy	-																		
<u>Small Intestine</u>	-																		
Large Intestine	-																		
Neumatodiasis	†																		
Impaction	-																		
<u>Periarteric Lymph Nodes</u>	-																		
Neumatoma	-																		
Fibrosis	-																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	I - Male - Control (Continued)																		
	4825 <sup>d</sup>	4826 <sup>d</sup>	4827 <sup>d</sup>	4828	4829 <sup>d</sup>	4830	4831	4832 <sup>d</sup>	4833	4834	4835	4836 <sup>d</sup>	4837	4839	4841 <sup>d</sup>	4842	4843 <sup>d</sup>	4844	4846
Urinary Bladder	0	-	-	-	0	-	-	0	-	0	0	0	-	-	0	-	0	-	0
Urolith																			
Cystitis																			
Testes																			
Neoplasms																			
Atrophy	+																		
Bone Marrow																			
Granulocytic hyperplasia																			
Erythroid hyperplasia																			
Lungs																			
Neoplasms																			
Alveolar histiocytosis																			
Brucnopneumonia																			
Metastatic abscesses																			
Intestines																			
Neoplasms																			
Pyogenic granuloma																			
Multiple Distribution																			
Polyarteritis																			
Metastatic calcification																			
Liver																			
Focal granulomatosis																			
Chronic abscesses																			

## TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

## Histological Findings

Group No.	1 - Male - Control (Continued)																		
Animal No.	4825 <sup>d</sup>	4826 <sup>d</sup>	4827 <sup>d</sup>	4828	4829 <sup>d</sup>	4830	4831	4832 <sup>d</sup>	4833	4834	4835	4836 <sup>d</sup>	4837	4839	4841 <sup>d</sup>	4842	4843 <sup>d</sup>	4844	4846

## Tissue Findings

Mammary Gland

Neoplasms

No Organ Specified

Neoplasms

Soft Tissue

Neoplasms

Parathyroid

Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LOI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose																									
Animal No.	4672	4673	4674	4675	4677	4678	4680	4681	4682	4683	4684	4685	4686	4687	4688	4689	4690	4691	4692	4693	4694	4695	4696	5223	5226	
Tissue Findings																										
Pituitary Neoplasms	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thyroids Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
C-cell hyperplasia				2																						
Heart Myocardial fibrosis				1								1														
Endocardial disease																										
Bacterial endocarditis																										
Liver Neoplasms																										
lyaline globules																										
Fatty change																										
Passive congestion																										
Central necrosis																										
Reactive foci																										
Spleen																										
Increased hemosiderin																										
Increased hemopoiesis																										
Atrophy																										
Reactive hyperplasia																										





TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																								
Animal No.	4672	4673 <sup>d</sup>	4674	4675	4677	4678	4680	4681	4682	4683 <sup>d</sup>	4684	4685 <sup>d</sup>	4686	4687 <sup>d</sup>	4688 <sup>d</sup>	4689	4690 <sup>d</sup>	4691	4692	4693 <sup>d</sup>	4694 <sup>d</sup>	4695	4696 <sup>d</sup>	5223 <sup>d</sup>	5226

Tissue Findings

- Skeleton
- Periostitis
- No Organ Specified
- Neoplasms
- Pyemia
- Parathyroid
- Neoplasms
- Soft Tissue
- Neoplasms
- Salivary Gland
- Neoplasms

+



180-YEAR TOXICITY STUDY IN RATS

LOI PROJECT #1400

Histological Findings

Group No.	4 - Male - High Dose (Continued)																									
	5227	5229	5230	5232	5233	5235	5236	5237	5238	5239	5246	5249	5250	5251	5253	5254	5255	5259	5260	5261	5262	5263	5265	5266	5268	
Organ Findings																										
Kidneys																										
Chronic inflammation	3	2	3	1	3	3	3	4	3	3	3	0	1	2	3	1	3	4	4	4	3	1	3	1	3	
Calcinosi																										
Metastatic abscesses																										
Suppurative pyelitis																										
Adrenals																										
Neoplasms																										
Capillary ectasia																										
Focal lipodyst																										
Focal hemorrhage																										
Focal medullary hyperplasia																										
Pancreas																										
Focal atrophy																										
Stomach																										
Neoplasms																										
Mucosal calcification																										
Small Intestine																										
Large Intestine																										
Benign nodules																										
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Benign nodules																										

TWO-YEAR TOXICITY STUDY IN RATS

(BI PROJECT #140)

Histological Findings

Group No. 4 - Male - High Dose (Continued)

