



Experimental Pathology Laboratories, Inc.

EPL ARCHIVES, INC.
BATTELLE NO. CN49730G
EPL PROJECT NUMBER 770-004

2-YEAR CHRONIC TOXICITY / CARCINOGENICITY STUDY
OF TOBACCO BLEND AND AQUEOUS TOBACCO EXTRACT
IN WISTAR HAN RATS: 1-YEAR TIME POINT:
HISTOPATHOLOGICAL EVALUATION OF ALL GROUPS

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PATHOLOGY REPORT

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FINAL REPORT

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PATHOLOGY SUMMARY



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1-YEAR TIME POINT: HISTOPATHOLOGICAL EVALUATION OF ALL GROUPS

PATHOLOGY SUMMARY

INTRODUCTION

The purpose of the overall study was to compare the toxicity of a tobacco blend (Blend), aqueous tobacco extract of that blend (Extract), and diet negative controls (Control) in rats at two time points: one year and two years.

This study is an extension of the 12-Month Repeated Dose Chronic Toxicity Study (for protocol, see [Appendix 1](#)). In the 1-year toxicity study reported by Battelle, only Control and High Dose groups were processed to slides and evaluated for histopathological changes. The purpose of this study is to prepare and evaluate slides for the remaining Low and Mid Dose groups sacrificed at the 1-year time point and to re-evaluate the previously processed slides from Battelle. To help achieve this objective, microscopic examinations were performed on selected tissues. This report presents the results and conclusions from those examinations.

MATERIALS AND METHODS

STUDY DESIGN AND CONDUCT

Wistar Hanover Charles River rats were randomized to groups as indicated in the following study design ([Table 1](#)) for the complete study (both 1-year and 2-year portions). For the 1-year portion of the study, 20 rats/sex were processed and examined from Group 1 (Control), Group 3 (Tobacco Blend Low Dose), Group 4 (Tobacco Blend Intermediate Dose), Group 5 (Tobacco Blend High Dose), Group 6 (Tobacco Extract Low Dose), Group 7 (Tobacco Extract Intermediate Dose), and Group 8 (Tobacco Extract High Dose).

Table 1: Study Design

Group	Target Dosage of Nicotine (mg/kg/day)	Number of Rats			
		Males		Females	
		Core	TK ^{a,b}	Core	TK ^{a,b}
1 – Control-A	0	<i>20/60</i>	10	<i>20/60</i>	10
2 – Control-B ^c	0	<i>0/60</i>	--	<i>0/60</i>	--
3 – Tobacco Blend Low Dose	0.2	<i>20/60</i>	10	<i>20/60</i>	10
4 – Tobacco Blend Intermediate Dose	2	<i>20/60</i>	10	<i>20/60</i>	10
5 – Tobacco Blend High Dose	5	<i>20/60</i>	10	<i>20/60</i>	10
6 – Tobacco Extract Low Dose	0.2	<i>20/60</i>	10	<i>20/60</i>	10
7 – Tobacco Extract Intermediate Dose	2	<i>20/60</i>	10	<i>20/60</i>	10
8 – Tobacco Extract High Dose	5	<i>20/60</i>	10	<i>20/60</i>	10
9 – Sentinels	0	30	--	30	--

^a Nicotine / cotinine analysis.

^b Five extra rats have been included in each dose group for potential replacement of any animal that may die or be unsuitable for blood sampling.

^c Control-B is an independent control group that duplicates Control-A for the carcinogenicity phase of the study.

Italics = 1 year study animals; **Bolded** = 2 year study animals

As part of the postmortem examination, samples of the following tissues were collected and fixed: adrenal glands, bone and marrow (femur), brain, clitoral gland, epididymides, esophagus, pharynx, and trachea, eyes, Harderian glands, heart, large intestine (cecum, colon, and rectum), small intestine (duodenum, jejunum, and ileum), kidneys, liver (median lobe and left lateral lobe), lungs with bronchi, mesenteric lymph node, mammary gland (females only), nose (nasal cavity and turbinates), ovaries, oral mucosa, pancreas, pituitary gland, preputial glands, prostate gland, salivary gland (mandibular), sciatic nerve, seminal vesicles, skeletal muscle (biceps femoris), skin, spinal cord (cervical, thoracic, and lumbar), spleen, sternum with marrow, stomach (fore-stomach and glandular), testes, thymus, thyroid (with parathyroids, if present in routine section), tongue, urinary bladder, uterus, vagina, Zymbal's glands, and all gross lesions.

HISTOLOGY AND HISTOPATHOLOGY

Fixed tissue samples from all rats were processed by routine methods, sectioned, mounted on slides, and stained with hematoxylin and eosin according to EPL SOPs. Slides from rats in Group 1 (Control), 5 (High Dose Blend), and 8 (High Dose Extract) were produced at Battelle. Slides from Group 3 (Low Dose Blend), 4 (Intermediate Dose Blend), 6 (Low Dose Extract), and 7 (Intermediate Dose Extract) were produced at EPL,

Inc. Slides were examined by light microscopy, and histopathologic findings were recorded.

Inflammatory or degenerative lesions were graded on a scale of one to four depending on severity (see [Appendix 2](#) for severity scale under “Codes and Symbols Used At Finding Level”). Nongradable lesions such as cysts were noted as “P” for “Present”. A few tissues were not available for examination. These tissues are indicated as “0” for “No Section” on the table of Individual Microscopic Findings (Animal Organ Finding Tables [AOFT]). These few missing tissues did not affect the overall evaluation of the study.

Following the completion of the microscopic examination of all of the tissues, a peer review was performed by another EPL pathologist. This peer review consisted of a complete review of all tissues from 20% of the Control rats of each sex and a complete review of all tissues from 60% of the High Dose Blend and High Dose Extract rats of each sex. Additionally, all hyperplastic and neoplastic lesions were reviewed from all animals in all groups and the ovaries and uterus were reviewed as potential target organs from all females. The results presented in this report represent the consensus diagnoses of both the study pathologist and the peer reviewing pathologist.

RESULTS

All findings were summarized by sex, group, non-tumor, and tumor categories in the Summary Tables ([Appendices 3 and 4](#)). Microscopic findings for each tissue are listed in the Table of Individual Microscopic Findings (AOFT) ([Appendix 5](#)). A tabulation of gross lesions observed at the time of necropsy, along with corresponding microscopic findings, if any, is provided in the Correlation Table: Necropsy-Microscopy ([Appendix 6](#)). This table shows only animals that had gross lesions noted at necropsy.

Because EPL Laboratories does not provide statistical analysis services, statistical analysis of the tumor pathology data was conducted by the sponsor and the results of this analysis are presented in [Appendix 7](#).

MORTALITY

Single male and female rats in the High Dose Blend group died during the study. Male animal no. 504 died on Day 142 and was cannibalized. The cause of death was a malignant schwannoma in the cervical area, extending into the throat muscles and Harderian gland. Female animal no. 1516 died on Day 297. The cause of death could not be determined. Two females in the High Dose Extract group were sacrificed in a moribund condition on Days 351 and 353. Animal no. 1802 was sacrificed due to a large necrotic fibroadenoma of the mammary gland and animal no. 1809 was diagnosed with a stromal sarcoma of the cervix resulting in a vaginal prolapse.

ONE-YEAR TERMINAL SACRIFICE

No histomorphologic tissue alterations attributable to the ingestion of Tobacco Blend or Tobacco extract at target dosages of nicotine of 0.2, 2, or 5 mg/kg/day were apparent in the tissues examined at the 1-year time point.

Female rats receiving either Tobacco Blend or Tobacco Extract at any of the dosage levels showed an increased incidence of ovarian cyclic dysfunction, characterized by a decrease in lutealization (corpora lutea) compared to the untreated controls. Following is a table of the incidence of this finding in all groups of female rats.

Table 2: Incidence of Decreased Corpora Lutea in Female Rats at 1-Year

	CONTROL	BLEND			EXTRACT		
Group No.	1	3	4	5	6	7	8
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
OVARIES (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Decreased Corpora Lutea	7	10	14	16	13	13	15

It should be noted that these findings in the ovaries are very common in Wistar Han female rats from six to eighteen months of age and are considered the normal consequence of aging ([Westwood, 2008](#), [Tucker, 1997](#)). There was no dose-response relationship and the increased incidence of ovarian cyclic dysfunction in all treated groups may simply reflect a lower than average incidence in the control animals. Because these finding are considered a normal consequence of aging, they are

frequently not diagnosed by pathologists and are considered background appropriate for age.

A few neoplasms of various types were noted in single animals in various groups without respect to treatment. These were the usual types of neoplasms commonly seen in rats of this age and strain. Analysis of the tumor incidence data by the sponsor found no significant trends in tumor incidence for either male or female Wistar Han rats given either the tobacco blend or the aqueous tobacco extract in the feed for one year. The following are tables of neoplasms diagnosed in rats of each sex.

Table 3: Incidence of Neoplasms in Male Rats at 1-Year

	CONTROL	BLEND			EXTRACT		
Group No.	1	3	4	5	6	7	8
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
ZYMBAL'S GLAND (NO. EXAMINED)	(20)	(18)	(18)	(17)	(19)	(18)	(19)
Squamous Papilloma	-	-	1	-	-	-	-
MESENTERIC LYMPH NODE (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Hemangiosarcoma	-	-	-	-	-	1	1
PITUITARY (NO. EXAMINED)	(20)	(18)	(19)	(20)	(18)	(18)	(20)
Adenoma; Pars Distalis	-	1	-	-	-	1	-
THYROID GLANDS (NO. EXAMINED)	(20)	(20)	(19)	(19)	(20)	(20)	(20)
Adenoma; C-Cell	-	1	1	-	-	-	-
SKELETAL MUSCLE, OTHER (NO. EXAMINED)	(0)	(0)	(0)	(1)	(0)	(0)	(0)
Malignant Schwannoma	-	-	-	1*	-	-	-
TESTES (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Interstitial Cell Adenoma	-	-	-	-	-	1	-
SKIN, OTHER (NO. EXAMINED)	(1)	(3)	(0)	(0)	(3)	(1)	(1)
Carcinoma; Sebaceous Gland	1	-	-	-	-	-	-
BONE, OTHER (NO. EXAMINED)	(0)	(0)	(0)	(1)	(1)	(0)	(0)
Osteosarcoma	-	-	-	-	1	-	-

*Malignant Schwannoma extended into the Harderian gland.

Table 4: Incidence of Neoplasms in Female Rats at 1-Year

	CONTROL	BLEND			EXTRACT		
Group No.	1	3	4	5	6	7	8
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
BONE, STERNUM (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
F fibroadenoma	-	-	-	-	-	1	-
MAMMARY GLAND (NO. EXAMINED)	(20)	(20)	(19)	(20)	(20)	(20)	(20)
Adenocarcinoma	-	-	-	1	-	-	-
F fibroadenoma	-	-	-	-	-	-	1
PITUITARY (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(18)	(20)
Adenoma; Pars Distalis	-	-	1	1	-	-	-
THYROID (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Carcinoma; Follicular Cell	-	-	-	-	-	1	-

Table 4: Incidence of Neoplasms in Female Rats at 1-Year (Continued)

	CONTROL	BLEND			EXTRACT		
Group No.	1	3	4	5	6	7	8
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
UTERUS (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Stromal Polyp	1	-	-	-	-	-	1
Stromal Polyp; Cervix	-	-	-	-	-	-	1
Stromal Sarcoma; Cervix	-	-	-	-	-	-	1
VAGINA (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(19)	(20)
Stromal Polyp	-	1	-	-	-	-	-
SKIN, OTHER (NO. EXAMINED)	(0)	(0)	(0)	(1)	(0)	(1)	(0)
Adenoma; Sebaceous Gland	-	-	-	1	-	-	-

A variety of spontaneous disease lesions and incidental findings were diagnosed in both treated and control rats. These findings were the usual number and type commonly seen in Wistar Han rats ([Charles River, 2011](#)). The most common findings (at least five rats in one group were affected) in male rats included increased alveolar macrophage in the lungs, nephropathy in the kidney, inflammation in the liver, tension lipidosis in the liver, cardiomyopathy in the heart, degeneration in the retina of the eye, and inflammation in the preputial glands. Following is a table with the incidence of the most common findings in male rats at the 1-year time point.

Table 5: Incidence of Common Findings in Male Rats at 1-Year

	CONTROL	BLEND				EXTRACT	
Group No.	1	3	4	5	6	7	8
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
LUNGS (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Alveolar Macrophages, Increased	5	1	3	3	2	4	4
KIDNEY (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Nephropathy	8	6	3	4	6	9	8
LIVER (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Inflammation	8	11	7	4	10	11	5
Tension Lipidosis	-	5	1	-	1	1	-
HEART (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Cardiomyopathy	5	6	2	7	2	3	2
EYE (NO. EXAMINED)	(20)	(20)	(20)	(19)	(20)	(20)	(20)
Degeneration; Retina	2	1	2	-	1	5	-
PREPUTIAL GLAND (NO. EXAMINED)	(20)	(20)	(19)	(20)	(20)	(20)	(20)
Inflammation	11	11	12	10	9	14	18

The most common findings in female rats included cysts in the thymus, increased alveolar macrophages in the lung, pigment deposition in the spleen, basophilic foci and inflammation in the liver, angiectasis in the adrenal cortex, inflammation in the clitoral

glands, dilatation of the uterine lumen, and the above mentioned decreased corpora lutea in the ovaries. Following is a table of the most common findings in female rats at the 1-year time point.

Table 6: Incidences of Common Findings in Female Rats at 1-Year

	CONTROL	BLEND			EXTRACT		
Group No.	1	3	4	5	6 7 8		
Dosage (nicotine mg/kg/day)	0	.2	2	5	.2	2	5
THYMUS (NO. EXAMINED)	(20)	(20)	(19)	(20)	(20)	(20)	(20)
Cyst(s)	4	4	8	1	5	6	5
LUNG (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Alveolar Macrophages; Increased	4	2	1	5	2	5	7
SPLEEN (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Pigment Deposition	6	13	6	3	6	4	8
LIVER (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Inflammation	6	9	6	1	6	10	4
Focus Foci; Basophilic Cell	4	5	2	2	1	1	5
ADRENAL GLAND (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Angiectasis; Cortex	3	7	4	1	6	9	1
CLITORAL GLANDS (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Inflammation	6	5	8	7	6	8	10
UTERUS (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Dilatation	4	3	4	2	4	5	3
OVARY (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Decreased Corpora Lutea	7	10	14	16	13	13	15

None of these findings were considered to be related to the ingestion of Tobacco Blend or Tobacco Extract at any of the targeted dosages of nicotine received.

DISCUSSION

COMPARISON WITH HISTOPATHOLOGY OF THE 1-YEAR STUDY BY BATTELLE

Both reports determined that none of the histomorphologic tissue alterations were considered to be related to the Tobacco Blend or the Tobacco Extract at a targeted dosage of nicotine of 5 mg/kg/day.

There were a number of diagnostic differences in various organs and tissues. The majority of these indicated that the Battelle pathologist had a higher threshold for various diagnoses. Some of the diagnoses that were not made by the Battelle pathologist include aspermia or hypospermia in the epididymides of rats with testicular atrophy, degeneration of the retina of the eye, inflammation in the Harderian gland, preputial gland, or clitoral gland, pigment deposition and extramedullary hematopoiesis in the

spleen, decreased corpora lutea in the ovaries (discussed previously), endometrial cysts and dilatation in the uterus, mucification in the vagina, and dilated ducts in the Zymbal's glands.

With respect to neoplasms, there were a few differences in diagnosis. In the liver, the biliary adenoma diagnosed in a Control female by Battelle was determined to be a multiloculated biliary cyst. In the uterus, the two stromal sarcomas diagnosed in High Dose Extract females by Battelle were considered to be a stromal sarcoma of the cervix and a stromal polyp of the cervix. In the mammary gland, the adenoma diagnosed in a High Dose Blend female by Battelle was determined to be an adenocarcinoma and the adenoma diagnosed in a High Dose Extract female was considered to be a fibroadenoma.

There were also differences in the number of animals diagnosed with various non-neoplastic findings by the Battelle pathologist compared to the EPL pathologist. Following is a table of differences in diagnoses from the Battelle pathologist (Path. 1) and the EPL pathologist (Path. 2). A few diagnoses that occurred singly are not included in the table. None of these differences affected the overall conclusions of the report.

Table 7: Differences Between Battelle and EPL Pathology Non-Neoplastic Findings

Group (Group No.) Pathologist	Males						Females					
	Control (1)		Blend (5)		Extract (8)		Control (1)		Blend (5)		Extract (8)	
	1	2	1	2	1	2	1	2	1	2	1	2
ADRENAL GLAND (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Angiectasis; Cortex	0	0	0	0	0	0	2	3	0	1	0	1
Hyperplasia; Cortex	1	0	1	0	0	0	0	0	0	0	0	0
Hypertrophy; Cortex	0	1	3	3	2	2	0	0	0	0	0	1
Vacuolation; Cortex	0	0	0	2	0	1	0	0	0	0	0	0
EPIDIDYMIS (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	-	-	-	-	-	-
Aspermia	0	0	0	1	0	2	-	-	-	-	-	-
Hypospermia	0	1	0	0	0	0	-	-	-	-	-	-
EYE (NO. EXAMINED)	(20)	(20)	(20)	(19)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Degeneration; Retina	0	2	0	0	0	0	0	1	0	0	0	1
HARDERIAN GLAND (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Inflammation	0	1	0	1	0	1	0	3	0	3	0	2
HEART (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Cardiomyopathy	5	5	4	7	2	2	1	2	0	1	2	2
KIDNEY (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Nephropathy	2	8	3	4	4	8	2	1	0	0	1	1

Table 7: Differences Between Battelle and EPL Pathology Non-Neoplastic Findings
(Continued)

Group (Group No.) Pathologist	Males						Females					
	Control (1)		Blend (5)		Extract (8)		Control (1)		Blend (5)		Extract (8)	
	1	2	1	2	1	2	1	2	1	2	1	2
LIVER (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Focus, Basophilic	0	2	0	1	0	1	0	4	0	2	2	5
Focus, Clear Cell	0	0	1	1	0	0	0	0	0	0	0	0
Focus, Mixed Cell	0	0	0	0	0	0	0	0	0	0	1	0
Focus, Eosinophilic	0	0	0	0	0	0	0	0	0	0	0	1
Hyperplasia, Bile Duct	2	0	1	2	1	2	0	0	0	0	1	0
Inflammation	0	8	0	4	1	5	1	6	0	1	1	4
LUNG (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Alveolar Macrophages, Increased	5	5	2	3	2	4	1	4	2	5	6	7
PITUITARY (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Hyperplasia, Pars Distalis	1	1	2	3	1	2	1	2	2	2	2	2
PREPUTIAL / CLITORAL GLAND (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Inflammation	0	11	0	10	1	18	0	6	0	7	0	10
SPLEEN (NO. EXAMINED)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Pigment Deposition	0	1	0	0	0	1	0	6	0	3	0	8
Increased Extramedullary Hematopoiesis	0	0	0	0	0	0	0	0	0	0	0	1
THYMUS (NO. EXAMINED)	(20)	(20)	(19)	(19)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
Cyst(s)	0	0	0	0	0	0	0	4	0	1	0	5
UTERUS (NO. EXAMINED)	-	-	-	-	-	-	(20)	(20)	(20)	(20)	(20)	(20)
Endometrial Hyperplasia, Cystic	-	-	-	-	-	-	2	1	3	1	2	0
Endometrial Cyst(s)	-	-	-	-	-	-	0	1	0	1	0	0
Dilatation	-	-	-	-	-	-	0	4	0	2	0	3
VAGINA (NO. EXAMINED)	-	-	-	-	-	-	(20)	(20)	(20)	(20)	(20)	(20)
Mucification	-	-	-	-	-	-	0	2	0	0	0	2
ZYMBAL'S GLAND (NO. EXAMINED)	(20)	(20)	(19)	(17)	(19)	(19)	(20)	(20)	(20)	(20)	(20)	(20)
Dilated Ducts	0	4	0	1	0	3	0	1	0	4	0	4

COMPARISON WITH HISTOPATHOLOGY OF THE 2-YEAR STUDY BY BATTELLE

The pathology conclusions of the 2-year study stated that there were no treatment-related gross or microscopic findings in either male or female rats on this study. A greater incidence of uterine carcinoma was observed in the High Dose Tobacco Blend and Tobacco Extract groups, however, there was no dose-response relationship and the total incidence was within the historical control background level for Wistar Han rats (Deerberg *et al*, 1981; Charles River Laboratories, 2011). These tumors were considered spontaneous and unrelated to the administration of the test article(s).

Regarding potential predictive value of the histopathology at the end of the 1-year study, no histomorphologic tissue alterations attributable to Tobacco Blend or Tobacco Extract at targeted doses up to 5mg/kg/day of nicotine were reported in either study.

The occurrence of cardiomyopathy, nephropathy, and increased alveolar macrophages in the lung at the 1-year time point predicted that these findings would be present and increased in incidence and severity at the 2-year time point. Likewise, the occurrence of C-cell hyperplasia and adenoma in the thyroids, hyperplasia and adenoma in the pars distalis of the pituitary, and stromal polyps, stromal sarcoma, and cystic endometrial hyperplasia of the uterus at the 1-year time point indicated that these findings would be present at the 2-year time point. There was no indication in the uterus that would have predicted the uterine carcinomas that occurred in the female rats at the 2-year time point. No precursor proliferative lesions for uterine carcinoma were present at the 1-year time point. This is typical for this type of tumor and is supported by the historical control data for the usual age of occurrence for this finding (Deerberg *et al*; Charles River Laboratories, 2011).

CONCLUSIONS

The administration of Tobacco Blend and Tobacco Extract to male and female Wistar Han rats at targeted nicotine dosages of 0.2, 2, or 5 mg/kg/day did not result in any test article-related histopathologic alterations in any of the tissue examined after one year on study. A variety of spontaneous disease lesion, aging changes, and incidental finding were noted in rats in all dose groups without respect to treatment.

Deborah A. Banas February 8, 2013
DEBORAH A. BANAS, DVM, MS, DABT, Diplomate, ACVP Date
Senior Pathologist

DAB/cb

REFERENCES

- Tucker, Mary J. (1997) The Female Genital System. *In: Diseases of the Wistar Rat.* pp. 145-148, Taylor and Francis, e-library, (2003) London.
- Charles River. (2011) Neoplastic and Non-Neoplastic Lesions in the Charles River Wistar Hannover [CrI:WI(Han)] Rat.
- Westwood, F.R. (2008) The Female Rat Reproductive Cycle: A Practical Histological Guide to Staging. *Toxicol Pathol.* 36: pp. 375-384.
- Deerberg F, Rehm S, and Pittermann W. (1981) Uncommon Frequency of Adenocarcinomas of the Uterus in Virgin Han:Wistar Rats. *Vet Pathol*, 18:707-713.
- Fallacara, D.M. (2011) Two-Year Chronic Toxicity / Carcinogenicity Feeding Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats: 12-Month Repeated Dose Chronic Toxicity Study (Study No. CN49730G). Battelle.
- Fallacara, D.M. (2012) Two-Year Chronic Toxicity / Carcinogenicity Feeding Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats: 2-Year Chronic Carcinogenicity Study (Study No. CN49730G). Battelle.

EPL ARCHIVES, INC.
STUDY NUMBER CN49730G
EPL PROJECT NUMBER 770-004

2-YEAR CHRONIC TOXICITY / CARCINOGENICITY STUDY OF TOBACCO BLEND AND
AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS: 1-YEAR TIME POINT:
HISTOPATHOLOGICAL EVALUATION OF ALL GROUPS

PEER REVIEW STATEMENT

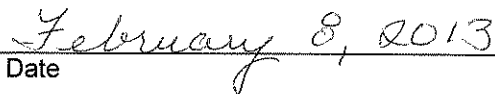
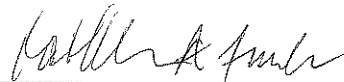
A microscopic peer review was performed as follows for this study:

1. Re-examination of all tissues from 20% of the control (Group 1) and 60% of the high-dose groups (Groups 5 and 8) by sex, selected randomly from the 1-year sacrifice:
Group 1 males: 106, 111, 112, 115
Group 5 males: 501, 502, 504, 507, 509, 510, 515, 516, 517, 518, 519, 520
Group 8 males: 802, 805, 806, 808, 810, 811, 812, 813, 816, 817, 818, 820
Group 1 females: 1106, 1108, 1113, 1119
Group 5 females: 1501, 1502, 1507, 1509, 1510, 1511, 1512, 1513, 1514, 1516, 1517, 1519
Group 8 females: 1802, 1803, 1805, 1807, 1808, 1809, 1811, 1812, 1813, 1815, 1818, 1820
2. Re-examination of all hyperplasias and neoplasias diagnosed by the study pathologist from all animals in Groups 1, 3, 4, 5, 6, 7, and 8 in both sexes.
3. Re-examination of the potential target tissues ovary and uterus from all females in Groups 1, 3, 4, 5, 6, 7, and 8.
4. There were no potential target organs diagnosed by the Study Pathologist for the male animals.

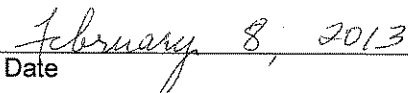
Following review of the microscopic findings reported by the study pathologist, the results were discussed and appropriate terminology and diagnoses mutually agreed on. Differences of opinion between the study and reviewing pathologists were resolved with agreement on the final diagnoses. The tables contained in the final report for the study reflect the mutually agreed-on diagnoses.



DEBORAH A. BANAS, DVM, MS, DABT, Diplomate, ACVP
Study Pathologist
Experimental Pathology Laboratories, Inc.


Date

KATHLEEN A. FUNK, DVM, PhD, Diplomate, ACVP
Reviewing Pathologist
Experimental Pathology Laboratories, Inc.


Date



COMPLIANCE STATEMENT

Client Name	<u>EPL Archives, Inc.</u>	EPL Principal Investigator	<u>Dr. Deborah A. Banas</u>
Client Study	<u>Battelle No. CN49730G</u>	EPL Pathologist	<u>Dr. Deborah A. Banas</u>
Species	<u>Rat</u>	EPL Project Number	<u>770-004</u>
Study Title	<u>2-Year Chronic Toxicity / Carcinogenicity Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats: 1-Year Time Point: Histopathological Evaluation of All Groups</u>		
Test Article	<u>Tobacco Blend and Aqueous Tobacco Extract</u>		

The Histopathology portions of the above-referenced study were conducted in compliance with the Good Laboratory Practice regulations of the Food and Drug Administration as stipulated by 21 CFR Part 58 and all applicable amendments.

Deborah A. Banas
EPL Principal Investigator

February 8, 2013
Date



QUALITY ASSURANCE FINAL CERTIFICATION

Study Title: 2-Year Chronic Toxicity / Carcinogenicity Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats: 1-Year Time Point: Histopathological Evaluation of All Groups

Client Study: Battelle No. CN49730G EPL Principal Investigator: Dr. Deborah A. Banas

EPL Project Number: 770-004 EPL Pathologist: Dr. Deborah A. Banas

The following aspects of this study were inspected by the Quality Assurance Unit of Experimental Pathology Laboratories, Inc. Dates inspections were performed and findings reported to the EPL Principal Investigator and Management are indicated below.

Area Inspected	Dates	
	Inspection	Reporting
Protocol	10/18,19/12; 10/22/12	10/19/12; 10/22/12
EPL Project Sheets	10/22,23/12; 11/30/12; 12/13/12	10/23/12; 12/3/12; 12/28/12
Project Setup	10/24/12; 10/25/12	10/24/12; 10/25/12
In-Process	11/1/12	11/2/12
Data Review	11/6/12; 11/7/12; 11/8/12; 11/9/12; 11/12/12; 11/13/12; 11/14/12	11/6/12; 11/7/12; 11/8/12; 11/9/12; 11/12/12; 11/13/12; 11/14/12
Peer Review	11/16,19/12; 11/30/12; 12/3/12	11/19/12; 12/3/12
Draft Pathology Report	11/28/12; 12/6,7/12; 12/13,14,17-20,27,28/12; 1/29/13	11/28/12; 12/7/12; 12/28/12; 1/29/13
Final Pathology Report	2/8,11/13	2/11/13
<hr/>		
Date reported to Study Director/Management	2/12/13	
Date of last quarterly facility inspection	11/12	


EPL Quality Assurance Unit


Date 2/12/13

APPENDIX 1:
EPL PROTOCOL

STUDY PROTOCOL

**2-YEAR CHRONIC TOXICITY/CARCINOGENICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO
EXTRACT IN WISTAR HAN RATS:**

1-YEAR TIME POINT: HISTOPATHOLOGICAL EVALUATION OF ALL GROUPS

TEST SITE:

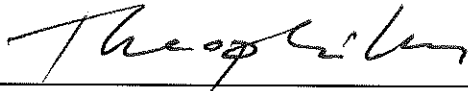
**EXPERIMENTAL PATHOLOGY LABORATORIES, INC. (EPL, Inc.)
45600 TERMINAL DRIVE
STERLING, VA 20166**

SPONSOR:

**R.J. REYNOLDS TOBACCO COMPANY
RESEARCH AND DEVELOPMENT
BOWMAN GRAY TECHNICAL CENTER
WINSTON-SALEM, NC 27102**

**Battelle Study No. CN49730G
EPL, Inc. Study No. 770-004**

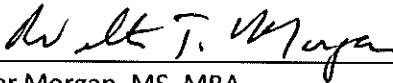
This protocol was approved by the following:



Suzana Theophilus, MS, PhD, DABT
Study Monitor
R.J. Reynolds Tobacco Company

10/23/12

Date



Walter Morgan, MS, MBA
Study Statistician
R.J. Reynolds Tobacco Company

10/23/2012

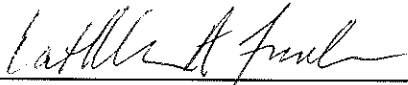
Date



Deborah A. Banas, DVM, MS, DABT, Diplomate ACVP
Study Director/Study Pathologist
Experimental Pathology Laboratories, Inc. (EPL, Inc.)

October 22, 2012

Date



Kathleen A. Funk, DVM, Ph.D., Diplomate ACVP
Manager, VA Laboratory Operations/Study Pathologist
Experimental Pathology Laboratories, Inc. (EPL, Inc.)

Oct. 22, 2012

Date

1.0 PERSONNEL

Study Monitor

Suzana Theophilus, MS, PhD, DABT
R.J. Reynolds Tobacco Company
Tel: 336-741-1536
E-mail: theophe@rjrt.com

Histology

Vivian English, Histology/Tissue Repository Supervisor
Experimental Pathology Laboratories, Inc. (EPL, Inc.)
Tel: 703-471-7060 ext. 222
Fax: 703-471-8447
E-mail: venglish@epl-inc.com

Study Director/Study Pathologist

Deborah A. Banas, DVM, MS, DABT, DACVP, Senior Pathologist
Experimental Pathology Laboratories, Inc. (EPL, Inc.)
Tel: 703-471-7060 ext. 205
Fax: 703-471-8447
E-mail: dbanas@epl-inc.com

Peer Review Pathologist

Kathleen A. Funk, DVM, PhD, DACVP, Senior Pathologist
Experimental Pathology Laboratories, Inc. (EPL, Inc.)
Tel: 703-471-7060 ext. 206
Fax: 703-471-8447
E-mail: kfunk@epl-inc.com

2.0 PURPOSE

The purpose of the overall study is to compare the toxicity of a tobacco blend (Blend), aqueous tobacco extract of that blend (Extract), and diet negative controls (Control) in rats at 2 time points: 1 year and 2 years.

This study is an extension of a 2-year rat chronic/carcinogenicity study with a 1-year chronic toxicity segment. Because in the previous study, for the 1-year segment, only Control and High Dose groups were processed to slides and evaluated from a histopathology perspective, the current study aims to complete the 1-year segment. This will be accomplished by preparing slides for the remaining Low and Mid dose groups and by re-evaluating all Control, Low, Mid, and High Dose groups (Blend and Extract) from a histopathological perspective and by preparing a 1-year histopathology report.

3.0 REGULATORY COMPLIANCE

This study will be conducted in compliance with the current version of the United States Food and Drug Administration's (FDA) Good Laboratory Practice (GLP) Regulations, 21 CFR Part 58, for the conduct of nonclinical laboratory studies.

The overall GLP study was conducted at Battelle, Columbus, OH. The in-life portion of the study was conducted at Battelle, OH, Battelle Study Number CN49730G, starting February 12, 2009, under the direction of Milton Hejtmancik, Ph.D., D.A.B.T. followed by Dawn Fallacara, Ph.D. Battelle has completed two final signed reports with partial to complete histopathology data for the 1-year and 2-year portions, respectively.

Accordingly, all portions of the current 1-year histopathology segment/study will be performed at EPL, Inc. and will adhere to this study protocol and any amendments, as well as to applicable EPL, Inc. facility Standard Operating Procedures (SOPs).

EPL, Inc.'s Quality Assurance will review the study protocol, the conduct for the histopathology portion of this study, the data, the final pathology report, and any other portions of the study deemed necessary to assure the integrity of the study. Appropriate documentation (e.g., QA reports) will be provided to the Study Director. The QA schedule, study phases audited, and final QA report signoff will be included in the final report. The sponsor, RJR, will be responsible for the audit of the statistical report.

4.0 TESTING SITE

Experimental Pathology Laboratories, Inc. (EPL, Inc.)
45600 Terminal Drive
Sterling, VA 20166

5.0 SPONSOR

R.J. Reynolds Tobacco Company
Research and Development
Bowman Gray Technical Center
Winston-Salem, NC 27102

6.0 PROPOSED SCHEDULE

The proposed dates for the following key events are listed below.

Year 1 Slide Reading Completed:	December, 2012
Peer Review Completed:	December, 2012
Data to RJRT for Statistical Analyses	December, 2012
Final Pathology Report:	January/February, 2013

7.0 EXPERIMENTAL DESIGN

Wistar Hanover, Charles River rats (4-5 weeks old, 50-200 grams) were randomized to groups as follows:

Group	Target Dosage of Nicotine (mg/kg/day)	Number of Rats			
		Males		Females	
		Core	TK ^{a,b}	Core	TK ^{a,b}
1 – Control-A	0	20/60	10	20/60	10
2 – Control-B ^c	0	0/60	--	0/60	--
3 – Tobacco Blend Low Dose	0.2	20/60	10	20/60	10
4 – Tobacco Blend Intermediate Dose	2	20/60	10	20/60	10
5 – Tobacco Blend High Dose	5	20/60	10	20/60	10
6 – Tobacco Extract Low Dose	0.2	20/60	10	20/60	10
7 – Tobacco Extract Intermediate Dose	2	20/60	10	20/60	10
8 – Tobacco Extract High Dose	5	20/60	10	20/60	10
9 – Sentinels	0	30	--	30	--

^a Nicotine / cotinine analysis.

^b Five extra rats have been included in each dose group for potential replacement of any animal that may die or be unsuitable for blood sampling.

^c Control-B was an independent control group that duplicates Control-A for the carcinogenicity phase of the study.

Bold font: 1-year study animals to be evaluated in this 1-year EPL histopathology study

Refer to Battelle Protocol and Study Number CN49730G for further details regarding the test and control articles, identification of the test system, diet and water, housing, animal numbering, types of analyses and measurements made during and at the termination of the in-life phase, and all other pertinent protocol-required information needed to conduct this study.

9.0 TISSUE PROCESSING

All fixed tissues of the 1-year chronic toxicity study animals from the Low dose (Groups 3 and 6) and Intermediate dose groups (Groups 4 and 7) will be processed to slides by EPL, Inc.

Adrenal glands
Bone and marrow (femur)
Brain
Clitoral gland
Epididymides
Esophagus, pharynx, and trachea
Eyes
Gross lesions
Harderian glands
Heart
Intestine, large (cecum, colon, and rectum)
Intestine, small (duodenum, jejunum, and ileum)
Kidneys
Liver (median lobe and left lateral lobe)
Lungs with bronchi
Lymph node (mesenteric)
Mammary gland (females only)
Nose (nasal cavity and turbinates)
Ovaries
Oral mucosa
Pancreas
Pituitary gland
Preputial glands
Prostate gland
Salivary gland (mandibular)
Sciatic nerve
Seminal vesicles
Skeletal muscle (biceps femoris)
Skin
Spinal cord (cervical, thoracic, and lumbar)
Spleen
Sternum with bone marrow
Stomach (fore-stomach and glandular)
Testes
Thymus
Thyroid gland (with parathyroids, if present in routine section)
Tongue

Urinary Bladder
Uterus
Vagina
Zymbal glands

Slides will be stained with hematoxylin and eosin according to EPL, Inc. facility SOPs for histology processing.

10.0 HISTOPATHOLOGICAL EVALUATION

Tissue slides from all unscheduled and scheduled necropsies of core rats in the 1-year chronic toxicity study from Groups 1, 3, 4, 5, 6, 7, and 8 will be examined histologically by a board-certified veterinary pathologist from EPL, Inc.