Animal No.	5227	5229 <sup>d</sup>	5230	5232	5233	5235 <sup>d</sup>	5236	5237 <sup>d</sup>	5238	5239	5246 <sup>d</sup>	5249 <sup>d</sup>	5250 <sup>d</sup>	5253	5254	5255	5259	5260	5261	5262	5263	5265 <sup>d</sup>	5266	5268 <sup>d</sup>	
Tissue Findings	0	-	0	-	-	-	-	-	0	0	-	0	-	-	-	-	0	0	0	0	-	-	0	-	
Urinary Bladder																									
Testes	*					*	*																		
Neoplasms																									
Atrophy	+																								
Bone Marrow																									
granulocytic hyper-																									
plasia																									
decreased cellularity																									
Yung																									
Neoplasms																									
Alveolar histio-																									
cytosis																									
Interstitial pneumonia																									
Hoine pneumonia																									
Integument																									
Neoplasms																									
Abscess																									
Multiple Distribution																									
Polyarteritis																									
Metastatic calcifi-																									
cation																									

TWO-YEAR TOXICITY STUDY IN RATS  
 LBI PROJECT #1400  
 Histological Findings

Group No. 4 - Male - High Dose (Continued)  
 Animal No. 5227 5229 5230 5232 5233 5235 5236 5237 5238 5239 5246 5249 5250 5251 5253 5254 5255 5259 5260 5261 5262 5263 5265 5266 5268

Tissue Findings

Skeleton

Periostitis

No Organ Specified

Neoplasms

Pyemia

Soft Tissue

Neoplasms

Salivary Gland

Neoplasms

Parathyroid

Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

101 PROJECT #1400

Histological Findings

Group No. 4 - Male - High Dose (Continued)

Animal No. 5269 5271 5272 5273 5274 5275 5276 5277 5278 5279 5280 5281 5284 5285 5286 5287 5289 5290 5291 5292 5293 5294 5295 5296

Tissue Findings	5269	5271	5272	5273	5274	5275	5276	5277	5278	5279	5280	5281	5284	5285	5286	5287	5289	5290	5291	5292	5293	5294	5295	5296
Pituitary	-	0	-	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thyroids	-	0	-	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis	-	-	-	-	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Endocardial disease	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bacterial endocarditis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dysplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hyaline globules	-	-	-	-	-	1	-	-	-	-	-	2	-	-	-	-	-	-	-	-	-	-	-	3
Fatty change	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Passive congestion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Central necrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Reactive foci	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemopoiesis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Atrophy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Reactive hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-





TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No. 4 - Male - High Dose (Continued)

Animal No. 5269 5271 5272 5273 5274 5275 5276 5277<sup>d</sup> 5278 5279 5280 5281 5284<sup>d</sup> 5285<sup>d</sup> 5286 5287<sup>d</sup> 5288<sup>d</sup> 5289 5290 5291 5292<sup>d</sup> 5293 5294 5295<sup>d</sup> 5296

Tissue Findings

- No Organ Specified
- Hepatocellular Neoplasms
- Pyromia
- Soft Tissue Neoplasms
- Salivary Gland Neoplasms
- Parathyroid Neoplasms



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																		
	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506 <sup>d</sup>	4507 <sup>d</sup>	4508	4509 <sup>d</sup>	4510	4511	4512	4513	4514 <sup>d</sup>	
<u>Tissue Findings</u>																			
<u>Adrenals</u>																			
<u>Neoplasms</u>																			
Capillary ectasia																			
Focal lipiodosis																			
Unilateral necrosis																			
<u>Pancreas</u>																			
Neoplasms																			
Focal acinar atrophy																			
Pancreatitis																			
<u>Stomach</u>																			
Mucosal calcification																			
<u>Small Intestine</u>																			
Large Intestine																			
Neumatodiasis																			
<u>Mesenteric Lymph Node</u>																			
Lymphoectasia																			
<u>Urinary Bladder</u>																			
Chronic ulcer																			
<u>Ovaries</u>																			
Neoplasms																			
Cysts																			
<u>Bone Marrow</u>																			
Erythroid hyperplasia																			

**TWO-YEAR TOXICITY STUDY IN RATS**

LRI PROJECT #1400

**Histological Findings**

		1 - females - Control (Continued)																	
Group No.	Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506 <sup>d</sup>	4507 <sup>d</sup>	4508	4509	4510	4511	4512	4513	4514 <sup>d</sup>
<b>Tissue Findings</b>																			
<u>Lung</u>																			
Alveolar histiocytosis																			
<u>Mammary Gland</u>																			
Neoplasms																			
Cystic hyperplasia																			
Chronic mastitis																			
<u>Uterus</u>																			
Neoplasms																			
Hydrometra																			
<u>Multiple Distribution</u>																			
Polyarteritis																			
<u>Integument</u>																			
Neoplasms																			
<u>No Organ Specified</u>																			
Neoplasms																			

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																			
	4515	4516 <sup>d</sup>	4517 <sup>d</sup>	4518	4519	4520 <sup>d</sup>	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717 <sup>d</sup>	4719		
Tissue Findings	-	0	+	+	+	+	-	-	0	+	-	0	0	0	0	-	-	-	-	
<u>Pituitary</u>																				
Neoplasms																				
Abscess																				
<u>Thyroids</u>																				
Neoplasms																				
C-cell hyperplasia																				
<u>Heart</u>																				
Myocardial fibrosis																				
<u>Liver</u>																				
Neoplasms																				
Hyaline globules																				
Fatty change																				
Passive congestion																				
Central necrosis																				
<u>Spleen</u>																				
Increased hemosiderin																				
Increased hemopoiesis																				
<u>Kidneys</u>																				
Chronic inflammation																				
Calcinosis																				
Suppurative pyelitis																				