11.0 PEER REVIEW

A board-certified pathologist from EPL, Inc., other than the study pathologist, will review the draft histopathology data and slides as follows:

- All tissues containing neoplastic findings.
- All tissues containing potential treatment-related findings.
- All remaining tissues from a subset of control and treated animals.

The peer review pathologist and the study pathologist will discuss and resolve any differences of opinion. The final histopathology data for the study will reflect the consensus of the study pathologist and the peer review pathologist.

12.0 STATISTICAL ANALYSIS

Statistical analyses will be supplied by the sponsor. Analyses will consist of evaluation of dose-response trends in treatment (Blend, Extract) vs. Control group. For tumor endpoints, analyses will be generally consistent with analyses of 2-year tumor endpoints. Cochran Armitage trend test will test for positive linear dose trends in prevalence rates of incidental (mortality-independent) tumors. Tarone's trend test will test for positive linear dose trends in fatal tumors. If a tumor is observed in a fatal context for some animals and in an incidental context for other animals, Peto's test will test for positive linear dose trends in tumor incidence, using the same time intervals applied for analysis of incidental tumors.

Tests for linear dose trends will be conducted separately for each gender and for Blend and Extract. Trend tests will be performed using proper contrasts applied to an analysis of the dosage groups involved (i.e., the control and the three treated dose groups). The p-value required for statistical significance for each trend test will be 0.05.

The statistical report will be written by the sponsor's statistician and will be included as an appendix to the EPL histopathology report.

13.0 PATHOLOGY REPORT

A stand-alone pathology report for the 1-year chronic toxicity study will be prepared by the EPL, Inc. study pathologist and submitted to Dr. Suzana Theophilus, Study Monitor. The statistical report will be prepared by RJR statistician, Walter Morgan, and the statistical report will be appended to the EPL, Inc 1-year histopathology report.

14.0 STORAGE OF STUDY MATERIALS AND RECORDS RETENTION

All residual study materials, records, and final pathology report will be sent for long-term storage to EPL Pathology Archives, Inc. (EPL Archives, Inc.) at the following address:

EPL Archives, Inc.
45610 Terminal Drive
Sterling, VA 20166
(703) 435-8780
Shipping@eplarchives.com

APPENDIX 2:
EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT TABLE LEVEL:

AOFT = Animal Organ Finding Table

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male Animal
F = Female Animal
K0 = Terminal Sacrifice Group
K1 K9 = Interim Sacrifice Group 1 . . . 9
R1 R9 = Recovery / Post-Treatment Group 1 . . . 9
+ = Intercurrent Death / Sacrificed Moribund

CODES AND SYMBOLS USED AT ORGAN LEVEL:

A = Organ autolytic, evaluation not possible
G = Gross finding evaluated histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present
! = No corresponding microscopic finding required
NAD = No abnormalities detected

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / mild / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large / moderately severe
P = Finding present, severity not scored
(= Finding unilateral in paired organs
B = Benign neoplasm
N = Malignant neoplasm
M = Metastasis
M58 = Metastasis from the Skeletal Muscle, Other

Tumor Indices:

Index 0 = Statistically an incidental tumor (terminal sacrifice)
Index 1 = Statistically certainly a non-fatal tumor
Index 2 = Statistically probably a non-fatal tumor
Index 3 = Statistically probably a fatal tumor
Index 4 = Statistically certainly a fatal tumor
Index 5 = Statistically an observable tumor (mortality-independent context)

CORRELATION TABLE: NECROPSY-MICROSCOPY:

Evaluation Not Required = No corresponding microscopic finding required

APPENDIX 3:
SUMMARY TABLES – NON-NEOPLASTIC LESIONS

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 3-1 / 7
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex	Males							
Dose Group	1	3	4	5	6	7	8	
No. Animals per Dose Group	20	20	20	20	20	20	20	
ADRENAL GLANDS No.Examined	20	20	20	20	20	20	20	20
- Hypertrophy; Cortex	1	1	—	3	—	—	—	2
- Vacuolation; Cortex	—	—	1	2	—	—	—	1
BONE, OTHER No.Examined	—	—	—	1	1	—	—	—
- Hemorrhage	—	—	—	1	—	—	—	—
BONE MARROW No.Examined	20	20	20	20	20	20	20	20
BONE, FEMUR No.Examined	20	20	20	20	20	20	20	20
BONE, STERNUM No.Examined	20	20	20	20	20	20	20	20
BRAIN No.Examined	20	20	20	20	20	20	20	20
CAUSE OF DEATH No.Examined	—	—	—	1	—	—	—	—
- Malignant Schwannoma	—	—	—	1	—	—	—	—
EPIDIDYMIDES No.Examined	20	20	20	20	20	20	20	20
- Aspermia	—	—	1	1	1	—	—	2
- Hypospermia	1	—	—	—	1	1	—	—
ESOPHAGUS No.Examined	20	20	20	19	20	20	20	20
EYES No.Examined	20	20	20	19	20	20	20	20
- Degeneration; Retina	2	1	2	—	1	5	—	—
HARDERIAN GLANDS No.Examined	20	20	20	20	20	20	20	20
- Inflammation	1	1	1	1	1	3	—	1
HEART No.Examined	20	20	20	20	20	20	20	20
- Cardiomyopathy	5	6	2	7	2	3	—	2
- Epicardium; Inflammation;	1	—	—	—	—	—	—	—
Chronic	—	—	—	—	—	—	—	—
- Valve; Inflammation	—	—	—	—	—	—	—	1
INTEST-LG, CECUM No.Examined	20	20	20	19	20	20	20	20
INTEST-LG, COLON No.Examined	20	20	20	19	20	20	20	20
- Metazoan Parasite	—	—	1	—	—	—	—	—
INTEST-LG, RECTUM No.Examined	20	20	20	20	20	20	20	20
INTEST-SM, DUODENUM No.Examined	20	20	20	19	20	20	20	20
INTEST-SM, ILEUM No.Examined	20	20	20	19	20	20	20	20
INTEST-SM, JEJUNUM No.Examined	20	20	20	19	20	20	20	20
- Inflammation	—	—	—	—	—	—	—	1
- Ulcer	—	—	—	—	—	—	—	1
KIDNEYS No.Examined	20	20	20	20	20	20	20	20
- Cyst(s)	—	—	1	1	—	—	—	—
- Inflammation; Pelvic	—	2	—	1	—	—	—	—
- Mineralization; Pelvic	—	—	—	—	1	—	—	—
- Nephropathy	8	6	3	4	6	9	—	8
- Pelvic Dilatation	1	—	—	1	—	—	—	—

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 3-2 / 7
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths							
Sex	Males						
Dose Group No. Animals per Dose Group	1 20	3 20	4 20	5 20	6 20	7 20	8 20
LIVER No.Examined	20	20	20	20	20	20	20
- Focus/Foci; Basophilic Cell	2	3	1	1	—	1	1
- Focus/Foci; Clear Cell	—	—	—	1	—	—	—
- Hepatodiaphragmatic Nodule	—	—	—	—	1	—	—
- Hyperplasia; Bile Duct	—	2	—	2	1	—	2
- Inflammation	8	11	7	4	10	11	5
- Lipidosis; Focal	—	1	—	—	—	—	—
- Lipidosis; Periportal	1	1	—	—	—	—	—
- Pigment; Periportal	1	—	—	—	—	—	1
- Tension Lipidosis	—	5	1	—	1	1	—
LN MESENTERIC No.Examined	20	20	20	20	20	20	20
- Angiomatous Hyperplasia	—	—	—	—	—	1	—
LUNG No.Examined	20	20	20	20	20	20	20
- Alveolar Macrophages; Increased	5	1	3	3	2	4	4
- Congestion	—	—	—	—	1	—	—
- Inflammation	1	1	3	—	2	1	—
- Osseous Metaplasia	—	2	—	—	2	1	1
- Pigmented Macrophages	—	1	—	—	1	—	1
NOSE/TURBINATES No.Examined	20	20	20	20	20	20	20
- Cyst(s); Mucosa	—	1	—	—	—	—	—
- Hemorrhage	—	—	—	1	—	—	—
- Inflammation	2	—	—	—	—	—	—
ORAL MUCOSA No.Examined	20	20	20	20	20	20	20
PANCREAS No.Examined	20	20	20	20	20	20	20
- Atrophy; Acinar Cell	—	2	1	1	1	1	1
PARATHYROID GLANDS No.Examined	15	19	19	11	19	20	14
PHARYNX No.Examined	20	20	20	19	20	20	20
- Foreign Material	—	—	1	—	—	—	—
- Increased Mucus; Mucosal Glands	1	—	—	—	—	—	—
- Inflammation	—	—	1	1	—	—	—
PITUITARY GLAND No.Examined	20	18	19	20	18	18	20
- Cyst(s)	—	—	1	—	1	—	—
- Hyperplasia; Pars Distalis	1	1	1	3	—	—	2
PREPUTIAL GLANDS No.Examined	20	20	19	20	20	20	20
- Inflammation	11	11	12	10	9	14	18
PROSTATE GLAND No.Examined	20	20	20	20	20	20	20
- Inflammation	—	2	—	—	2	2	1
- Inflammation; Chronic	—	—	—	3	—	—	1
SALIVARY GLAND No.Examined	20	20	20	19	20	20	20
SCIATIC NERVE No.Examined	20	20	20	20	20	20	20

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

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SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex		Males						
Dose Group No. Animals per Dose Group		1 20	3 20	4 20	5 20	6 20	7 20	8 20
SEMINAL VESICLES	No.Examined	20	20	20	20	20	20	20
- Distention		-	-	1	-	-	-	-
SKEL MUSCLE, OTHER	No.Examined	-	-	-	1	-	-	-
SKELETAL MUSCLE	No.Examined	20	20	20	20	20	20	20
SKIN	No.Examined	20	20	20	20	20	20	20
SKIN, OTHER	No.Examined	1	3	-	-	3	1	1
- Epidermal Ulceration		-	-	-	-	1	-	1
- Fat Infiltration		-	1	-	-	-	-	-
- Hyperkeratosis		-	2	-	-	1	-	-
- Hyperplasia; Epithelial		-	-	-	-	-	-	1
- Hyperplasia; Sebaceous Gland		-	-	-	-	1	-	-
- Inflammation		-	2	-	-	1	-	-
SPINAL CORD	No.Examined	20	20	20	20	20	20	20
SPLEEN	No.Examined	20	20	20	20	20	20	20
- Lymphoid Depletion		-	-	-	1	-	-	-
- Pigment Deposition		1	1	-	-	-	1	1
STOMACH	No.Examined	20	20	20	20	20	20	20
- Inflammation		-	-	-	1	-	-	-
- Mucosal Cyst; Glandular		-	-	-	1	-	-	-
TESTES	No.Examined	20	20	20	20	20	20	20
- Atrophy		1	-	1	1	2	1	3
- Interstitial Fluid		-	1	-	-	-	-	-
THYMUS	No.Examined	20	19	19	19	18	19	20
- Atrophy		-	-	1	-	-	-	-
- Cyst(s)		-	2	1	-	2	1	-
THYROID GLAND	No.Examined	20	20	19	19	20	20	20
- Follicular Cyst(s)		-	-	-	1	-	1	-
TONGUE	No.Examined	20	20	20	19	20	20	20
TRACHEA	No.Examined	20	20	20	20	20	20	20
URINARY BLADDER	No.Examined	20	20	20	20	19	20	20
- Hemorrhage; Mucosa		-	-	-	1	-	-	-
ZYMBAL'S GLANDS	No.Examined	20	18	18	17	19	18	19
- Dilated Duct(s)		4	2	3	1	2	4	3

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex	Females							
Dose Group	1	3	4	5	6	7	8	
No. Animals per Dose Group	20	20	20	20	20	20	20	
ADRENAL GLANDS No.Examined	20	20	20	20	20	20	20	20
- Angiectasis; Cortex	3	7	4	1	6	9	1	
- Degeneration; Cortex	-	1	-	-	-	-	-	
- Hyperplasia; Cortex	-	-	-	-	-	1	-	
- Hypertrophy; Cortex	-	1	-	-	3	-	1	
- One Medulla Examined	-	-	-	-	1	-	-	
- Pigment Deposition	1	-	-	-	-	-	-	
- Three Adrenals Submitted in Wet	-	-	-	-	-	1	-	
- Vacuolation; Cortex	-	-	-	-	1	-	-	
BONE MARROW No.Examined	20	20	20	20	20	20	20	20
BONE, FEMUR No.Examined	20	20	20	20	20	20	20	20
BONE, STERNUM No.Examined	20	20	20	20	20	20	20	20
BRAIN No.Examined	20	20	20	20	20	20	20	20
CAUSE OF DEATH No.Examined	-	-	-	1	-	-	2	
- Fibroadenoma	-	-	-	-	-	-	1	
- Stromal Sarcoma	-	-	-	-	-	-	1	
- Undetermined	-	-	-	1	-	-	-	
CLITORAL GLANDS No.Examined	20	20	20	20	20	20	20	20
- Inflammation	6	5	8	7	6	8	10	
ESOPHAGUS No.Examined	20	20	20	20	20	20	20	20
EYES No.Examined	20	20	20	20	20	20	20	20
- Degeneration; Retina	1	2	1	-	3	1	1	
HARDERIAN GLANDS No.Examined	20	20	20	20	20	20	20	20
- Inflammation	3	-	2	3	2	1	2	
HEART No.Examined	20	20	20	20	19	20	20	20
- Cardiomyopathy	2	-	-	1	1	1	2	
INTEST-LG, CECUM No.Examined	20	20	20	20	20	20	20	20
INTEST-LG, COLON No.Examined	20	20	20	20	20	20	20	20
INTEST-LG, RECTUM No.Examined	20	20	20	20	20	20	20	20
- Metazoan Parasites	2	-	1	-	-	1	-	
INTEST-SM, DUODENUM No.Examined	20	20	20	20	20	20	20	20
INTEST-SM, ILEUM No.Examined	20	20	20	20	20	20	20	20
INTEST-SM, JEJUNUM No.Examined	20	20	20	20	20	20	20	20
KIDNEYS No.Examined	20	20	20	20	20	20	20	20
- Cyst(s)	-	-	-	-	-	1	-	
- Hyperplasia; Urothelium	-	1	-	-	-	-	-	
- Inflammation; Pelvic	-	1	-	-	-	-	-	
- Mineralization; Pelvic	1	2	-	1	1	-	-	
- Mineralization; Tubular	1	1	-	-	-	-	1	

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex	Females							
Dose Group	1	3	4	5	6	7	8	
No. Animals per Dose Group	20	20	20	20	20	20	20	
KIDNEYS cont.d	20	20	20	20	20	20	20	
- Nephropathy	1	1	4	—	—	3	1	
- Pelvic Dilatation	—	1	—	—	—	—	—	
LIVER No.Examined	20	20	20	20	20	20	20	
- Angiectasis; Focal	—	—	—	1	—	—	—	
- Cyst; Multilocular; Bile	1	—	—	—	—	—	—	
- Focus/Foci; Basophilic Cell	4	5	2	2	1	1	5	
- Focus/Foci; Eosinophilic Cell	—	—	—	—	—	—	1	
- Hyperplasia; Bile Duct	—	—	—	—	1	1	—	
- Inflammation	6	9	6	1	6	10	4	
- Lipidosis; Focal	—	1	—	—	—	—	—	
- Pigment; Periportal	—	2	—	—	—	—	—	
LN MESENTERIC No.Examined	20	20	20	20	20	20	20	
LUNG No.Examined	20	20	20	20	20	20	20	
- Alveolar Macrophages; Increased	4	2	1	5	2	5	7	
- Inflammation	2	—	1	1	—	1	—	
- Pigmented Macrophages	—	—	1	1	—	—	—	
MAMMARY GLAND No.Examined	20	20	19	20	20	20	20	
- Galactoceles(s)	—	—	—	—	1	—	—	
- Hyperplasia	—	—	1	—	1	—	1	
- Inflammation	—	—	—	—	—	1	—	
- Lactation	—	—	1	—	—	—	—	
NOSE/TURBINATES No.Examined	20	20	20	20	20	20	20	
ORAL MUCOSA No.Examined	20	20	20	20	20	20	20	
OVARIES No.Examined	20	20	20	20	20	20	20	
- Atrophy	—	—	—	1	—	—	—	
- Cyst(s)	—	1	—	—	1	—	—	
- Cyst(s); Parovarian	2	—	—	2	—	—	1	
- Cystic Bursa	1	1	—	—	—	—	1	
- Decreased Corpora Lutea	7	10	14	16	13	13	15	
- Hematocyst(s)	—	—	—	—	1	—	—	
- Insufficient Tissue	—	1	—	—	—	—	—	
- Persistent Corpora Lutea	1	1	1	—	—	—	2	
- Pigment Deposition	—	—	—	1	—	—	—	
PANCREAS No.Examined	20	20	20	20	20	20	20	
- Atrophy; Acinar Cell	1	1	—	1	—	1	—	
PARATHYROID GLANDS No.Examined	17	20	19	16	20	18	16	
PHARYNX No.Examined	20	19	20	20	20	19	20	
PITUITARY GLAND No.Examined	20	20	20	20	20	18	20	
- Angiectasis	—	—	—	—	—	1	—	
- Cyst(s)	—	1	—	—	—	—	—	
- Hyperplasia; Pars Distalis	2	—	—	2	3	2	2	

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex		Females						
Dose Group No. Animals per Dose Group		1	3	4	5	6	7	8
		20	20	20	20	20	20	20
SALIVARY GLAND	No.Examined	20	20	20	20	20	20	20
- Atrophy		1	-	-	-	-	-	-
- Inflammation		1	-	-	-	-	-	-
SCIATIC NERVE	No.Examined	20	20	20	20	20	20	20
SKELETAL MUSCLE	No.Examined	20	20	20	20	20	20	20
SKIN	No.Examined	20	20	20	20	20	20	20
SKIN, OTHER	No.Examined	-	-	-	1	-	1	-
- Hyperkeratosis		-	-	-	-	-	1	-
SPINAL CORD	No.Examined	20	20	20	20	20	20	20
SPLEEN	No.Examined	20	20	20	20	20	20	20
- Increased Extramedullary Hematopoiesis		-	-	-	-	2	1	1
- Pigment Deposition		6	13	6	3	6	4	8
STOMACH	No.Examined	20	20	20	20	20	20	20
- Erosion; Glandular		1	-	-	-	-	-	-
- Inflammation		1	-	-	-	-	-	-
- Mineralization; Mucosa		-	-	-	-	-	3	-
- Mucosal Cyst; Non-Glandular		1	-	-	-	-	-	-
THYMUS	No.Examined	20	20	19	20	20	20	20
- Cyst(s)		4	4	8	1	5	6	5
THYROID GLAND	No.Examined	20	20	20	20	20	20	20
- Hyperplasia; C-Cell		1	-	-	2	-	-	-
- Hyperplasia; Follicular Cell		1	-	-	-	-	-	-
TONGUE	No.Examined	20	20	20	20	20	20	20
- Inflammation; Chronic		1	-	-	-	-	-	-
TRACHEA	No.Examined	20	20	20	20	20	20	20
URETERS	No.Examined	-	1	-	-	-	-	-
- Dilatation		-	1	-	-	-	-	-
- Hyperplasia; Urothelium		-	1	-	-	-	-	-
- Inflammation		-	1	-	-	-	-	-
URINARY BLADDER	No.Examined	20	20	20	20	20	19	20
- Calculi		-	1	-	-	-	-	-
- Hyperplasia; Urothelium		-	1	-	-	-	-	-
- Inflammation		-	1	-	-	-	-	-
UTERUS	No.Examined	20	20	20	20	20	20	20
- Cyst(s); Endometrial		1	4	1	1	1	2	-
- Dilatation		4	3	4	2	4	5	3
- Endometrial Hyperplasia; Cystic		1	-	4	1	1	1	-
- Fibrosis; Cervix		-	1	1	-	-	-	-
- Hyperplasia; Epithelial		-	-	1	-	-	-	-

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NON-NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex		Females						
Dose Group		1	3	4	5	6	7	8
No. Animals per Dose Group		20	20	20	20	20	20	20
VAGINA	No.Examined	20	20	20	20	20	19	20
- Metazoan Parasite		-	-	-	-	1	-	-
- Mucification		2	1	1	-	1	-	2
- Prolapse		-	-	-	-	-	-	1
ZYMBAL'S GLANDS	No.Examined	20	20	19	20	20	20	20
- Dilated Duct(s)		1	3	1	4	3	1	4

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
 Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
 Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
 Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
 Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
 Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
 Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

APPENDIX 4:
SUMMARY TABLES – NEOPLASTIC LESIONS

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SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex		Males						
Dose Group No. Animals per Dose Group		1 20	3 20	4 20	5 20	6 20	7 20	8 20
ADRENAL GLANDS	No. Examined	20	20	20	20	20	20	20
BONE, OTHER	No. Examined	—	—	—	1	1	—	—
— Osteosarcoma		—	—	—	—	1	—	—
BONE MARROW	No. Examined	20	20	20	20	20	20	20
BONE, FEMUR	No. Examined	20	20	20	20	20	20	20
BONE, STERNUM	No. Examined	20	20	20	20	20	20	20
BRAIN	No. Examined	20	20	20	20	20	20	20
CAUSE OF DEATH	No. Examined	—	—	—	1	—	—	—
EPIDIDYIMIDES	No. Examined	20	20	20	20	20	20	20
ESOPHAGUS	No. Examined	20	20	20	19	20	20	20
EYES	No. Examined	20	20	20	19	20	20	20
HARDERIAN GLANDS	No. Examined	20	20	20	20	20	20	20
— Malignant Schwannoma; Invasive		—	—	—	1	—	—	—
HEART	No. Examined	20	20	20	20	20	20	20
INTEST-LG, CECUM	No. Examined	20	20	20	19	20	20	20
INTEST-LG, COLON	No. Examined	20	20	20	19	20	20	20
INTEST-LG, RECTUM	No. Examined	20	20	20	20	20	20	20
INTEST-SM, DUODENUM	No. Examined	20	20	20	19	20	20	20
INTEST-SM, ILEUM	No. Examined	20	20	20	19	20	20	20
INTEST-SM, JEJUNUM	No. Examined	20	20	20	19	20	20	20
KIDNEYS	No. Examined	20	20	20	20	20	20	20
LIVER	No. Examined	20	20	20	20	20	20	20
LN MESENTERIC	No. Examined	20	20	20	20	20	20	20
— Hemangiosarcoma		—	—	—	—	—	1	1
LUNG	No. Examined	20	20	20	20	20	20	20
NOSE/TURBINATES	No. Examined	20	20	20	20	20	20	20
ORAL MUCOSA	No. Examined	20	20	20	20	20	20	20

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex	Males							
Dose Group	1	3	4	5	6	7	8	
No. Animals per Dose Group	20	20	20	20	20	20	20	
PANCREAS No. Examined	20	20	20	20	20	20	20	
PARATHYROID GLANDS No. Examined	15	19	19	11	19	20	14	
PHARYNX No. Examined	20	20	20	19	20	20	20	
PITUITARY GLAND No. Examined	20	18	19	20	18	18	20	
- Adenoma; Pars Distalis	-	1	-	-	-	1	-	
PREPUTIAL GLANDS No. Examined	20	20	19	20	20	20	20	
PROSTATE GLAND No. Examined	20	20	20	20	20	20	20	
SALIVARY GLAND No. Examined	20	20	20	19	20	20	20	
SCIATIC NERVE No. Examined	20	20	20	20	20	20	20	
SEMINAL VESICLES No. Examined	20	20	20	20	20	20	20	
SKEL MUSCLE, OTHER No. Examined	-	-	-	1	-	-	-	
- Malignant Schwannoma	-	-	-	1	-	-	-	
SKELETAL MUSCLE No. Examined	20	20	20	20	20	20	20	
SKIN No. Examined	20	20	20	20	20	20	20	
SKIN, OTHER No. Examined	1	3	-	-	3	1	1	
- Carcinoma; Sebaceous Gland	1	-	-	-	-	-	-	
SPINAL CORD No. Examined	20	20	20	20	20	20	20	
SPLEEN No. Examined	20	20	20	20	20	20	20	
STOMACH No. Examined	20	20	20	20	20	20	20	
TESTES No. Examined	20	20	20	20	20	20	20	
- Interstitial Cell Adenoma	-	-	-	-	-	1	-	
THYMUS No. Examined	20	19	19	19	18	19	20	
THYROID GLAND No. Examined	20	20	19	19	20	20	20	
- Adenoma; C-Cell	-	1	1	-	-	-	-	
TONGUE No. Examined	20	20	20	19	20	20	20	
TRACHEA No. Examined	20	20	20	20	20	20	20	
URINARY BLADDER No. Examined	20	20	20	20	19	20	20	

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

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CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData@System V6.2d2

NUMBER OF ANIMALS WITH NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths							
Sex	Males						
Dose Group	1	3	4	5	6	7	8
No. Animals per Dose Group	20	20	20	20	20	20	20
ZYMBAL'S GLANDS No. Examined	20	18	18	17	19	18	19
- Squamous Papilloma	-	-	1	-	-	-	-

Group 1, Control-A (C), males: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), males: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), males: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), males: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 4-4 / 5
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex		Females						
Dose Group No. Animals per Dose Group		1 20	3 20	4 20	5 20	6 20	7 20	8 20
ADRENAL GLANDS	No. Examined	20	20	20	20	20	20	20
BONE MARROW	No. Examined	20	20	20	20	20	20	20
BONE, FEMUR	No. Examined	20	20	20	20	20	20	20
BONE, STERNUM - Fibrolipoma	No. Examined	20 -	20 -	20 -	20 -	20 -	20 1	20 -
BRAIN	No. Examined	20	20	20	20	20	20	20
CAUSE OF DEATH	No. Examined	-	-	-	1	-	-	2
CLITORAL GLANDS	No. Examined	20	20	20	20	20	20	20
ESOPHAGUS	No. Examined	20	20	20	20	20	20	20
EYES	No. Examined	20	20	20	20	20	20	20
HARDERIAN GLANDS	No. Examined	20	20	20	20	20	20	20
HEART	No. Examined	20	20	20	20	19	20	20
INTEST-LG, CECUM	No. Examined	20	20	20	20	20	20	20
INTEST-LG, COLON	No. Examined	20	20	20	20	20	20	20
INTEST-LG, RECTUM	No. Examined	20	20	20	20	20	20	20
INTEST-SM, DUODENUM	No. Examined	20	20	20	20	20	20	20
INTEST-SM, ILEUM	No. Examined	20	20	20	20	20	20	20
INTEST-SM, JEJUNUM	No. Examined	20	20	20	20	20	20	20
KIDNEYS	No. Examined	20	20	20	20	20	20	20
LIVER	No. Examined	20	20	20	20	20	20	20
LN MESENTERIC	No. Examined	20	20	20	20	20	20	20
LUNG	No. Examined	20	20	20	20	20	20	20
MAMMARY GLAND - Adenocarcinoma - Fibroadenoma	No. Examined	20 - -	20 - -	19 - -	20 1 -	20 - -	20 - -	20 - 1
NOSE/TURBINATES	No. Examined	20	20	20	20	20	20	20
ORAL MUCOSA	No. Examined	20	20	20	20	20	20	20

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

PATHOLOGY REPORT
SUMMARY TABLES

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

NUMBER OF ANIMALS WITH NEOPLASTIC LESIONS BY ORGAN/GROUP/SEX Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Incl. Deaths								
Sex	Females							
Dose Group No. Animals per Dose Group	1 20	3 20	4 20	5 20	6 20	7 20	8 20	
OVARIES No. Examined	20	20	20	20	20	20	20	20
PANCREAS No. Examined	20	20	20	20	20	20	20	20
PARATHYROID GLANDS No. Examined	17	20	19	16	20	18	16	
PHARYNX No. Examined	20	19	20	20	20	19	20	
PITUITARY GLAND No. Examined - Adenoma; Pars Distalis	20 -	20 -	20 1	20 1	20 -	18 -	20 -	
SALIVARY GLAND No. Examined	20	20	20	20	20	20	20	20
SCIATIC NERVE No. Examined	20	20	20	20	20	20	20	20
SKELETAL MUSCLE No. Examined	20	20	20	20	20	20	20	20
SKIN No. Examined	20	20	20	20	20	20	20	20
SKIN, OTHER No. Examined - Adenoma; Sebaceous Gland	- -	- -	- -	1 1	- -	1 -	- -	
SPINAL CORD No. Examined	20	20	20	20	20	20	20	20
SPLEEN No. Examined	20	20	20	20	20	20	20	20
STOMACH No. Examined	20	20	20	20	20	20	20	20
THYMUS No. Examined	20	20	19	20	20	20	20	20
THYROID GLAND No. Examined - Carcinoma; Follicular Cell	20 -	20 -	20 -	20 -	20 -	20 1	20 -	
TONGUE No. Examined	20	20	20	20	20	20	20	20
TRACHEA No. Examined	20	20	20	20	20	20	20	20
URETERS No. Examined	-	1	-	-	-	-	-	-
URINARY BLADDER No. Examined	20	20	20	20	20	19	20	
UTERUS No. Examined - Stromal Polyp - Stromal Polyp; Cervix - Stromal Sarcoma; Cervix	20 1 - -	20 - - -	20 - - -	20 - - -	20 - - -	20 - - -	20 - - -	20 1 1 1
VAGINA No. Examined - Stromal Polyp	20 -	20 1	20 -	20 -	20 -	19 -	20 -	
ZYMBAL'S GLANDS No. Examined	20	20	19	20	20	20	20	20

Group 1, Control-A (C), females: Tobacco Blend & Aqueous Tobacco Extract (0 mg/kg/day)
Group 3, Tobacco Blend Low Dose (B0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 4, Tobacco Blend Intermed (B2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 5, Tobacco Blend High Dose (B5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)
Group 6, Tobacco Extract Low (E0.2), females: Tobacco Blend & Aqueous Tobacco Extract (0.2 mg/kg/day)
Group 7, Tobacco Extract Intermed (E2), females: Tobacco Blend & Aqueous Tobacco Extract (2 mg/kg/day)
Group 8, Tobacco Extract High Dose (E5), females: Tobacco Blend & Aqueous Tobacco Extract (5 mg/kg/day)

APPENDIX 5:
TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 1, Control-A (C)

ANIMAL NUMBER :

	101 MK0	102 MK0	103 MK0	104 MK0	105 MK0	106 MK0	107 MK0	108 MK0	109 MK0	110 MK0
ADRENAL GLANDS	:	-	-	-	-	-	-	-	+	-
- Hypertrophy; Cortex	:	(1.	.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
EPIDIDYIMIDES	:	-	-	-	-	-	-	-	+	-
- Hypospermia	:	4.	.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	-
HARDERIAN GLANDS	:	-	-	-	+	-	-	-	-	-
- Inflammation.	:	.	.	.	1.
HEART	:	-	-	-	-	-	-	+	+	-
- Cardiomyopathy	:	1.	2.	.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	+	-	+	+	-	+	-	+
- Nephropathy	:	.	1.	.	1.	1.	.	1.	.	1.
- Pelvic Dilatation	:	.	(1.
LIVER	:	+	+	+	+	-	+	+	-	+
- Focus/Foci; Basophilic Cell.	:	.	1.	.	.	.	1.	.	.	.
- Inflammation.	:	1.	.	.	1.	.	.	1.	.	1.
- Pigment; Periportal	:	.	.	2.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	+	+	-	-	-	-	-	-
- Alveolar Macrophages; Increased	:	.	1.	1.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	+	-
- Inflammation.	:	1.	.
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	-	-	-	0	-	-	0	0

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1. Control-A (C)

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 1, Control-A (C)

ANIMAL NUMBER :

	111	112	113	114	115	116	117	118	119	120
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PITUITARY GLAND	:	-	-	+	-	-	-	-	-	-
- Hyperplasia; Pars Distalis	:	.	.	2.
PREPUTIAL GLANDS	:	-	+	+	-	+	-	+	+	+
- Inflammation.	:	.	2.	2.	.	1.	1.	.	1.	1.
PROSTATE GLAND	:	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-G	-	-	-	-	-	-	-	-
SKIN, OTHER	:	+	+	+	+	+	+	+	+	+
- Carcinoma; Sebaceous Gland	:	N0.								
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	+	-	(-	-	+	+	-	-
- Dilated Duct(s).	:	.	(P.	.	.	.	(P.	(P.	.	.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM      : Tobacco Blend & Aqueous Tobacco E  PATHOL. NO.: 90279 DAB
TEST SYSTEM    : RAT, 1-Year, Orally in feed        DATE       : 08-FEB-13
SPONSOR        : EPL Archives, Inc.                 PathData@System V6.2d2

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)

DOSE GROUP : 1, Control-A (C)

ANIMAL NUMBER :

[illegible]

Organ	1	2	3	4	5	6	7	8	9	10
ADRENAL GLANDS							+			
- Angiectasis; Cortex							2.			
BONE MARROW							-			
BONE, FEMUR							-			
BONE, STERNUM							-			
BRAIN							-			
CLITORAL GLANDS			+				+			
- Inflammation.			3.				2.			
ESOPHAGUS			-				-			
EYES			+				-			
- Degeneration; Retina			2.							
HARDERIAN GLANDS			-				-	+		
- Inflammation.								(1.		
HEART			-				+			+
- Cardiomyopathy							1.			1.
INTEST-LG, CECUM			-				-			
INTEST-LG, COLON			-				-			
INTEST-LG, RECTUM			+				-			+
- Metazoan Parasites.			P.							P.
INTEST-SM, DUODENUM			-				-			
INTEST-SM, ILEUM			-				-			
INTEST-SM, JEJUNUM			-				-			
KIDNEYS			-			+	-			
- Nephropathy						1.				
LIVER		+	G	-	+	+	-	+	+	+
- Cyst; Multilocular; Bile.		P.								
- Focus/Foci; Basophilic Cell.								1.		
- Inflammation.				1.	1.		1.		1.	
LN MESENTERIC			-				-			
LUNG		+		-			+		+	
- Alveolar Macrophages; Increased		1.							1.	
- Inflammation.							1.			
MAMMARY GLAND			-				-			
NOSE/TURBINATES			-				-			
ORAL MUCOSA			-				-			

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-6 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 1, Control-A (C)

ANIMAL NUMBER :

	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
OVARIES	:	+	-	+	-	+G	-	+	-	+
- Cyst(s); Parovarian	:	(P.
- Decreased Corpora Lutea	:	P.	.	P.	.	.	P.	.	.	P.
PANCREAS	:	-	-	-	-	-	+	-	-	-
- Atrophy; Acinar Cell	:	1.	.	.	.
PARATHYROID GLANDS	:	-	-	-	-	(-	0	-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	+	-	-	-
- Hyperplasia; Pars Distalis	:	1.	.	.	.
SALIVARY GLAND	:	-	-	-	-	+	-	-	-	-
- Atrophy	:	(1.
- Inflammation.	:	(1.
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	-	-	-	-	-	-	+	+
- Pigment Deposition.	:	1.	2.	1.
STOMACH	:	-	-	-	-	-	+G	-	-	-
- Mucosal Cyst; Non-Glandular.	:	P.	.	.	.
THYMUS	:	-	+	-	-	+	-	-	-	-
- Cyst(s)	:	.	P.	.	.	P.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	+	-
- Inflammation; Chronic.	:	1.	.
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	+	+	-	+	-	+	-	-
- Dilatation	:	.	3.	.	.	3.	.	.	2.	.
- Stromal Polyp	:	.	.	B0.
VAGINA	:	-	-	-	-	+	-	-	-	-
- Mucification.	:	P.
ZYMBAL'S GLANDS	:	-	-	-	-	(-	-	-	-	-

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 1, Control-A (C)

ANIMAL NUMBER :

	1111 FK0	1112 FK0	1113 FK0	1114 FK0	1115 FK0	1116 FK0	1117 FK0	1118 FK0	1119 FK0	1120 FK0	
OVARIES	:	-	+	-	+G	-	-	-	+G	+	+
- Cyst(s); Parovarian	:	(P.	.	.	.
- Cystic Bursa.	:	.	.	.	P.
- Decreased Corpora Lutea	:	.	P.	.	P.	P.
- Persistent Corpora Lutea.	:	P.	.	.
PANCREAS	:	-	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	-	(-	0	-	0	-	-	(-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	-	+	-
- Hyperplasia; Pars Distalis	:	2.	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	+	-	+	-	-	+
- Pigment Deposition.	:	1.	.	1.	.	.	1.
STOMACH	:	-	+	-	-	-	-	-	-	-	-
- Erosion; Glandular.	:	.	1.
- Inflammation.	:	.	1.
THYMUS	:	-	-	-	+	+	-	-	-	-	-
- Cyst(s)	:	.	.	.	P.	P.	-	.	.	.	-
THYROID GLAND	:	-	+	-	-	-	-	-	-	+	-
- Hyperplasia; C-Cell	:	(2.	.	.
- Hyperplasia; Follicular Cell	:	.	(1.
TONGUE	:	-	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	+	-	-	+	-	-	-	+
- Cyst(s); Endometrial	:	.	.	P.
- Dilatation	:	1.
- Endometrial Hyperplasia; Cystic	:	2.
VAGINA	:	-	-	-	-	-	-	-	-	+	-
- Mucification.	:	P.	.
ZYMBAL'S GLANDS	:	-	-	-	-	-	-	(+	-	-	-
- Dilated Duct(s).	:	(P.	.	.	.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	301	302	303	304	305	306	307	308	309	310
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
ADRENAL GLANDS	:	-	-	-	-	-	-	-	-	-
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES	:	-	-	-	-	-	-	-	-	-
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	-
HARDERIAN GLANDS	:	-	-	-	+	-	-	-	-	-
- Inflammation.	:	.	.	.	(1.
HEART	:	+	-	+	+	-	-	+	+	-
- Cardiomyopathy	:	1.	.	1.	1.	.	.	1.	1.	.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	+	+	-	+	-	+	-	-	+
- Inflammation; Pelvic	:	.	.	.	(2.
- Nephropathy	:	1.	1.	.	.	1.	.	.	.	1.
LIVER	:	+	-	+	+	+	+	-	+	+
- Focus/Foci; Basophilic Cell	:	.	.	.	1.	.	1.	.	1.	.
- Hyperplasia; Bile Duct	:	1.
- Inflammation	:	1.	.	1.	.	1.	1.	.	.	.
- Lipidosis; Focal	:	1.
- Tension Lipidosis	:	.	.	.	2.	.	1.	.	.	.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	+	+	-	+	-	-	-
- Alveolar Macrophages; Increased	:	.	.	1.
- Osseous Metaplasia	:	.	.	.	P.	.	P.	.	.	.
NOSE/TURBINATES	:	+	-	-	-	-	-	-	-	-
- Cyst(s); Mucosa	:	P.
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	+	-	-	-	-	-	-	-	-
- Atrophy; Acinar Cell	:	1.