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4515	4516 <sup>d</sup>	4517 <sup>d</sup>	4518	4519	4520 <sup>d</sup>	4521	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717 <sup>d</sup>	4719
<u>Tissue Findings</u>	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-
<u>Ovaries</u>																		
Neoplasms																		
Cysts				+					+									
<u>Bone Marrow</u>																		
Erythroid hyperplasia																		
<u>Lung</u>																		
Alveolar histiocytosis																		
<u>Mammary Gland</u>																		
Neoplasms	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Cystic hyperplasia																		
Chronic mastitis																		
<u>Uterus</u>																		
Neoplasms																		
Hydronephra																		
<u>Multiple Distribution</u>																		
Polyarteritis																		
<u>Integument</u>																		
Neoplasms																		
<u>No Organ Specified</u>																		
Neoplasms																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4720	4722 <sup>d</sup>	4723 <sup>d</sup>	4726	4728	4729 <sup>d</sup>	4731	4732	4733	4734	4735	4736	4737 <sup>d</sup>	4738 <sup>d</sup>	4739 <sup>d</sup>	4740	4741	4742 <sup>d</sup>
<u>Pituitary</u>																		
Neoplasms	*	*	-	0	*	*	-	-	*	0	-	-	-	*	-	0	0	-
Abscess																		
<u>Thyroids</u>																		
Neoplasms	-	-	0	-	-	-	-	-	-	*	-	-	-	-	-	-	0	-
C-cell hyperplasia																		
<u>Heart</u>																		
Myocardial fibrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Liver</u>																		
Neoplasms	-	-	-	-	-	-	-	*	*									0
Lipaline globules									2									
Fatty change																		
Passive congestion																		
Central necrosis																		
<u>Spleen</u>																		
Increased hemostatin																		
Increased hemopoiesis	+	-	-	-	-	-	+	-	+	-	-	-	+	-	-	-	-	+
<u>Kidneys</u>																		
Chronic inflammation																		
Calcinosis																		
Suppurative pyelitis	2	-	-	2	-	-	-	-	2	1	-	-	-	2	-	1	2	

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4720	4722 <sup>d</sup>	4723 <sup>d</sup>	4726	4728	4729 <sup>d</sup>	4731	4732	4733	4734	4735	4736	4737 <sup>d</sup>	4738 <sup>d</sup>	4739 <sup>d</sup>	4740	4741	4742 <sup>d</sup>
Tissue Findings																		
Adrenals	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																		
Capillary ectasia				4	1	3	3	4	1	4	3	2	1	1	1	3	4	
Focal lipidosis															1	2	2	
Unilateral necrosis																		
Pancreas	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Neoplasms																		
Focal acinar atrophy							1											
Pancreatitis																		
Stomach																		
Mucosal calcification																		
Small Intestine	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Large Intestine	0	0	-	-	-	-	-	-	-	-	-	0	-	0	-	-	-	-
Nematodiasis																		
Mesenteric Lymph Node	0	0	-	0	-	0	-	0	-	-	0	-	0	-	0	-	0	-
Lymphoecytosis																		
Urinary Bladder																		
Chronic ulcer	+	-	-	0	-	0	-	-	-	0	-	-	-	-	-	-	-	0
Ovaries																		
Neoplasms	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Cysts	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
Animal No.	4743	4744	4745	4746	4747	4748	4749	4750	4757	4758	4760	4761	4764	4765	4766	4769	4770	4771

Tissue Findings

Pituitary	-	+	+	+	+	-	-	-	+	-	-	-	-	+	+	+	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abscess	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroids	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C-cell hyperplasia	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-
Heart	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hyaline globules	1	-	-	-	3	-	-	-	-	1	-	-	-	-	-	-	1	-
Fatty change	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	-
Passive congestion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Central necrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemopoiesis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Kidneys	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic inflammation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Calcinosis	3	3	2	-	2	1	1	-	3	1	-	-	-	-	-	2	1	1
Suppurative pyelitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	1 - Females - Control (Continued)																	
	4743	4744 <sup>d</sup>	4745	4746	4747	4748	4749	4750	4757 <sup>d</sup>	4758	4760	4761	4764	4765	4767 <sup>d</sup>	4769 <sup>d</sup>	4770	4771
Tissue Findings																		
<u>Adrenals</u>																		
Neoplasms																		
Capillary ectasia	1		3		2	3	3	3	3	3	3	3	3	3		5	3	
focal lipoidosis										2				1				
Unilateral necrosis																		
<u>Pancreas</u>																		
Neoplasms																		
Focal atinar atrophy																		
Pancreatitis																		
<u>Stomach</u>																		
Mucosal calcification									0									†
<u>Small Intestine</u>																		
Large Intestine																		
Nematodiasis					0					0		0	0					
<u>Mesenteric Lymph Node</u>																		
Lymphoectasia	0		0	0			0		0		0							0
<u>Urinary Bladder</u>																		
Chronic ulcer																		
<u>Ovaries</u>																		
Neoplasms																		
Cysts																		