PATHOLOGY REPORT
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	301	302	303	304	305	306	307	308	309	310
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PARATHYROID GLANDS	:	-	-	(-	0	-	-	-	(-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	0	-
PREPUTIAL GLANDS	:	+	-	+	-	+	+	-	-	+
- Inflammation.	:	(2.	-	(1.	-	(1.	1.	-	-	(1.
PROSTATE GLAND	:	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	+	-	-	-	-	-
- Interstitial Fluid.	:	-	-	-	(2.	-	-	-	-	-
THYMUS	:	-	-	-	-	+	-	-	0G	+
- Cyst(s)	:	-	-	-	-	P.	-	-	-	P.
THYROID GLAND	:	-	-	(-	-	+	-	-	-	-
- Adenoma; C-Cell.	:	-	-	-	-	(B0.	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	-	-	-	0	-	(-	-	-

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PAGE : 5-11 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	311	312	313	314	315	316	317	318	319	320
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
ADRENAL GLANDS	:	-	-	+	-	-	-	-	-	-
- Hypertrophy; Cortex	:	.	.	(1.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
EPIDIDYIMIDES	:	-	-	-	-	-	-	-	-	-
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	+	-	-	-	-	-	-	-	-
- Degeneration; Retina	:	1.
HARDERIAN GLANDS	:	-	-	-	-	-	-	-	-	-
HEART	:	-	-	+	-	-	-	-	-	-
- Cardiomyopathy	:	.	.	1.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	+	-	+	-	-	-	-	-	+
- Inflammation; Pelvic	:	1.
- Nephropathy	:	1.	.	1.
LIVER	:	+	+	+	+	+	+	+	+	+
- Hyperplasia; Bile Duct	:	.	.	.	1.
- Inflammation.	:	1.	1.	1.	1.	1.	1.	1.	1.	1.
- Lipidosis; Periportal.	:	.	.	.	1.
- Tension Lipidosis	:	.	.	2.	.	.	1.	.	1.	.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	-	+	-	-	+	-	-
- Inflammation.	:	.	.	.	1.
- Pigmented Macrophages.	:	2.	.	.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	-	-	-	-	+	-	-	-	-
- Atrophy; Acinar Cell	:	1.
PARATHYROID GLANDS	:	-	-	-	-	(-	-	-	-	-

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	311	312	313	314	315	316	317	318	319	320
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	0	+	-	-	+	-	-
- Adenoma; Pars Distalis	:	B0.	.	.
- Hyperplasia; Pars Distalis	:	.	.	.	1.
PREPUTIAL GLANDS	:	+	-	+	-	+	-	+	+	+
- Inflammation.	:	2.	.	(2.	.	2.	.	(1.	1.	(1.
PROSTATE GLAND	:	+	-	+	-	-	-	-	-	-
- Inflammation.	:	1.	.	1.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-G	-G	-	-G	-	-	-	-	-
SKIN, OTHER	:	+	+	.	+
- Fat Infiltration	:	.	.	.	P.
- Hyperkeratosis	:	2.	2.
- Inflammation.	:	2.	1.
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	+	-	-	-	-	-
- Pigment Deposition.	:	.	.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	(-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	0	(-	-	-	-	-	+	+	-
- Dilated Duct(s).	:	P.	(P.	.

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INDIVIDUAL ANIMAL DATA

PAGE : 5-14 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
OVARIES	:	+	-	+	-	(+	-	(+
- Decreased Corpora Lutea	:	.	.	P.	(P.
- Insufficient Tissue	:	(P.	.	.	.
- Persistent Corpora Lutea.	:	P.
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	-	-	-	-	-	-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	+	+	-	-	+	-	-	+
- Pigment Deposition.	:	1.	1.	1.	.	.	1.	.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	+	-	-	-	+
- Cyst(s)	:	P.	.	.	P.	.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URETERS	:	+G
- Dilatation	:	(4.
- Hyperplasia; Urothelium	:	(4.
- Inflammation.	:	(2.
URINARY BLADDER	:	+G	-	-	-	-	-	-	-	-
- Calculi	:	P.
- Hyperplasia; Urothelium	:	3.
- Inflammation.	:	2.
UTERUS	:	-	+	+	+	-	-	+	+	+G
- Cyst(s); Endometrial	:	.	P.	(P.	(P.	.	.	P.
- Dilatation	:	.	.	.	2.	.	.	2.	2.	.
- Fibrosis; Cervix	:	4.
VAGINA	:	+	-	-	-	-	-	-	-	+G
- Mucification.	:	P.
- Stromal Polyp	:	B0.
ZYMBAL'S GLANDS	:	-	+	-	-	-	-	-	-	-
- Dilated Duct(s).	:	.	(P.

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INDIVIDUAL ANIMAL DATA

PAGE : 5-15 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	1311	1312	1313	1314	1315	1316	1317	1318	1319	1320
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	-	+	-	+	-	+	-	+	-
- Angiectasis; Cortex	:	.	2.	.	1.	.	1.	.	2.	(1.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	+	-	-	-	-	-	+	-	-
- Inflammation.	:	(1.	(1.	.	.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	+	-	-	-	-	-
- Degeneration; Retina	:	.	.	.	1.
HARDERIAN GLANDS	:	-	-	-	-	-	-	-	-	-
HEART	:	-	-	-	-	-	-	-	-	-
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	-	+	-	-	+	-	+
- Mineralization; Pelvic	:	(2.	.	(1.
- Nephropathy	:	.	.	.	1.
LIVER	:	+	-	-	+	+	+	+	-	+
- Focus/Foci; Basophilic Cell.	:	1.	1.	.	1.	.
- Inflammation.	:	1.	.	.	.	1.	1.	1.	.	1.
- Pigment; Periportal	:	.	.	.	4.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	-	-	-	-	+	+	-
- Alveolar Macrophages; Increased	:	1.	1.	.
MAMMARY GLAND	:	-	-	-	-	-	-	-	-	-
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	+G	+	+G	+	-	-	+	+	-
- Cyst(s)	:	.	.	(P.
- Cystic Bursa.	:	P.
- Decreased Corpora Lutea	:	P.	P.	P.	P.	.	.	P.	P.	.

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 3, Tobacco Blend Low Dose (B0.2)

ANIMAL NUMBER :

	1311	1312	1313	1314	1315	1316	1317	1318	1319	1320
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PANCREAS	:	-	-	-	-	+	-	-	-	-
- Atrophy; Acinar Cell	:	1.
PARATHYROID GLANDS	:	-	(-	-	-	-	(-	-	-	(-
PHARYNX	:	0	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	+	-	-	-
- Cyst(s)	:	P.	.	.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	-	+	-	+	+	+	+	+
- Pigment Deposition.	:	2.	.	1.	.	1.	1.	1.	2.	2.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	+	-	-	+
- Cyst(s)	:	P.	.	.	P.
THYROID GLAND	:	-	(-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	-	-	-	-	-	-	-
VAGINA	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	(+	(-	-	-	-	-	-	+
- Dilated Duct(s).	:	.	(P.	(P.

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, Tobacco Blend Intermed (B2)

[illegible]

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

	401	402	403	404	405	406	407	408	409	410
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PITUITARY GLAND	:	-	0	-	-	-	-	-	-	-
PREPUTIAL GLANDS	:	+	+	+	-	+	+	+	-	+
- Inflammation.	:	1.	(2.	1.	(2.	(1.	(2.	.	(1.	.
PROSTATE GLAND	:	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	+G	-	-	-	-
- Atrophy	:	1.
THYROID GLAND	:	0	-	(-	-	-	-	+	(-	-
- Adenoma; C-Cell.	:	(B0.	.	.
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	+	+	(-	(-	0	-	(-	-	(-
- Dilated Duct(s).	:	P.	(P.	(P.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)

DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

	411	412	413	414	415	416	417	418	419	420
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
ADRENAL GLANDS	:	-	-	-	-	-	+	-	-	-
- Vacuolation; Cortex	:	(1.	.	.	.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
EPIDIDYIMIDES	:	-	-	-	-	-	-	-	-	+
- Aspermia	:	(P.	.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	+	-	-	-	-	-	-	-
- Degeneration; Retina	:	.	1.
HARDERIAN GLANDS	:	-	-	-	-	-	-	-	-	-
HEART	:	-	-	-	-	-	-	-	-	-
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	+	-	-	-	-	-	-
- Metazoan Parasite	:	.	.	P.
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	+	-	-	+	-	-	-	+
- Cyst(s)	:	.	.	.	(P.
- Nephropathy	:	.	1.	1.
LIVER	:	-	+	+	-	+	-	+	-	+
- Focus/Foci; Basophilic Cell.	:	.	.	1.
- Inflammation.	:	.	1.	1.	.	1.	.	1.	.	.
- Tension Lipidosis	:	2.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	+	-	+	-	-	-	-
- Alveolar Macrophages; Increased	:	.	.	1.	.	2.
- Inflammation.	:	1.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	-	-	-	-	-	-	-	-	+
- Atrophy; Acinar Cell	:	2.
PARATHYROID GLANDS	:	(-	-	-	(-	-	(-	-	-	-

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TEST ITEM      : Tobacco Blend & Aqueous Tobacco E  PATHOL. NO.: 90279 DAB
TEST SYSTEM    : RAT, 1-Year, Orally in feed        DATE       : 08-FEB-13
SPONSOR        : EPL Archives, Inc.                 PathData@System V6.2d2

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DOSE GROUP : 4, Tobacco Blend Intermed (B2)

[illegible]

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TEST ITEM      : Tobacco Blend & Aqueous Tobacco E  PATHOL. NO.: 90279 DAB
TEST SYSTEM    : RAT, 1-Year, Orally in feed        DATE       : 08-FEB-13
SPONSOR        : EPL Archives, Inc.                 PathData@System V6.2d2

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DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

[illegible][illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

	1401 FK0	1402 FK0	1403 FK0	1404 FK0	1405 FK0	1406 FK0	1407 FK0	1408 FK0	1409 FK0	1410 FK0	
PARATHYROID GLANDS	:	-	(-	-	(-	0	-	(-
PHARYNX	:	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	+	-	+	-	-	-	-
- Pigment Deposition.	:	.	.	.	2.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-	-
THYMUS	:	0	+	+	-	-	+	-	+	+	+
- Cyst(s)	:	.	P.	P.	.	.	P.	.	P.	P.	P.
THYROID GLAND	:	-	(-	-	-	(-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	-	+	+	-	+	+	-	-
- Cyst(s); Endometrial	:	.	.	.	(P.
- Dilatation	:	3.	.	.	(1.	.
- Endometrial Hyperplasia; Cystic	:	(2.	.	.
VAGINA	:	-	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	(-	-	0	(-	-	-	-	-

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-23 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

	1411	1412	1413	1414	1415	1416	1417	1418	1419	1420
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	-	-	-	-	-	+	-	-	-
- Angiectasis; Cortex	:	(2.	.	.	.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	-	-	+	+	-	+	-	-	-
- Inflammation.	:	.	(1.	1.	.	(1.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	+	-
- Degeneration; Retina	:	1.	.	.
HARDERIAN GLANDS	:	-	-	-	-	-	-	+	-	-
- Inflammation.	:	(1.	.	.	.
HEART	:	-	-	-	-	-	-	-	-	-
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	+	-	-
- Metazoan Parasites.	:	P.	.	.
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	-	-	+	+	-	-	-
- Nephropathy	:	.	.	.	1.	1.
LIVER	:	-	-	-	+	-	+	-	+	-
- Inflammation.	:	.	.	1.	.	.	1.	.	1.	.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	-	-	+	-	-	-	-
- Inflammation.	:	1.
MAMMARY GLAND	:	-	-	-	-	-	+	-	+	-
- Hyperplasia	:	1.	.
- Lactation.	:	1.	.	.	.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	+	-	+	+	+	+	+	+	-
- Decreased Corpora Lutea	:	P.	.	P.	P.	P.	.	P.	P.	.
- Persistent Corpora Lutea.	:	P.

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, Tobacco Blend Intermed (B2)

ANIMAL NUMBER :

	1411	1412	1413	1414	1415	1416	1417	1418	1419	1420
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	-	-	-	-	-	(-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	+G	-
- Adenoma; Pars Distalis	:	B0.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	-	-	-	+	-	-	+	-
- Pigment Deposition.	:	2.	.	.	.	1.	.	1.	1.	.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	+	-	-	+	+	-	-	-	-
- Cyst(s)	:	P.	.	.	P.	P.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	+G	+	-	-	-	+	+	-	+
- Dilatation	:	.	2.	(2.
- Endometrial Hyperplasia; Cystic	:	.	1.	.	.	.	1.	1.	.	.
- Fibrosis; Cervix	:	3.
- Hyperplasia; Epithelial	:	2.
VAGINA	:	-	-	-	-	-	+	-	-	-
- Mucification.	:	P.	.	.	.
ZYMBAL'S GLANDS	:	+	-	-	-	-	-	(-	-	-
- Dilated Duct(s).	:	(P.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-25 / 56
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	501 MK0	502 MK0	503 MK0	504 MK0+	505 MK0	506 MK0	507 MK0	508 MK0	509 MK0	510 MK0
ADRENAL GLANDS	:	+	-	-	+	-	-	-	-	+
- Hypertrophy; Cortex	:	.	.	.	(1.
- Vacuolation; Cortex	:	(1.	(1.
BONE, OTHER	:	.	.	.	+G
- Hemorrhage	:	.	.	.	2.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CAUSE OF DEATH	:	.	.	.	+
- Malignant Schwannoma	:	.	.	.	P.
EPIDIDYIMIDES	:	+	-	-	-	-	-	-	-	-
- Aspermia	:	(P.
ESOPHAGUS	:	-	-	-	0	-	-	-	-	-
EYES	:	-	-	-	(A	-	-	-	-	-
HARDERIAN GLANDS	:	-	-	-	(+	-	-	-	-	-
- Malignant Schwannoma; Invasive.	:	.	.	.	M58.
HEART	:	+	+	+	-	-	-	-	+	-
- Cardiomyopathy	:	1.	1.	1.	1.	.
INTEST-LG, CECUM	:	-	-	-	A	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	A	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	A	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	A	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	A	-	-	-	-	-
KIDNEYS	:	-	-	-	+G	-	-	+	+	-
- Nephropathy	:	1.	1.	.	.
- Pelvic Dilatation	:	.	.	.	(2.
LIVER	:	-	-	+	-	+	-	-	-	+
- Focus/Foci; Basophilic Cell.	:	1.
- Focus/Foci; Clear Cell	:	1.
- Hyperplasia; Bile Duct	:	.	.	1.
- Inflammation.	:	.	.	1.	1.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	+	+	-	-	-	-	-	-
- Alveolar Macrophages; Increased	:	.	1.	1.

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INDIVIDUAL ANIMAL DATA

PAGE : 5-26 / 56
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	501 MK0	502 MK0	503 MK0	504 MK0+	505 MK0	506 MK0	507 MK0	508 MK0	509 MK0	510 MK0
NOSE/TURBINATES	:	-	-	+	-	-	-	-	-	-
- Hemorrhage	:	.	.	1.
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	-	-	-	-	-	+	-	-	-
- Atrophy; Acinar Cell	:	1.	.	.	.
PARATHYROID GLANDS	:	-	-	0	-	-	-	-	0	0
PHARYNX	:	-	+	-	A	-	-	-	-	-
- Inflammation.	:	.	1.
PITUITARY GLAND	:	-	-	+	-	-	-	-	-	-
- Hyperplasia; Pars Distalis	:	.	.	1.
PREPUTIAL GLANDS	:	-	+	-	+	-	-	-	-	+
- Inflammation.	:	.	1.	(2.	1.	.	.	.	1.
PROSTATE GLAND	:	+	-	-	-	-	-	-	-	+
- Inflammation; Chronic.	:	1.	1.
SALIVARY GLAND	:	-	-	-	0	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKEL MUSCLE, OTHER	:	.	.	.	+
- Malignant Schwannoma	:	.	.	N4.
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	+	-	-	-	-	-
- Lymphoid Depletion.	:	.	.	.	3.
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	+G	-	-	-	-	-	-	-	-
- Atrophy	:	(3.
THYMUS	:	-	-	-	0	-	-	-	-	-
THYROID GLAND	:	-	-	-	0	-	+	-	-	-
- Follicular Cyst(s).	:	(P.	.	.
TONGUE	:	-	-	-	0	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	+	-	-
- Hemorrhage; Mucosa.	:	2.	.	.
ZYMBAL'S GLANDS	:	-	-	-	0	-	(0	-	(

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 5, Tobacco Blend High Dose (B5)

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-28 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	511	512	513	514	515	516	517	518	519	520
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PITUITARY GLAND	:	-	+	-	-	-	-	-	+	-
- Hyperplasia; Pars Distalis	:	.	3.	3.	.
PREPUTIAL GLANDS	:	(-	-	-	+	+	+	+	+
- Inflammation.	:	1.	(1.	1.	2.	1.
PROSTATE GLAND	:	-	-	-	-	-	-	-	+	-
- Inflammation; Chronic.	:	1.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	+	-	-	-	+	-	-	-	-
- Inflammation.	:	1.
- Mucosal Cyst; Glandular	:	P.
TESTES	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	0	-	(-	(+	-	-	-
- Dilated Duct(s).	:	(P.	.	.	.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-29 / 56
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	1501	1502	1503	1504	1505	1506	1507	1508	1509	1510
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	-	-	-	-	-	-	-	-	-
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	+	-	-	-	-	-	-	-	-
- Inflammation.	:	1.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	-
HARDERIAN GLANDS	:	-	-	+	-	-	-	-	-	-
- Inflammation.	:	.	.	(1.
HEART	:	-	-	-	-	-	-	-	+	-
- Cardiomyopathy	:	1.	.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	+	-	-	-	-	-	-
- Mineralization; Pelvic	:	.	.	1.
LIVER	:	-	-	+	-	-	-	-	-	+
- Focus/Foci; Basophilic Cell.	:	.	.	1.
- Inflammation.	:	1.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	+	+	+	-	-	+	-	-	-
- Alveolar Macrophages; Increased	:	1.	1.	1.	.	.	1.	.	.	.
- Inflammation.	:	1.
- Pigmented Macrophages.	:	.	1.
MAMMARY GLAND	:	-	-	-	-	-	-	-	-	-
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	+	+	-	+G	+	+	+	+	+
- Cyst(s); Parovarian	:	.	.	.	P.
- Decreased Corpora Lutea	:	P.	P.	.	P.	P.	P.	P.	P.	P.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	1501	1502	1503	1504	1505	1506	1507	1508	1509	1510
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PANCREAS	:	-	+	-	-	-	-	-	-	-
- Atrophy; Acinar Cell	:	.	1.
PARATHYROID GLANDS	:	(-	-	0	-	-	0	-	0
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	+G	-	-	-	-	+	-
- Adenoma; Pars Distalis	:	.	.	B0.
- Hyperplasia; Pars Distalis	:	2.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-G	-	-	-	-	-
SKIN, OTHER	:	.	.	.	+
- Adenoma; Sebaceous Gland.	:	.	.	.	B0.
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	+	-	-
- Cyst(s)	:	P.	.	.
THYROID GLAND	:	-	-	-	+	-	-	-	-	-
- Hyperplasia; C-Cell	:	.	.	.	(2.
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	-	-	+	-	-	-	+
- Dilatation	:	3.
- Endometrial Hyperplasia; Cystic	:	2.
VAGINA	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	(-	-	(-	-	-	(-

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 5, Tobacco Blend High Dose (B5)

1511	1512	1513	1514	1515	1516	1517	1518	1519	1520
FK0	FK0	FK0	FK0	FK0	FK0+	FK0	FK0	FK0	FK0

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 5, Tobacco Blend High Dose (B5)

ANIMAL NUMBER :

	1511	1512	1513	1514	1515	1516	1517	1518	1519	1520
	FK0	FK0	FK0	FK0	FK0	FK0+	FK0	FK0	FK0	FK0
OVARIES	:	+	+	+	+	+	+G	-	+	-
- Atrophy	:	(2.	.
- Cyst(s); Parovarian	:	P.	.	.	.
- Decreased Corpora Lutea	:	P.	P.	P.	P.	P.	.	P.	(P.	.
- Pigment Deposition.	:	(2.	.
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	(-	(-	(-	-	(-	-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	-	+G
- Hyperplasia; Pars Distalis	:	2.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	-	-	-	-	-	+	+	-
- Pigment Deposition.	:	1.	1.	1.	.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	+	-	-	-	-	-	-
- Hyperplasia; C-Cell	:	.	.	(2.
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	-	+	-	-	-	-	+
- Cyst(s); Endometrial	:	.	.	.	P.
- Dilatation	:	2.
VAGINA	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	-	(+	+	-	+	+	(-	-
- Dilated Duct(s).	:	.	.	(P.	(P.	.	P.	(P.	.	.

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CN49730G (770-004)

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 6, Tobacco Extract Low (E0.2)

[illegible]

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TEST ITEM      : Tobacco Blend & Aqueous Tobacco E  PATHOL. NO.: 90279 DAB
TEST SYSTEM    : RAT, 1-Year, Orally in feed        DATE       : 08-FEB-13
SPONSOR        : EPL Archives, Inc.                 PathData@System V6.2d2

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DOSE GROUP : 6, Tobacco Extract Low (E0.2)

ANIMAL NUMBER :

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 6, Tobacco Extract Low (E0.2)

ANIMAL NUMBER :

	611 MK0	612 MK0	613 MK0	614 MK0	615 MK0	616 MK0	617 MK0	618 MK0	619 MK0	620 MK0
PARATHYROID GLANDS	:	-	-	-	-	-	-	(-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	+	-	-	-
- Cyst(s)	:	P.	.	.	.
PREPUTIAL GLANDS	:	+	+	-	-	+	-	+	+	+
- Inflammation.	:	(1.	1.	.	(2.	.	(3.	.	(1.	1.
PROSTATE GLAND	:	-	-	-	-	-	-	-	-	+
- Inflammation.	:	1.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-G	-	-	-	-	-	-	-
SKIN, OTHER	:	!	+	!	!	!	!	!	!	!
- Hyperplasia; Sebaceous Gland	:	.	1.
SPINAL CORD	:	-	-	-	-	-	-	-G	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	+	-	-	-	-	-	-
- Atrophy	:	.	.	3.
THYMUS	:	-	-	-	-	-	-	-	-	0
THYROID GLAND	:	-	-	-	-	-	-	(-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	-	-	(-	+	-	(-	(-	(-
- Dilated Duct(s)	:	(P.

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 6, Tobacco Extract Low (E0.2)

[illegible]

ADRENAL GLANDS		:	-	+	-	-	+	-	+	+	-	+
- Angiectasis; Cortex		:	1.	.	1.	1.	1.	.
- Hypertrophy; Cortex		:	.	(1.
- One Medulla Examined		:	P.	.
.....												
BONE MARROW		:	-	-	-	-	-	-	-	-	-	-
.....												
BONE, FEMUR		:	-	-	-	-	-	-	-	-	-	-
.....												
BONE, STERNUM		:	-	-	-	-	-	-	-	-	-	-
.....												
BRAIN		:	-	-	-	-	-	-	-	-	-	-
.....												
CLITORAL GLANDS		:	-	+	-	-	+	+	+	-	-	-
- Inflammation.		:	.	(2.	.	(1.	1.	2.	.	.
.....												
ESOPHAGUS		:	-	-	-	-	-	-	-	-	-	-
.....												
EYES		:	+	-	-	-	-	+	-	+	-	-
- Degeneration; Retina		:	1.	1.	.	1.	.	.
.....												
HARDERIAN GLANDS		:	-	-	-	-	+	+	-	-	-	-
- Inflammation.		:	(1.	(1.	.	.
.....												
HEART		:	-	-	-	-	-	-	-	-	-	+
- Cardiomyopathy		:	2.
.....												
INTEST-LG, CECUM		:	-	-	-	-	-	-	-	-	-	-
.....												
INTEST-LG, COLON		:	-	-	-	-	-	-	-	-	-	-
.....												
INTEST-LG, RECTUM		:	-	-	-	-	-	-	-	-	-	-
.....												
INTEST-SM, DUODENUM		:	-	-	-	-	-	-	-	-	-	-
.....												
INTEST-SM, ILEUM		:	-	-	-	-	-	-	-	-	-	-
.....												
INTEST-SM, JEJUNUM		:	-	-	-	-	-	-	-	-	-	-
.....												
KIDNEYS		:	-	-	-	-	-	-	+	-	-	-
- Mineralization; Pelvic		:	1.	.	.	.
.....												
LIVER		:	-	+	+	-	-	-	+	-	-	-
- Focus/Foci; Basophilic Cell.		:	.	.	1.
- Hyperplasia; Bile Duct		:	.	1.
- Inflammation.		:	.	.	1.	.	.	.	1.	.	.	.
.....												
LN MESENTERIC		:	-	-	-	-	-	-	-	-	-	-
.....												
LUNG		:	-	-	-	-	-	-	-	+	-	-
- Alveolar Macrophages; Increased		:	1.	.	.
.....												
MAMMARY GLAND		:	+	-	-	-	-	-	-	-	+	-
- Galactoceles		:	P.	.
- Hyperplasia		:	1.
.....												
NOSE/TURBINATES		:	-	-	-	-	-	-	-	-	-	-
.....												
ORAL MUCOSA		:	-	-	-	-	-	-	-	-	-	-
.....												

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-38 / 56
 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 6, Tobacco Extract Low (E0.2)

ANIMAL NUMBER :

	1601	1602	1603	1604	1605	1606	1607	1608	1609	1610
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
OVARIES	:	+	+	-	+	+	+	+	+	-
- Cyst(s)	:	(P.	.	.	.
- Decreased Corpora Lutea	:	P.	P.	.	P.	P.	.	P.	P.	.
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	(-	-	-	-	-	-	(-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	+	-	-	+	-	-	-	-
- Hyperplasia; Pars Distalis	:	.	1.	.	.	3.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	+	+	-	+	-	-	-	-
- Increased Extramedullary Hematopoiesis	:	.	1.
- Pigment Deposition.	:	.	2.	1.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	+	-	-	+	-	+	-	+
- Cyst(s)	:	.	P.	.	.	P.	.	P.	.	P.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	+	-	+	+	-	-	+
- Cyst(s); Endometrial	:	(P.	.
- Dilatation	:	1.	2.	.	.	.
- Endometrial Hyperplasia; Cystic	:	.	.	(2.
VAGINA	:	-	-	-	-	-	-	+	-	+
- Metazoan Parasite	:	P.	.	.
- Mucification.	:	P.
ZYMBAL'S GLANDS	:	-	-	-	+	(-	-	-	+	(-
- Dilated Duct(s).	:	.	.	.	(P.	.	.	.	P.	.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-39 / 56
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 6, Tobacco Extract Low (E0.2)

ANIMAL NUMBER :

	1611	1612	1613	1614	1615	1616	1617	1618	1619	1620
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	+	-	-	-	+	-	+	+	-
- Angiectasis; Cortex	:	2.	.	2.	.
- Hypertrophy; Cortex	:	(1.	.	.	.	(1.
- Vacuolation; Cortex	:	(1.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	-	-	-	-	+	-	-	-	+
- Inflammation.	:	1.	.	.	.	(2.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	-
HARDERIAN GLANDS	:	-	-	-	-	-	-	-	-	-
HEART	:	-	-	-	-	-	-	-	-	0
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	-	-	-	-	-	-	-
LIVER	:	+	-	-	-	-	+	-	+	+
- Inflammation.	:	1.	1.	.	1.	1.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	+	-	-	-	-	-	-	-	-
- Alveolar Macrophages; Increased	:	1.
MAMMARY GLAND	:	-	-	-	-	-	-	-	-	-
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	-	-	+	+G (+	+	+	+	+
- Decreased Corpora Lutea	:	.	.	P.	.	P.	P.	P.	P.	P.
- Hematocyst(s)	:	.	.	.	(P.
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	-	-	-	-	-	-	(-	-	(-

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-40 / 56
 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 6, Tobacco Extract Low (E0.2)

ANIMAL NUMBER :

	1611	1612	1613	1614	1615	1616	1617	1618	1619	1620
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	+	-	-	-
- Hyperplasia; Pars Distalis	:	1.	.	.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	+	-	+	+	-	-	+
- Increased Extramedullary Hematopoiesis	:	.	.	1.
- Pigment Deposition.	:	1.	1.	.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	+G	-	-	-	-	+G	-	-
- Dilatation	:	.	(4.	4.	.	.
VAGINA	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	+	-	-	(-	(-	(-	-	(-
- Dilated Duct(s).	:	.	(P.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-41 / 56
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	701 MK0	702 MK0	703 MK0	704 MK0	705 MK0	706 MK0	707 MK0	708 MK0	709 MK0	710 MK0
ADRENAL GLANDS	:	-	-	-	-	-	-	-	-	-
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES	:	-	-	-	-	-	-	-	-	-
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	+	+	-	-	-	-	-	-
- Degeneration; Retina	:	.	1.	1.
HARDERIAN GLANDS	:	-	-	-	+	+	-	-	-	-
- Inflammation	:	.	.	.	(1.	(1.
HEART	:	-	-	+	+	-	-	+	-	-
- Cardiomyopathy	:	.	.	1.	2.	.	.	1.	.	.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	+	+	-	+	-	+	-
- Nephropathy	:	.	.	1.	1.	.	1.	.	1.	1.
LIVER	:	-	+	-	-	+	-	+	-	+
- Focus/Foci; Basophilic Cell	:	1.	.	.
- Inflammation	:	.	1.	.	.	1.	.	1.	.	1.
- Tension Lipidosis	:	1.	.	.
LN MESENTERIC	:	-	-	-	-	-	-	+	-	-
- Angiomatous Hyperplasia	:	2.	.	.
- Hemangiosarcoma	:	N0.	.	.
LUNG	:	+	+	+	-	+	-	-	-	-
- Alveolar Macrophages; Increased	:	.	2.	1.
- Inflammation	:	1.
- Osseous Metaplasia	:	P.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
PANCREAS	:	-	-	+	-	-	-	-	-	-
- Atrophy; Acinar Cell	:	.	.	2.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	701 MK0	702 MK0	703 MK0	704 MK0	705 MK0	706 MK0	707 MK0	708 MK0	709 MK0	710 MK0
PARATHYROID GLANDS	:	-	(-	-	-	-	-	(-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	0	-	-	-	0	-
PREPUTIAL GLANDS	:	+	+	+	+	+	+	+	-	+
- Inflammation.	:	(1.	(1.	(3.	(2.	(
PROSTATE GLAND	:	-	-	-	-	-	-	+	-	-
- Inflammation.	:	2.	.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	(-	-	-	+	-	(-
- Follicular Cyst(s).	:	(P.	.	.
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	(-	(-	+	-	(-	(
- Dilated Duct(s).	:	.	.	.	P.

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 7, Tobacco Extract Intermed (E2)

[illegible]

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	711	712	713	714	715	716	717	718	719	720
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PREPUTIAL GLANDS	:	-	+	+	+	-	-	+	+	-
- Inflammation.	:	.	1.	(1.	1.	.	.	2.	(1.	1.
PROSTATE GLAND	:	-	-	-	-	-	+	-	-	-
- Inflammation.	:	1.	.	.	.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-G	-	-	-	-	-	-	-
SKIN, OTHER	:	.	-G
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	+	-	-	-	-	-
- Pigment Deposition.	:	.	.	.	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	+	G	-	-	-
- Atrophy	:	(4.
- Interstitial Cell Adenoma	:	(B0.
THYMUS	:	-	-	-	0	-	-	+	-	-
- Cyst(s)	:	P.	.	.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	0	+	(-	+	+	-	-	(-	-
- Dilated Duct(s).	:	.	P.	.	(P.	(P.

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	1701	1702	1703	1704	1705	1706	1707	1708	1709	1710
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	-	(+	+	+	+	-	-	-	+
- Angiectasis; Cortex	:	.	(1.	(1.	1.	1.	2.	.	.	1.
- Three Adrenals Submitted in Wet	:	.	.	P.	1.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-	-	-
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	+	-	+	-	-	+	-	+	+
- Inflammation.	:	(3.	.	(1.	.	.	(1.	.	(1.	2.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	+
- Degeneration; Retina	:	1.
HARDERIAN GLANDS	:	-	-	-	-	-	-	-	-	-
HEART	:	-	-	-	-	-	-	-	-	-
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	+	-
- Metazoan Parasites.	:	P.	.
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	+G	-	-	-	-	-	-
- Cyst(s)	:	.	.	(P.
LIVER	:	+	+	+	-	-	+	+	-	+
- Focus/Foci; Basophilic Cell.	:	.	.	2.
- Hyperplasia; Bile Duct	:	1.
- Inflammation.	:	1.	1.	.	.	.	1.	1.	.	1.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	-	-	-	-	-	-	+	+
- Alveolar Macrophages; Increased	:	1.	1.
MAMMARY GLAND	:	-	-	-	-	-	-	-	-	-
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	+	+	(+	+	+	+	-	+	-
- Decreased Corpora Lutea	:	P.	P.	(P.	P.	P.	P.	.	P.	.

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INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	1701	1702	1703	1704	1705	1706	1707	1708	1709	1710
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PANCREAS	:	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	:	0	-	-	-	(-	(-	-
PHARYNX	:	0	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	0	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	+	-	-	-	+	-	-	-
- Pigment Deposition.	:	.	1.	.	.	.	1.	.	.	.
STOMACH	:	-	-	-	-	-	-	-	+	-
- Mineralization; Mucosa	:	1.	.
THYMUS	:	-	+	-	-	+	-	+	+	-
- Cyst(s)	:	.	P.	.	.	P.	.	P.	P.	.
THYROID GLAND	:	(-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
UTERUS	:	-	-	+	-	-	-	-	-	-
- Cyst(s); Endometrial	:	.	.	P.
VAGINA	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	-	-	(-	(-	-	(-

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	1711	1712	1713	1714	1715	1716	1717	1718	1719	1720
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	:	+	-	+	-	-	+	-	-	+
- Angiectasis; Cortex	:	1.	.	1.	.	.	1.	.	.	.
- Hyperplasia; Cortex	:	(1.	.
BONE MARROW	:	-	-	-	-	-	-	-	-	-
BONE, FEMUR	:	-	-	-	-	-	-	-	-	-
BONE, STERNUM	:	-	+G	-	-	-	-	-	-	-
- Fibrolipoma	:	.	B0.
BRAIN	:	-	-	-	-	-	-	-	-	-
CLITORAL GLANDS	:	-	(-	+	+	-	-	+	-	-
- Inflammation.	:	.	.	1.	1.	.	(1.	.	.	.
ESOPHAGUS	:	-	-	-	-	-	-	-	-	-
EYES	:	-	-	-	-	-	-	-	-	(-
HARDERIAN GLANDS	:	-	-	-	-	-	-	+	-	-
- Inflammation.	:	(1.	.	.
HEART	:	-	+	-	-	-	-	-	-	-
- Cardiomyopathy	:	.	1.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-	-	-
KIDNEYS	:	-	-	+	+	-	-	-	-	+
- Nephropathy	:	.	.	1.	1.	1.
LIVER	:	+	+	+	+	-	-	-	+	-
- Inflammation.	:	1.	1.	1.	1.	.	.	.	1.	.
LN MESENTERIC	:	-	-	-	-	-	-	-	-	-
LUNG	:	-	+	+	-	+	-	+	-	-
- Alveolar Macrophages; Increased	:	.	1.	1.	.	1.
- Inflammation.	:	1.	.	.
MAMMARY GLAND	:	-	-	-	-	+	-	-	-	-
- Inflammation.	:	3.
NOSE/TURBINATES	:	-	-	-	-	-	-	-	-	-
ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-
OVARIES	:	+	+	-	+	-	+	+	-	+
- Decreased Corpora Lutea	:	P.	P.	.	P.	.	P.	P.	.	P.