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No. I - Females - Control (Continued)

Animal No. 4743 4744<sup>d</sup> 4745 4746 4747 4748 4749 4750 4757<sup>d</sup> 4758 4760 4761 4764 4765 4767<sup>d</sup> 4769<sup>d</sup> 4770 4771

Tissue Findings

Bone Marrow  
 Erythroid hyperplasia  
 Lung  
 Alveolar histiocytosis +  
 Mammary Gland  
 Neoplasms \* \* \* \* \*  
 Cystic hyperplasia \*  
 Chronic mastitis +  
 Uterus  
 Neoplasms +  
 Hydrometra  
 Multiple Distribution  
 Polyarteritis  
 Integument  
 Neoplasms  
 No Organ Specified  
 Neoplasms

180-MONTH TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose																			
	4647	4648	4649 <sup>d</sup>	4650	4651	4652	4653	4654	4655	4656 <sup>d</sup>	4657	4658	4660 <sup>d</sup>	4661 <sup>d</sup>	4662 <sup>d</sup>	4663	4664	4665 <sup>d</sup>	4667 <sup>d</sup>	4668 <sup>d</sup>
Tissue Findings																				
Pituitary	0	+	+	0	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasms																				
Cyst																				
Thyroids																				
Neoplasms																				
C-cell hyperplasia																				
Heart																				
Myocardial fibrosis																				
Liver																				
Neoplasms																				
Elyaline globules																				
Fatty change																				
Passive congestion																				
Central necrosis																				
Bile duct proliferation																				
Increased hemosiderin																				
Infection																				
Conventional cyst																				
Spleen																				
Increased hemosiderin																				
Increased hemopoiesis																				
Increased granulopoiesis																				

180-MONTH TOXICITY STUDY IN RATS

LEI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	4647	4648	4649 <sup>d</sup>	4650	4651	4652	4653	4654	4655	4656 <sup>d</sup>	4657	4658	4660 <sup>d</sup>	4661 <sup>d</sup>	4662 <sup>d</sup>	4663	4664	4665 <sup>d</sup>	4667 <sup>d</sup>	4668 <sup>d</sup>
Tissue Findings																				
<b>Kidneys</b>																				
Chronic inflammation																				
Calcinosis																				
Suppurative pyelitis																				
Interstitial nephritis																				
Congenital cyst																				
<b>Adrenals</b>																				
Capillary ectasia																				
Focal lipidosis																				
<b>Pancreas</b>																				
Focal atinar atrophy																				
<b>Stomach</b>																				
Neoplasms																				
Chronic inflammation																				
<b>Small Intestine</b>																				
Large Intestine																				
Neumatodiasis																				
Chronic Colitis																				
<b>Mesenteric Lymph Node</b>																				
Reactive hyperplasia																				
Increased pigmentation																				

180-MONTH TOXICITY STUDY IN RATS

LN1 PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
	4647	4648	4649 <sup>d</sup>	4650	4651	4652	4653	4654	4655	4656 <sup>d</sup>	4657	4658	4660 <sup>d</sup>	4661 <sup>d</sup>	4662 <sup>d</sup>	4663	4664	4665 <sup>d</sup>	4667 <sup>d</sup>	4668 <sup>d</sup>
Tissue Findings	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cystitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Droplet	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovaries	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cyst/s	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Erythroid hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Granulocytic hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased cellularity	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lung	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Alveolar histiocytosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bronchiopneumonia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Abscess	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Galactocele	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Endometrial polyp	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

180-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

4 - Female - High Dose (Continued)

Group No.	Animal No.	4647	4648	4649	4650	4651	4652	4653	4654	4655	4656	4657	4658	4660	4661	4662	4663	4664	4665	4667	4668

Tissue Findings

- Thymus
- Neoplasms
- No Organ Specified
- Neoplasms
- Chronic abscess
- Acute peritonitis
- Chronic hepatitis
- Fat necrosis
- Integument
- Neoplasms
- Soft Tissue
- Neoplasms