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 7, Tobacco Extract Intermed (E2)

ANIMAL NUMBER :

	1711	1712	1713	1714	1715	1716	1717	1718	1719	1720
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PANCREAS	:	-	-	-	-	-	-	-	+	-
- Atrophy; Acinar Cell	:	1.	.
PARATHYROID GLANDS	:	(-	-	-	-	-	(0	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	0	-	-	-	+	+G
- Angiectasis	:	3.	3.
- Hyperplasia; Pars Distalis	:	2.	2.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-G	-	-	-	-	-
SKIN, OTHER	:	.	.	.	+
- Hyperkeratosis	:	.	.	.	2.
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	+	-	+	+	-	-	-	-
- Increased Extramedullary Hematopoiesis	:	.	.	.	1.
- Pigment Deposition.	:	.	1.	.	.	1.
STOMACH	:	-	-	-	-	-	+	-	+	-
- Mineralization; Mucosa	:	1.	.	1.	.
THYMUS	:	+	-	-	+	-	-	-	-	-
- Cyst(s)	:	P.	.	.	P.
THYROID GLAND	:	+	G	-	-	-	-	-	-	-
- Carcinoma; Follicular Cell	:	(N0.
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	0	-	-	-	-
UTERUS	:	+	+G	-	+	+	-	+	G	+
- Cyst(s); Endometrial	:	P.
- Dilatation	:	.	4.	.	3.	3.	.	4.	.	2.
- Endometrial Hyperplasia; Cystic	:	2.
VAGINA	:	-	-	-	-	0	-	-	-	-
ZYMBAL'S GLANDS	:	-	-	-	-	-	(+	-	(
- Dilated Duct(s).	:	(P.	.	.

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INDIVIDUAL ANIMAL DATA

PAGE : 5-50 / 56
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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

ANIMAL NUMBER :

	801	802	803	804	805	806	807	808	809	810
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PANCREAS	:	+	-	-	-	-	-	-	-	-
- Atrophy; Acinar Cell	:	1.
PARATHYROID GLANDS	:	0	0	-	-	-	-	-	-	-
PHARYNX	:	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	+	-	-	-	-
- Hyperplasia; Pars Distalis	:	.	.	.	1.
PREPUTIAL GLANDS	:	+	+	+	+	+	+	+	+	+
- Inflammation.	:	2.	2.	2.	1.	1.	1.	1.	1.	1.
PROSTATE GLAND	:	-	+	-	-	+	-	-	-	-
- Inflammation.	:	.	2.
- Inflammation; Chronic.	:	1.
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	-	-	-	-	-
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	+G	-	-	-	-	+
- Atrophy	:	.	.	.	3.	3.
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	0	-	-	-	(-	-	-	(

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

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PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

ANIMAL NUMBER :

	811	812	813	814	815	816	817	818	819	820
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
PREPUTIAL GLANDS	:	+	+	-	+	+	+	+	(+
- Inflammation.	:	(1.	(1.	.	1.	(3.	(1.	(1.	.	(1.
PROSTATE GLAND	:	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	:	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-G	-	-	-	-
SKIN, OTHER	:	+
- Epidermal Ulceration	:	3.
- Hyperplasia; Epithelial	:	2.
SPINAL CORD	:	-	-	-	-	-	-	-	-	-
SPLEEN	:	-	-	-	-	+	-	-	-	-
- Pigment Deposition.	:	1.
STOMACH	:	-	-	-	-	-	-	-	-	-
TESTES	:	-	-	-	-	-	-	-	-	+
- Atrophy	:	2.
THYMUS	:	-	-	-	-	-	-	-	-	-
THYROID GLAND	:	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLANDS	:	+	-	+	(-	-	-	-	+
- Dilated Duct(s).	:	(P.	.	(P.	(P.

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CN49730G (770-004)

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

1801	1802	1803	1804	1805	1806	1807	1808	1809	1810
FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0+	FK0

ADRENAL GLANDS								
- Angiectasis; Cortex	:	1.
- Hypertrophy; Cortex	:	(1.	.	.
BONE MARROW								
BONE, FEMUR	:	-	-	-	-	-	-	-
BONE, STERNUM	:	-	-	-	-	-	-	-
BRAIN								
CAUSE OF DEATH	:	'	+	'	'	'	'	+
- Fibroadenoma.	:	P.						.
- Stromal Sarcoma.	:	.						P.
CLITORAL GLANDS								
- Inflammation.	:	(1.	. (1.	.	. (1.	(1.	. (1.	.
ESOPHAGUS								
EYES	:	-	-	-	-	-	-	-
HARDERIAN GLANDS	:	+	-	-	+	-	-	-
- Inflammation.	:	(1.	.	.	(1.	.	.	.
HEART								
- Cardiomyopathy	:	1.	.	.
INTEST-LG, CECUM	:	-	-	-	-	-	-	-
INTEST-LG, COLON	:	-	-	-	-	-	-	-
INTEST-LG, RECTUM	:	-	-	-	-	-	-	-
INTEST-SM, DUODENUM	:	-	-	-	-	-	-	-
INTEST-SM, ILEUM	:	-	-	-	-	-	-	-
INTEST-SM, JEJUNUM	:	-	-	-	-	-	-	-
KIDNEYS								
- Mineralization; Tubular	:	.	.	.	(1.	.	.	.
- Nephropathy	:	1.	.	.
LIVER								
- Focus/Foci; Basophilic Cell.	:	.	2.	1.
- Focus/Foci; Eosinophilic Cell	:	.	1.
- Inflammation.	:	.	1.	.	.	1.	.	.
LN MESENTERIC								
LUNG	:	+	-	+	+	+	-	-
- Alveolar Macrophages; Increased	:	1.	.	1.	1.	1.	.	.
MAMMARY GLAND	:	-	+G	-	-	-	-	-
- Fibroadenoma.	:	.	B3.
NOSE/TURBINATES								

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CN49730G (770-004)

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

1801	1802	1803	1804	1805	1806	1807	1808	1809	1810
FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0+	FK0

ORAL MUCOSA	:	-	-	-	-	-	-	-	-	-	-
.....	:										
OVARIES	:	+	+	+G	+	+	-	+	-G	+	+
- Cyst(s); Parovarian	:			(P.							
- Decreased Corpora Lutea	:	P.	P.	(P.	P.			P.		P.	P.
- Persistent Corpora Lutea	:					P.					
.....	:										
PANCREAS	:	-	-	-	-	-	-	-	-	-	-
.....	:										
PARATHYROID GLANDS	:	-	-	(-	-	(-	-	0	-	(-	-
.....	:										
PHARYNX	:	-	-	-	-	-	-	-	-	-	-
.....	:										
PITUITARY GLAND	:	-	-	-	-	-	+	+	-	-	-
- Hyperplasia; Pars Distalis	:						1.	3.			
.....	:										
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-	-
.....	:										
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-	-
.....	:										
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-	-
.....	:										
SKIN	:	-	-	-	-	-	-	-	-	-	-
.....	:										
SPINAL CORD	:	-	-	-	-	-	-	-	-	-	-
.....	:										
SPLEEN	:	-	-	-	-	-	+	-	+	+	+
- Increased Extramedullary Hematopoiesis	:									1.	
- Pigment Deposition	:						1.		2.		2.
.....	:										
STOMACH	:	-	-	-	-	-	-	-	-	-	-
.....	:										
THYMUS	:	-	-	+	-	-	-	+	-	+	+
- Cyst(s)	:			P.				P.		P.	P.
.....	:										
THYROID GLAND	:	-	-	-	-	-	-	-	-	-	-
.....	:										
TONGUE	:	-	-	-	-	-	-	-	-	-	-
.....	:										
TRACHEA	:	-	-	-	-	-	-	-	-	-	-
.....	:										
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-	-
.....	:										
UTERUS	:	+	-	+G	-	-	-	-	-	+G	-
- Dilatation	:	1.		4.							
- Stromal Sarcoma; Cervix	:									N4.	
.....	:										
VAGINA	:	-	-	-	+	-	-	-	-	+G	-
- Mucification	:					P.					
- Prolapse	:									P.	
.....	:										
ZYMBAL'S GLANDS	:	+	(-	+	-	-	-	-	-	-	+
- Dilated Duct(s)	:	(P.		(P.							P.

PAGE : 5-55 / 56
CN49730G (770-004)

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 8, Tobacco Extract High Dose (E5)

[illegible][illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 5-56 / 56
 CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E PATHOL. NO.: 90279 DAB
 TEST SYSTEM : RAT, 1-Year, Orally in feed DATE : 08-FEB-13
 SPONSOR : EPL Archives, Inc. PathData©System V6.2d2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 8, Tobacco Extract High Dose (E5)

ANIMAL NUMBER :

	1811	1812	1813	1814	1815	1816	1817	1818	1819	1820	
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	
PARATHYROID GLANDS	:	(-	0	-	(-	0	(0	-
PHARYNX	:	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	:	-	-	-	-	-	-	-	-	-	-
SALIVARY GLAND	:	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	:	-	-	-	-	-	-	-	-	-	-
SKELETAL MUSCLE	:	-	-	-	-	-	-	-	-	-	-
SKIN	:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD	:	-	-	-	-	-	-	-	-	-	-
SPLEEN	:	+	-	+	-	+	-	-	+	-	+
- Pigment Deposition.	:	1.	.	2.	.	2.	.	.	1.	.	2.
STOMACH	:	-	-	-	-	-	-	-	-	-	-
THYMUS	:	-	-	-	-	-	-	-	-	-	+
- Cyst(s)	:	P.
THYROID GLAND	:	-	-	-	-	-	-	-	-	-	-
TONGUE	:	-	-	-	-	-	-	-	-	-	-
TRACHEA	:	-	-	-	-	-	-	-	-	-	-
URINARY BLADDER	:	-	-	-	-	-	-	-	-	-	-
UTERUS	:	+	-	+G	+	-	-	-	-	-	-
- Dilatation	:	.	.	.	4.
- Stromal Polyp	:	B0.
- Stromal Polyp; Cervix.	:	.	.	B0.
VAGINA	:	-	-	-	-	+	-	-	-	-	-
- Mucification.	:	P.
ZYMBAL'S GLANDS	:	-	-	+	-	-	-	-	-	-	-
- Dilated Duct(s).	:	.	.	(P.

APPENDIX 6:
CORRELATION TABLE: NECROPSY-MICROSCOPY

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-1 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 1, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 111

SKIN

- 01: Nodules, dorsal, pale, G1/ 5 x 5 x 2 mm. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Carcinoma; Sebaceous Gland (malignant neoplasm).

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-2 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 1, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1101

LIVER

- 01: Hdn, median lobe, G1/ 10 x 8 x 4 mm. - Cyst; Multilocular; Bile.

ANIMAL NO: 1105

OVARIES

- 01: Cyst(s), right, clear, G1/ 30 x 20 x 20 mm. - Cyst(s); Parovarian, unilateral.

ANIMAL NO: 1107

STOMACH

- 01: Nodule, glandular, pale, G1/ 3 x 3 x 1 mm. - Mucosal Cyst; Non-Glandular.

ANIMAL NO: 1114

OVARIES

- 01: Cyst(s), bilateral, clear, G1/ 8 x 8 x 8 mm. - Cystic Bursa, bilateral.

ANIMAL NO: 1118

OVARIES

- 01: Cyst(s), right, clear, G1/ 20 x 20 x 20 mm. - Cyst(s); Parovarian, unilateral.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-3 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 3, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 309

THYMUS

- 01: Small, G1/ 0.5x.

- Not submitted for examination.

ANIMAL NO: 311

SKIN

- 01: Crust(s), pedal (foot), dark, bilateral, G1/ 4 x 4 mm, rear foot. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Hyperkeratosis, grade 2.

Finding 01 in SKIN

- Inflammation, grade 2.

ANIMAL NO: 312

SKIN

- 01: Crust(s), pedal (foot), brown, G1/ 3 x 3 mm, rear foot. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Hyperkeratosis, grade 2.

Finding 01 in SKIN

- Inflammation, grade 1.

ANIMAL NO: 314

SKIN

- 01: Nodule, pedal (foot), pale, left, G1/ left rear foot, 2 x 2x 1 mm. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Fat Infiltration.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-4 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 3, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1301

KIDNEYS

- 01: Dilatation, plevis, G2/ 3x.

- Pelvic Dilatation, bilateral, grade 2.

URETERS

- 01: Calculus, lumen, one, dark, G3/ 5 x 2 x 2 mm.

- Dilatation, unilateral, grade 4.
Hyperplasia; Urothelium, unilateral, grade 4. Inflammation, unilateral, grade 2.

URINARY BLADDER

- 01: Calculus, lumen, one, G1/ 2 x 2 x 2 mm.

- Calculi. Hyperplasia; Urothelium, grade 3. Inflammation, grade 2.

ANIMAL NO: 1310

UTERUS

- 01: Mass, cervix, tan, G1/ 12 x 10 x 8 mm.

- SEE UNDER: VAGINA.

VAGINA

- 01: Distended and filled with soft material (noted at gross trimming).
Finding 01 in UTERUS

- Stromal Polyp (benign neoplasm).
- Stromal Polyp (benign neoplasm).

ANIMAL NO: 1311

OVARIES

- 01: Cyst(s), bilateral, clear, G1/ 8 x 8 x 8 mm.

- Cystic Bursa, bilateral.

ANIMAL NO: 1313

OVARIES

- 01: Cyst(s), right, clear, G1/ 10 x 10 x 10 mm.

- Cyst(s), unilateral.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-5 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 4, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 405

THYMUS
- 01: Small, G1/ 0.5x.

- Atrophy, grade 1.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-6 / 14
CN49730G (770-004)

TEST ITEM : Tobacco Blend & Aqueous Tobacco E
TEST SYSTEM : RAT, 1-Year, Orally in feed
SPONSOR : EPL Archives, Inc.

PATHOL. NO.: 90279 DAB
DATE : 08-FEB-13
PathData@System V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 4, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1411

UTERUS

- 01: Enlarged, cervix, pale, G1/ 2x.

- Fibrosis; Cervix, bilateral, grade 3.
Hyperplasia; Epithelial, bilateral, grade 2.

ANIMAL NO: 1419

PITUITARY GLAND

- 01: Focus, dark, G1/ 4 x 3 mm.

- Adenoma; Pars Distalis (benign neoplasm).

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-7 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 5, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 501

TESTES

- 01: Small, left, G1/ 0.5x.

- Atrophy, unilateral, grade 3.

ANIMAL NO: 504

BONE, OTHER

- 01: Hemorrhage, cranium, G1/ 20 x 15 mm;
hemorrhage noted on floor of cranial
(cranium) cavity.

- Hemorrhage, grade 2.

KIDNEYS

- 01: Dilatation, right, G2/ 15 x 8 x 8 mm.

- Pelvic Dilatation, unilateral, grade 2.

ANIMAL NO: 515

KIDNEYS

- 01: Focus, right, tan, G1/ 1 x 1 mm.

- Nephropathy, bilateral, grade 2.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-8 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 5, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1503

PITUITARY GLAND

- 01: Focus, dark, G1/ 3 x 2 mm.

- Adenoma; Pars Distalis (benign neoplasm).

ANIMAL NO: 1504

OVARIES

- 01: Cyst(s), bilateral, clear, G2/ 8 x 8 x 8 mm.

- Cyst(s); Parovarian, bilateral.

SKIN

- 01: Nodule, dorsal, red, G1/ 5 x 4 x 2 mm.

- SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Adenoma; Sebaceous Gland (benign neoplasm).

ANIMAL NO: 1516

OVARIES

- 01: Cyst(s), bilateral, clear, G1/ 10 mm.

- Cyst(s); Parovarian, bilateral.

ANIMAL NO: 1520

PITUITARY GLAND

- 01: Focus, dark, G1/ 1 x 1 mm.

- Hyperplasia; Pars Distalis, grade 2.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-9 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 6, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 603

SKIN

- 01: Discoloration(s), pedal (foot), red, G1/
3 x 2 mm. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN - Hyperkeratosis, grade 2.

ANIMAL NO: 604

LUNG

- 01: Discoloration(s), diffuse, red, G1. - Congestion, grade 1.

ANIMAL NO: 605

LUNG

- 01: Discoloration(s), diffuse, red, G2. - No corresponding finding.

SKIN

- 01: Crust(s), pedal (foot), dark, bilateral,
G1/ 7 x 7 mm. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN - Epidermal Ulceration, grade 2.

Finding 01 in SKIN - Inflammation, grade 2.

ANIMAL NO: 612

SKIN

- 01: Nodule, labial (lip), pale, G1/ 2 x 2 x
2 mm. - SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN - Hyperplasia; Sebaceous Gland, grade 1.

ANIMAL NO: 615

LIVER

- 01: Hdn, median lobe, G1/ 10 x 6 x 4 mm. - Hepatodiaphragmatic Nodule.

ANIMAL NO: 618

BONE, OTHER

Finding 01 in SPINAL CORD - Osteosarcoma (malignant neoplasm).

SPINAL CORD

- 01: Cervical spinal cord - black - SEE UNDER: BONE, OTHER.

discoloration in muscle adjacent to
spinal cord 1.4 x 7.0 x 1.5 cm (noted
at gross trimming).

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-10 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 6, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1612

UTERUS

- 01: Dilatation, horn, pink, right, G1/ 6 x 6 x 6 mm.	- Dilatation, unilateral, grade 4.
--	------------------------------------

ANIMAL NO: 1614

OVARIES

- 01: Enlarged, left, dark, G1/ 12 x 10 x 10 mm.	- Hematocyst(s), unilateral.
--	------------------------------

ANIMAL NO: 1618

UTERUS

- 01: Dilatation, horn, pink, bilateral, G1/ 8 x 8 x 8 mm.	- Dilatation, bilateral, grade 4.
--	-----------------------------------

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-11 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 7, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 712

SKIN

- 01: Crust(s), pedal (foot), brown, right,
G1/ 3 x 2 mm, rear foot.