140-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

		4 - Female - High Dose (Continued)																		
Group No.	Animal No.	4669 <sup>d</sup>	4670	5147	5148	5149 <sup>d</sup>	5151	5152	5154 <sup>d</sup>	5155	5158	5160	5163 <sup>d</sup>	5164	5166	5167	5169 <sup>d</sup>	5170	5172	5173 <sup>d</sup>
<b>Tissue Findings</b>																				
Pituitary	-	-	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-
Neoplasms	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cyst	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroids	-	-	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C-cell hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-
Myocardial fibrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hyaline globules	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fatty change	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Passive congestion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Central necrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bile duct proliferation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Infarction	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Congenital cyst	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemopoiesis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased granulopoiesis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.		4 - Female - High Dose (Continued)																			
Animal No.		4669 <sup>d</sup>	4670	4671 <sup>d</sup>	5147	5148	5149 <sup>d</sup>	5151	5152	5154 <sup>d</sup>	5155	5158	5160	5163 <sup>d</sup>	5164	5166	5167	5169 <sup>d</sup>	5170	5172	5173 <sup>d</sup>
Tissue Findings																					
<u>Kidneys</u>																					
Chronic inflammation	1										1				1						
Calcinosis			2												2				2	2	
Suppurative pyelitis			3																		
Interstitial nephritis																					+
Congenital cyst																					
<u>Adrenals</u>																					
Capillary ectasia	1	3	2		2	2	4	2					5				1				5
Focal lipidosis																					
<u>Pancreas</u>																					
Focal acinar atrophy	0	1						2		0			0								
<u>Stomach</u>																					
Neoplasms																					
Chronic inflammation																					
<u>Small Intestine</u>																					
Large Intestine																					
Nematodiasis		0		0				0		0									0		0
Chronic colitis																					
<u>Mesenteric Lymph Node</u>																					
Reactive hyperplasia	0			0						0										0	0
Increased pigmentation																					
<u>Urinary Bladder</u>																					
Cystitis																					
Urolith																					



## TWO-YEAR TOXICITY STUDY IN RATS

L81 PROJECT #1400

## Histological Findings

Group No. 4 - Female - High Dose (Continued)

Animal No.	4667	4670	4671 <sup>d</sup>	5147	5148	5149 <sup>d</sup>	5151	5152	5154 <sup>d</sup>	5155	5158	5160	5163 <sup>d</sup>	5164	5166	5167	5169 <sup>d</sup>	5170	5172	5173 <sup>d</sup>
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## Tissue Findings

Integument  
Neoplasms  
Soft Tissue  
Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

		4 - Female - High Dose (Continued)																				
Group No.	Animal No.	5175	5176	5178 <sup>d</sup>	5179	5181	5182	5183 <sup>d</sup>	5185	5189	5190 <sup>d</sup>	5191	5192 <sup>d</sup>	5193 <sup>d</sup>	5194	5195	5196	5197	5198 <sup>d</sup>	5199	5200	
Tissue Findings																						
Pituitary		-	*	-	*	0	-	0	0	0	0	*	*	*	-	-	*	-	-	*	-	*
Neoplasms																						
Cyst																						
Thyroids		-	-	-	-	-	-	-	0	-	-	-	-	-	-	*	-	-	-	-	-	-
Neoplasms																						
C-cell hyperplasia																						
Heart		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myocardial fibrosis																						
Liver		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasms																						
Hyaline globules																						
Fatty change																						
Passive congestion																						
Central necrosis																						
Bile duct proliferation																						
Increased hemosiderin																						
Infarction																						
Congenital cyst																						
Spleen		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased hemosiderin																						
Increased hemopoiesis																						
Increased granulopolesis																						



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	5175	5176	5178 <sup>d</sup>	5179	5181	5182	5183 <sup>d</sup>	5185	5189	5190 <sup>d</sup>	5191	5192 <sup>d</sup>	5193 <sup>d</sup>	5194	5195	5196	5197	5198 <sup>d</sup>	5199	5200
<b>Tissue Findings</b>																				
Urinary Bladder	-	0	-	-	-	0	-	-	-	0	-	-	-	-	-	-	-	0	0	-
Cystitis	-																			
Urolith	-																			
Ovaries	-	-	-	-	-	-	-	-	-	0	-	+	-	-	-	-	-	0	-	-
Cyst/s	-																			
Bone Marrow	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Erythroid hyperplasia																				
Granulocytic hyperplasia																				
Decreased cellularity																				
<b>Lung</b>																				
Alveolar histiocytosis																				
Bronchopneumonia																				
Abscess																				
<b>Primary Gland</b>																				
Neoplasms										*	*	*	*	*	*	*	*	*	*	*
Galactocele																				
<b>Uterus</b>																				
Neoplasms	*																			
Endometrial polyp																				
<b>Thyroid</b>																				
Neoplasms																				

180-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No. 4 - Female - High Dose (Continued)

Animal No.	5175	5176	5178 <sup>d</sup>	5179	5181	5182	5183 <sup>d</sup>	5185	5189	5190 <sup>d</sup>	5191	5192 <sup>d</sup>	5193 <sup>d</sup>	5194	5195	5196	5197	5198 <sup>d</sup>	5199	5200
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Tissue Findings

- No Organ Specified
- Neoplasms
- Chronic abscess
- Acute peritonitis
- Chronic peritonitis
- Fat necrosis
- Integument
- Neoplasms
- Soft Tissue
- Neoplasms

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

Histological Findings

Group No.	4 - Female - High Dose (Continued)																				
	5201 <sup>d</sup>	5202	5203 <sup>d</sup>	5204 <sup>d</sup>	5205	5206	5207	5208	5209	5210 <sup>d</sup>	5211	5212 <sup>d</sup>	5213	5214	5215	5216 <sup>d</sup>	5218 <sup>d</sup>	5219	5220	5221	
Tissue Findings																					
Pituitary neoplasms Cyst	-	*	-	-	*	-	*	*	-	0	*	-	0	-	0	*	-	*	-	*	-
Thyroids neoplasms C-cell hyperplasia	-	0	0	-	*	-	-	0	-	0	-	0	*	-	0	0	0	-	-	-	-
Heart Myocardial fibrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver Neoplasms Hyaline globules Fatty change Passive congestion Central necrosis Bile duct proliferation Increased hemosiderin Infarction Congenital cyst	*														*						
	+										+										3
																					2
Spleen Increased hemosiderin Increased hemopoiesis Increased granulopoiesis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TWO-YEAR TOXICITY STUDY IN RATS

LB1 PROJECT #1400

Histological Findings

4 - Female - High Dose (Continued)

Group No.	4 - Female - High Dose (Continued)																			
Animal No.	5201	5202	5203	5204	5205	5206	5207	5208	5209	5210	5211	5212	5213	5214	5215	5217	5218	5219	5220	5221
Kidneys	-	-	-	-	2	2	-	1	-	3	1	-	-	2	-	2	1	2	-	-
Chronic inflammation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Calcinosis	-	-	-	-	2	2	-	1	-	3	1	-	-	2	-	2	1	2	-	-
Suppurative pyelitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Interstitial nephritis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Congenital cyst	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Adrenals	-	2	5	1	2	2	-	2	3	3	3	4	2	2	0	1	-	4	3	3
Capillary ectasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
focal lipidosis	-	-	-	-	2	2	-	2	3	3	3	4	2	1	0	1	-	4	3	3
Pancreas	-	-	-	0	-	-	-	-	-	-	0	-	-	-	-	-	-	-	-	-
focal acinar atrophy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach	-	-	-	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Neoplasias	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic inflammation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Small Intestine	-	-	-	0	-	-	-	0	0	-	0	-	-	-	-	-	-	-	-	-
Large Intestine	-	0	-	-	0	-	-	0	0	-	0	0	0	0	-	-	-	0	0	-
Neumatodiasis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chronic colitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesenteric Lymph Node	-	-	-	0	0	-	-	0	0	0	-	0	0	0	0	0	0	0	0	-
Reactive hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
increased pigmentation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-







## TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	I - Male - Control (Continued)																			
Animal No.	4522	4523	4525	4526	4527	4528 <sup>d</sup>	4529	4530	4531	4532 <sup>d</sup>	4533 <sup>d</sup>	4535	4537	4538	4539	4540	4541 <sup>d</sup>	4542	4543	4544

## Tissue Findings

No Organ Specified  
 Multiple plasmacytoma  
 Myeloid leukemia  
 Carcinoma  
 Adenocarcinoma  
 Synovial sarcoma  
 Soft Tissue  
 fibroma  
 Integument  
 Squamous cell carcinoma  
 Parathyroid  
 Adenoma



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No. 1 - Male - Control (Continued)

Animal No. 4545 4546 4773 4774 4776 4777 4778 4780 4782 4783 4785 4786 4788 4791 4792 4794 4795 4796 4797 4798 4800

Tissue Findings

Lung Alveolar bronchiolar adenoma †

No Organ Specified †

Multiple plasmacytoma †

Myeloid leukemia †

Carcinoma †

Adenocarcinoma †

Synovial sarcoma †

Soft Tissue †

Fibroma †

Integument †

Squamous cell carcinoma †

Parathyroid †

Adenoma †

TWO-YEAR TOXICITY STUDY IN RATS

LB1 PROJECT #1400

NEOPLASMS

Group No. I - Male - Control (Continued)

Animal No. 4825<sup>d</sup> 4826<sup>d</sup> 4827<sup>d</sup> 4828 4829<sup>d</sup> 4830 4831 4832<sup>d</sup> 4833 4834 4835 4836<sup>d</sup> 4837 4839 4841<sup>d</sup> 4842 4843<sup>d</sup> 4844 4846

Tissue Findings

Pituitary Adenoma

Thyroids C-cell adenoma

Liver - Preneoplastic Alterations

Basophilic focus  
Eosinophilic focus  
Clear cell focus

Liver - Neoplasms  
Hepatocellular carcinoma

Adrenals

Cortical adenoma  
Pheochromocytoma  
Cortical carcinoma

Pancreas Islet cell adenoma

Testes

Interstitial cell tumor

Mammary Gland

Adenocarcinoma

TWO-YEAR TOXICITY STUDY IN RATS

L81 PROJECT #1400

NEOPLASMS

Group No. 1 - Male - Control (Continued)

Animal No. 4825<sup>d</sup> 4826<sup>d</sup> 4827<sup>d</sup> 4828 4829<sup>d</sup> 4830 4831 4832<sup>d</sup> 4833 4834 4835 4836<sup>d</sup> 4837 4839 4841<sup>d</sup> 4842 4843<sup>d</sup> 4844 4846

Tissue Findings

Lung  
Alveolar bronchiolar adenoma

No Organ Specified  
Multiple plasmacytoma  
Myeloid leukemia  
Carcinoma  
Adenocarcinoma  
Synovial sarcoma

Soft Tissue  
Fibroma

Integument  
Squamous cell carcinoma

Parathyroid  
Adenoma

+

+

+

+

+

+

180-YEAR TOXICITY STUDY IN RATS

LB1 PROJECT #1400

NEOPLASMS

Group No.	1 - Male - Control (Continued)																		
Anima; No.	4801	4803 <sup>d</sup>	4804	4806	4807	4808 <sup>d</sup>	4809	4810	4811	4814	4815 <sup>d</sup>	4817	4818 <sup>d</sup>	4819 <sup>d</sup>	4820 <sup>d</sup>	4821	4822	4823 <sup>d</sup>	4824 <sup>d</sup>
Tissue Findings		+			+			+	+		+		+				+		+
Pituitary Adenoma																			
Thyroids C-cell adenoma																			
Liver - Preneoplastic Alterations																			
Basophilic focus																			
Eosinophilic focus																			
Clear cell focus																			
Liver - Neoplasms																			
Hepatocellular carcinoma																			
Adrenals																			
Cortical adenoma																			
Pheochromocytoma																			
Cortical carcinoma																			
Pancreas																			
Islet cell adenoma																			
Testes																			
Interstitial cell tumor																			
Mammary Gland																			
Adenocarcinoma																			

TWO-YEAR TOXICITY STUDY IN RATS  
LBI PROJECT #1400

NEOPLASMS

Group No. 1 - Male - Control (Continued)  
Animal No. 4801 4803 4804 4806 4807 4808 4809 4810 4811 4814 4815 4817 4818 4819 4820 4821 4822 4823 4824

Tissue Findings

Lung  
Alveolar bronchiolar adenoma  
No Organ Specified  
Multiple plasmacytoma  
Myeloid leukemia  
Carcinoma  
Adenocarcinoma  
Synovial sarcoma  
Soft Tissue  
Fibroma  
Integument  
Squamous cell carcinoma  
Parathyroid  
Adenoma



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

4 - Male - High Dose

Group No. 4672 4673 4674 4675 4677 4678 4680 4681 4682 4683 4684 4685 4686 4687 4688 4689 4690 4691 4692 4693 4694 4695 4696 5223 5226

Tissue Findings

No Organ Specified

Sarcoma

Lymphosarcoma

Carcinoma

Soft tissue

Fibroma

Integument

Squamous cell

carcinoma

Parathyroid

Adenoma





100-YEAR DURABILITY STUDY IN BAYS

101 PROJECT #7000

REPLACES

4 - Male - High Base (Continued)

Group No. 509 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600

Tissue Findings

Prostatic Adenoma

Dysplasia (Cell Adh.)

Uter - Prostatic Adenoma

Uter - Benign

Prostatic Adenoma

Prostatic Adenoma

Prostatic Adenoma

Prostatic Adenoma

Prostatic Adenoma

Prostatic Adenoma

Prostatic Adenoma

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## TWO-YEAR TOXICITY STUDY IN RATS

LDI PROJECT #1400

NEOPLASMS

Group No. 4 - Male - High Dose (Continued)

Animal No. 5269 5271 5272 5273 5274 5275 5276 5277 5278 5279 5280 5281 5284 5285 5286 5287 5288 5289 5290 5291 5292 5293 5294 5295 5296

## Tissue Findings

## No. Organ Specified

Sarcoma  
Lymphosarcoma  
Carcinoma

Soft Tissue  
Fibroma

## Integument

Squamous cell  
Carcinoma

## Parathyroid

Adenoma

TWO-YEAR TOXICITY STUDY IN RATS  
LBI PROJECT #1400  
NEOPLASMS

Group No.	Females - Control																		
Animal No.	4497	4498	4499	4500	4501	4502	4503	4504	4505	4506 <sup>d</sup>	4507 <sup>d</sup>	4508	4509 <sup>d</sup>	4510	4511	4512	4513	4514 <sup>d</sup>	
Tissue Findings	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary Adenoma																			
Thyroids																			
C-cell adenoma																			
Liver - Preneoplastic Alterations																			
Clear cell focus																			
Basophilic focus																			
Liver - Neoplasms																			
Neoplastic nodule																			
Hepatocellular carcinoma																			
Adrenals																			
Cortical adenoma																			
Pancreas																			
Islet cell adenoma																			
Ovaries																			
Sarcoma																			
Integument																			
Basal cell carcinoma																			
Fibrosarcoma																			
Primary Gland																			
Fibroadenoma																			
Adenocarcinoma																			

THO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)
Animal No.	4497 4498 4499 4500 4501 4502 4503 4504 4505 4506 <sup>d</sup> 4507 <sup>d</sup> 4508 4509 <sup>d</sup> 4510 4511 4512 4513 4514 <sup>d</sup>

Tissue Findings

Uterus

Leiomyoma

No Organ Specified

Sarcoma

Lymphosarcoma

Reticulum cell sarcoma

Malignant lymphoma

Myeloid leukemia

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No.	Females - Control (Continued)																
	4515	4516 <sup>d</sup>	4517 <sup>d</sup>	4518	4519	4520 <sup>d</sup>	4701	4702	4704	4708	4710	4711	4713	4714	4716	4717 <sup>d</sup>	4719
Tissue Findings																	
Pituitary Adenoma			+	+	+	+			+								+
Thyroids																	
C-cell adenoma																	
Liver - Preneoplastic Alterations																	
Clear cell focus																	+
Basophilic focus																	+
Liver - Neoplasms																	
Neoplastic nodule																	
Hepatocellular carcinoma																	
Adrenals																	
Cortical adenoma																	+
Pancreas																	
Islet cell adenoma																	
Ovaries																	
Sarcoma																	
Integument																	
Basal cell carcinoma																	
Fibrosarcoma																	







TWO-YEAR TOXICITY STUDY IN RATS

LB1 PROJECT #1400

NEOPLASMS

Group No. Females - Control (Continued)

Animal No. 4743 4744<sup>d</sup> 4745 4746 4747 4748 4749 4750 4757<sup>d</sup> 4758 4760 4761 4764 4765 4767<sup>d</sup> 4769<sup>d</sup> 4770 4771

Tissue Findings

Pituitary

Adenoma + + + + + + + + + + +

Thyroids

C-cell adenoma

Liver - Preneoplastic Alterations

Clear cell focus

Basophilic focus

Liver - Neoplasms

Neoplastic nodule

Hepatocellular carcinoma

Adrenals

Cortical adenoma

Pancreas

Islet cell adenoma

Ovaries

Sarcoma

Intestine

Basal cell carcinoma

Fibrosarcoma

Mammary Gland

Fibroadenoma

Adenocarcinoma

+ + + + + + + + + + + + + + + + +

## TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

| Group No. | Animal No.  | Females - Control (Continued) |
|-----------|---|-------------------------------|
|           | 4743 4744 4745 4746 4747 4748 4749 4750 4757 4758 4760 4761 4764 4765 4767 4769 4770 4771 |                               |

## Tissue Findings

Uterus

Leiomyoma

No organ specified

Sarcoma

Lymphosarcoma

Reticulum cell sarcoma

Malignant lymphoma

Myeloid leukemia



TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No. 4 - Female - High Dose (Continued)

Animal No. 4647 4648 4649<sup>d</sup> 4650 4651 4652 4653 4654 4655 4656<sup>d</sup> 4657 4658 4660<sup>d</sup> 4661 4662<sup>d</sup> 4663 4664<sup>d</sup> 4665<sup>d</sup> 4667<sup>d</sup> 4668<sup>d</sup> 4669

Tissue Findings

Mammary Gland

Adenoma

Fibroadenoma

Adenocarcinoma

No Organ Specified

Sarcoma

Myeloid Sarcoma

Malignant Lymphoma

Adenocarcinoma

Soft Tissue

Sarcoma

+

+

+

+

+

+

+

TWO-YEAR TOXICITY STUDY IN RATS

LBI PROJECT #1400

NEOPLASMS

Group No. 4 - Female - High Dose (Continued)

Anima: No. 4670 4671 5147 5148 5149<sup>d</sup> 5151 5152 5154<sup>d</sup> 5155 5158 5160 5163<sup>d</sup> 5164 5166 5167 5169<sup>d</sup> 5170 5172 5173<sup>d</sup> 5175

Tissue Findings

Pituitary  
Adenoma

Thyroids  
C-cell adenoma

Thymus  
Thymoma

Liver - Preneoplastic Alterations  
Lymphophilic focus

Liver - Neoplasms  
Neoplastic nodule  
Carcinoma

Stomach  
Squamous cell carcinoma

Integument  
Fibroma  
Squamous cell carcinoma

Uterus  
Leiomyosarcoma  
Adenocarcinoma  
Carcinoma

+

+

+

+

+

+

+

+

TWO-YEAR TOXICITY STUDY IN RATS

LB1 PROJECT #1400

NEOPLASMS

4 - Female - High Dose (Continued)

| Group No. | Animal No. | 4670 | 4671 | 5147 | 5148 | 5149 | 5151 | 5152 | 5154 | 5155 | 5158 | 5160 | 5163 | 5164 | 5166 | 5167 | 5169 | 5170 | 5172 | 5173 | 5175 |
|-----------|------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|-----------|------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|

Tissue Findings

Primary Gland

Adenoma

Fibroadenoma

Adenocarcinoma

No Organ Specified

Sarcoma

Pyeliosarcoma

Polypoid Lymphoma

Adenocarcinoma

Soft Tissue

Sarcoma

+                    +                    +                    +  
 +                    +                    +                    +