- SEE UNDER: SKIN, OTHER

SKIN, OTHER

- 01: Finding 01 in SKIN.

- No corresponding finding

ANIMAL NO: 716

TESTES

- 01: Discoloration(s), left, mottled, G1.

- Interstitial Cell Adenoma, unilateral
(benign neoplasm).

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-12 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 7, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1703

KIDNEYS

- 01: Cyst(s), right dark, G1/ 1 x 1 mm.

- Cyst(s), unilateral.

ANIMAL NO: 1711

THYROID GLAND (BOTH LOBES)

- 01: Enlarged, right, tan, G1/ 3x.

- Carcinoma; Follicular Cell, unilateral
(malignant neoplasm).

ANIMAL NO: 1712

BONE (STERNUM)

- 01: Mass, tan, G2/ 10 x 5 x 5 mm.

- Fibrolipoma (benign neoplasm).

UTERUS

- 01: Dilatation, horn, pink, bilateral, G1/
9x 9 x 9 mm.

- Dilatation, bilateral, grade 4.

ANIMAL NO: 1714

SKIN

- 01: Discoloration(s), caudal (tail), tan,
G1/ 12 x 5 mm.

- SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Hyperkeratosis, grade 2.

ANIMAL NO: 1718

UTERUS

- 01: Dilatation, horn, pink, bilateral, G1/
7 x 7 x 7 mm.

- Dilatation, bilateral, grade 4.

ANIMAL NO: 1720

PITUITARY GLAND

- 01: Focus, dark, G1/ 3 x 3 mm.

- Angiectasis, grade 3. Hyperplasia; Pars
Distalis, grade 2.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-13 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 8, MALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 801

ADRENAL GLANDS

- 01: Small, right, G1/ 0.5x.

- No corresponding finding.

ANIMAL NO: 804

TESTES

- 01: Small, bilateral, G1/ 0.5x.

- Atrophy, bilateral, grade 3.

ANIMAL NO: 814

LYMPH NODE, MESENTERIC

- 01: Enlarged, dark, G1/ 3x.

- Hemangiosarcoma (malignant neoplasm).

ANIMAL NO: 815

SKIN

- 01: Ulcer, dorsal, dark, G1/ 5 x 5 x 2 mm.

- SEE UNDER: SKIN, OTHER.

SKIN, OTHER

Finding 01 in SKIN

- Epidermal Ulceration, grade 3.

Finding 01 in SKIN

- Hyperplasia; Epithelial, grade 2.

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 6-14 / 14
CN49730G (770-004)

TEST ITEM	: Tobacco Blend & Aqueous Tobacco E	PATHOL. NO.:	90279 DAB
TEST SYSTEM	: RAT, 1-Year, Orally in feed	DATE	: 08-FEB-13
SPONSOR	: EPL Archives, Inc.	PathData@System	V6.2d2

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 8, FEMALE

NECROPSY OBSERVATION

CORRESPONDING MICROSCOPIC FINDING

ANIMAL NO: 1802

MAMMARY GLAND

- 01: Mass, thoracic, G1/ 80 x 70 x 40 mm.

- Fibroadenoma (benign neoplasm, probably fatal).

ANIMAL NO: 1803

OVARIES

- 01: Cyst(s), left, clear, G1/ 10 x 10 x 10 mm.

- Cyst(s); Parovarian, unilateral.

UTERUS

- 01: Dilatation, horn, dark, bilateral, G2/ 8 x 8 x 8 mm.

- Dilatation, bilateral, grade 4.

ANIMAL NO: 1808

OVARIES

- 01: Cyst(s), right, clear, G1/ 10 x 8 x 8 mm.

- No corresponding finding.

ANIMAL NO: 1809

UTERUS

- 01: Mass, cervix, pale, G2/ 35 x 25 x 25 mm.

- Stromal Sarcoma; Cervix, bilateral (malignant neoplasm, definitely fatal).

VAGINA

- 01: Prolapse, G1.

- Prolapse.

ANIMAL NO: 1812

OVARIES

- 01: Cyst(s), bilateral, clear, G1/ 15 x 15 x 15 mm.

- Cystic Bursa, bilateral.

ANIMAL NO: 1813

UTERUS

- 01: Mass, cervix, tan, G1/ 15 x 12 x 10 mm.

- Stromal Polyp; Cervix, bilateral (benign neoplasm).

APPENDIX 7:
STATISTICAL ANALYSIS REPORT

AMENDED STATISTICAL ANALYSIS REPORT

**2-YEAR CHRONIC TOXICITY/CARCINOGENICITY STUDY OF TOBACCO BLEND
AND AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS:**

1-YEAR TIME POINT: HISTOPATHOLOGICAL EVALUATION OF ALL GROUPS

TEST SITE:

EXPERIMENTAL PATHOLOGY LABORATORIES, INC. (EPL, Inc.)

45600 TERMINAL DRIVE

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R.J. REYNOLDS TOBACCO COMPANY

RESEARCH AND DEVELOPMENT

BOWMAN GRAY TECHNICAL CENTER

WINSTON-SALEM, NC 27102

Battelle Study No. CN49730G

EPL, Inc. Study No. 770-004

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January 7, 2013

Prepared By:

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Statistician

01-07-2013

Date

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Theophilus

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Study Monitor

1/7/13

Date

Reason for Changes

Animal ID 1518 in Table 1 (Early Deaths, page 8) was corrected to 1516. No other changes were made.

Walter T. Morgan
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01-07-2013
Date

Theophilus
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11/7/13
Date

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1.0 INTRODUCTION

This report summarizes the statistical analysis of tumor incidence data from the 1-year time point of a 2-year chronic toxicity/carcinogenicity study of two separate test articles, a tobacco blend and an aqueous tobacco extract from that blend, administered in the diet to Wistar Han rats. A total of 280 rats were used in this study for the core dosage groups for the 1-year time point, of which 140 were females and 140 were males. Animals were randomly assigned to seven core dosage groups by sex and body weight using a computer algorithm (PATH/TOX SYSTEM, Version 4.2.2), such that there were 20 rats per sex per group at 1 year. The seven dosage groups were fed diets without test articles, Control (Group 1), or diets with two separate test articles, tobacco blend low dose (0.2 mg nicotine/kg/day, Group 3), tobacco blend intermediate dose (2 mg nicotine/kg/day, Group 4), tobacco blend high dose (5 mg nicotine/kg/day, Group 5), tobacco extract low dose (0.2 mg nicotine/kg/day, Group 6), tobacco extract intermediate dose (2 mg nicotine/kg/day, Group 7), and tobacco extract high dose (5 mg nicotine/kg/day, Group 8). In each core dosage group for the 1-year time point, 20 animals of each sex were used to assess potential toxicity and carcinogenicity.

1.1 Objectives of the Analysis

The objective of the analysis was to determine if significant linear dose response trends existed in incidences of tumors among groups given each test article vs. control group. For the tobacco blend test article, the groups statistically compared were Group 1 and Groups 3 to 5, while for the aqueous tobacco extract test article the groups compared were Group 1 and Groups 6 to 8. These analyses were conducted separately for males and females.

2.0 METHODS

This section describes the statistical methods applied in the analysis of tumor incidence data. Statistical analyses were performed using SAS (Version 9.2) software.

2.1 Tumor Incidence

This section describes the methods used to determine whether positive linear dose-response trends in tumor incidence were present. The statistical methods applied depend on the context in which tumors were observed. In this study, each tumor observed in each animal was classified as incidental, fatal, or mortality independent. Tumors that were not directly or indirectly responsible for the animal's death but were merely observed at the autopsy of the animal after it died of an unrelated cause are incidental tumors. Fatal tumors were assumed to have caused the early (unscheduled) death of the animal. Tumors whose detection occurred at times other than when the animal died and which, therefore, could not have been responsible for the animal's death, were classified as mortality independent tumors. Tumors classified as mortality independent by the study pathologist were treated as incidental tumors in the statistical analysis. Both tumor classifications were not the cause of death of the animal, but were associated with a day of death at which the tumor was observed, which was used as the temporal component (time interval) in the statistical model.

While some types of tumors were observed in only one context (incidental or fatal), others may have been observed in both contexts. The methods used for the analysis of incidental, fatal, and combined tumor data are described below. These methods are consistent with those currently recommended by the Food and Drug Administration (FDA) for tumor analysis ([Lin, 2000](#); [CDER, 2001](#)).

Tests for linear dose trends were conducted separately for the tobacco blend and the tobacco extract groups. Trend tests were performed using proper contrasts applied to an analysis of the dosage groups involved in the test (i.e., the control group and the three treated dose groups). The effects of tobacco blend or tobacco extract were each assessed through their respective trend tests. P-values less than 0.05 were required for statistical significance for each test article.

2.1.1 Incidental Methods

Cochran Armitage trend tests, using the Mantel-Haentzel method to pool results over time intervals, were used to test for positive linear dose trends in prevalence rates of incidental tumors. However, since early death was observed for only four animals, the study period was divided into only two intervals of death days for this analysis: [0, 359], and [360,368].

2.1.2 Fatal Methods

Tarone's trend tests were used to test for positive linear dose trends in tumors observed in a fatal context.

2.1.3 Combined Methods

When a tumor was observed in a fatal context for some animals and was observed in an incidental context for the other animals, Peto's method was used to test for positive linear dose trends in tumor incidences. The time intervals above (see Section 2.1.1, Incidental Methods) were used in this analysis.

2.1.4 General Comments

For each tumor type, tumor data were analyzed separately for the tobacco blend and the tobacco extract. A given trend test was conducted using only the data for the groups that were included in that trend test. For example, the dose trend among Group 1 (Control-A) and the tobacco blend groups was tested using data for animals from only Groups 1, 3, 4, and 5. For each trend test, the appropriate method was used, depending on whether tumors were observed in the incidental, fatal, or both contexts among the groups which were involved in the trend test.

Animals having multiple incidences of a specific tumor were considered to be with tumor and were counted only once in the analysis of that tumor type. An animal with both fatal and incidental tumors of a specific tumor type was considered to have a fatal tumor of that tumor type. When analysis was conducted for a specific tumor type, animals without this type of tumor were considered to be without tumor even though the animal may have had another type of tumor.

3.0 RESULTS

3.1 Macroscopic Findings

Macroscopic findings were summarized by treatment group. Numbers of animals in each group with each non-normal finding are listed in [Appendix A](#).

3.2 Early Deaths

Death day was calculated as the number of days from the start of the study (March 3, 2009) to the date that animal deaths were recorded. [Table 1](#) presents information about the four animals that died before the 1-year time point and their disposition. It shows that only one male animal and three female animals out of 140 of each sex died before the terminal sacrifice at the 1-year time point.

3.3 Tumor Analysis

[Table 2](#) and [Table 3](#) present the results of statistical analyses of tumor incidence data for tobacco blend for females and males, respectively, for tissue types for which at least one animal with tumor was observed. [Table 4](#) and [Table 5](#) present the results of statistical analyses of tumor incidence data for the aqueous tobacco extract for females and males, respectively, for tissue types for which at least one animal with tumor was observed. Also provided in these tables are the numbers of animals in each dose group with tumors for each tumor type as well as the number of animals for which the tumor of interest was not observed. Tumors were reported for tissues "Skin, Other", Skeletal Muscle, Other", and "Bone" since they were observed in some cases, but those tissues were reported as "not done" for most animals, so no statistical analysis was performed in those cases. Results for some tissues were not reported for some animals if those tissues were missing or not present on the slides. The tables present p-values for the tests

for trends for the other tissues. P-values less than 0.05 were required for statistical significance. The data set used for the tumor incidence statistical analysis is presented in [Appendix B](#).

3.3.1 Results for Tobacco Blend

[Tables 2](#) and [3](#) show low tumor counts for animals given the tobacco blend feed, with either zero or one animal found with each type of tumor across the four groups (80 animals) in most cases. One female animal in each of the intermediate and high tobacco blend feed groups was found to have ADENOMA; PARS DISTALIS (benign neoplasm) in the PITUITARY GLAND, while one male animal in each of the low and intermediate tobacco blend feed groups was found to have ADENOMA; C-CELL, UNILATERAL (benign neoplasm) in the THYROID GLAND. Tests for linear trend were not statistically significant for these two cases ($P > 0.05$) or any of the other tumor types, for which only one animal with tumor was observed across the four groups tested.

3.3.2 Results for Aqueous Tobacco Extract

Similarly, [Tables 4](#) and [5](#) show low tumor counts for animals given the aqueous tobacco extract feed, with either zero or one animal found with each type of tumor across the four groups (80 animals) in most cases. One female animal in each of the control and high tobacco extract feed groups was found to have STROMAL POLYP (benign neoplasm) in the UTERUS, while one male animal in each of the intermediate and high tobacco extract feed groups was found to have HEMANGIOSARCOMA (malignant neoplasm) in the LYMPH NODE MESENTERIC. Tests for linear trend were not statistically significant for these two cases ($P > 0.05$) or any of the other tumor types, for which only one animal with tumor was observed across the four groups tested.

4.0 CONCLUSIONS

Analysis of the tumor incidence data found no significant trends in tumor incidence for either males or females given either the tobacco blend or aqueous tobacco extract feed.

5.0 REFERENCES

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Table 1. Early Deaths

Animal ID	Gender	Group Number	Group Name	Disposition	Death Day
504	Male	5	Tobacco Blend High Dose	Natural Death	142
1516	Female	5	Tobacco Blend High Dose	Natural Death	297
1802	Female	8	Tobacco Extract High Dose	Moribund Sacrifice	351
1809	Female	8	Tobacco Extract High Dose	Moribund Sacrifice	353

Table 2. Results of Analysis of Tumor Data – Females, Tobacco Blend

Tissue	Diagnosis	Tumor Type+	Number of Animals with Indicated Result				P: Linear Trend
			Control	Tobacco Blend 0.2 mg	Tobacco Blend 2.0 mg	Tobacco Blend 5.0 mg	
Mammary Gland	Adenocarcinoma (malignant neoplasm)	None I	20 0	20 0	19 0	19 1	0.1723
Pituitary Gland	Adenoma; Pars Distalis (benign neoplasm)	None I	20 0	20 0	19 1	19 1	0.1922
Skin, Other	Adenoma; Sebaceous Gland (benign neoplasm)	ND	20	20	20	19	NA
		None	0	0	0	0	
		I	0	0	0	1	
Uterus	Stromal Polyp (benign neoplasm)	None I	19 1	20 0	20 0	20 0	0.1830
Vagina	Stromal Polyp (benign neoplasm)	None I	20 0	19 1	20 0	20 0	0.6654

+Tumor Type I = Incidental, F = Fatal, None = no tumors were reported, ND = tissue was not examined, reported as “NOT DONE”

Table 3. Results of Analysis of Tumor Data – Males, Tobacco Blend

Tissue	Diagnosis	Tumor Type+	Number of Animals with Indicated Result				P: Linear Trend
			Control	Tobacco Blend 0.2 mg	Tobacco Blend 2.0 mg	Tobacco Blend 5.0 mg	
Pituitary Gland	Adenoma; Pars Distalis (benign neoplasm)	None I	20 0	17 1	19 0	20 0	0.6665
Skel. Muscle, Other	Malignant Schwannoma (malignant neoplasm)	ND F	20 0	20 0	20 0	19 1	NA
Skin, Other	Carcinoma; Sebaceous Gland (malignant neoplasm)	ND	19	17	20	20	NA
		None	0	3	0	0	
		I	1	0	0	0	
Thyroid Gland	Adenoma; C-Cell, unilateral (benign neoplasm)	None I	20 0	19 1	18 1	19 0	0.9739
Zymbal's Glands	Squamous Papilloma, unilateral (benign neoplasm)	None I	20 0	18 0	17 1	17 0	0.6168

+Tumor Type I = Incidental, F = Fatal, None = no tumors were reported, ND = tissue was not examined, reported as "NOT DONE"

Table 4. Results of Analysis of Tumor Data – Females, Aqueous Tobacco Extract

Tissue	Diagnosis	Tumor Type+	Number of Animals with Indicated Result				P: Linear Trend
			Control	Tobacco Extract 0.2 mg	Tobacco Extract 2.0 mg	Tobacco Extract 5.0 mg	
Bone, Sternum	Fibrolipoma (benign neoplasm)	None I	20 0	20 0	19 1	20 0	0.6263
Mammary Gland	Fibroadenoma (benign neoplasm)	None F	20 0	20 0	20 0	19 1	0.1797
Thyroid Gland	Carcinoma; Follicular Cell, unilateral (malignant neoplasm)	None I	20 0	20 0	19 1	20 0	0.6263
Uterus	Stromal Polyp (benign neoplasm)	None I	19 1	20 0	20 0	19 1	0.9605
	Stromal Polyp; Cervix (benign neoplasm)	None I	20 0	20 0	20 0	19 1	0.1642
	Stromal Sarcoma; Cervix (malignant neoplasm)	None F	20 0	20 0	20 0	19 1	0.1720

+Tumor Type I = Incidental, F = Fatal, None = no tumors were reported, ND = tissue was not examined, reported as “NOT DONE”

Table 5. Results of Analysis of Tumor Data – Males, Aqueous Tobacco Extract

Tissue	Diagnosis	Tumor Type+	Number of Animals with Indicated Result				P: Linear Trend
			Control	Tobacco Extract 0.2 mg	Tobacco Extract 2.0 mg	Tobacco Extract 5.0 mg	
Bone	Osteosarcoma (malignant neoplasm)	ND	20	19	20	20	NA
		None	0	0	0	0	
		I	0	1	0	0	
LN Mesenteric	Hemangiosarcoma (malignant neoplasm)	None	20	20	19	19	0.2030
		I	0	0	1	1	
Pituitary Gland	Adenoma; Pars Distalis (benign neoplasm)	None	20	18	17	20	0.6613
		I	0	0	1	0	
Skin, Other	Carcinoma; Sebaceous Gland (malignant neoplasm)	ND	19	17	19	19	NA
		None	0	3	1	1	
		I	1	0	0	0	
Testes	Interstitial Cell Adenoma, unilateral (benign neoplasm)	None	20	20	19	20	0.6547
		I	0	0	1	0	

+Tumor Type I = Incidental, F = Fatal, None = no tumors were reported, ND = tissue was not examined, reported as “NOT DONE”

Appendix A. Macroscopic Findings

Sex	Organ	Finding	Control	Tobacco Blend 0.2	Tobacco Blend 2.0	Tobacco Blend 5.0	Tobacco Extract 0.2	Tobacco Extract 2.0	Tobacco Extract 5.0
Female	KIDNEYS	cyst(s), right dark, g1/ 1 x 1 mm	0	0	0	0	0	1	0
		dilatation, plevi, g2/ 3x	0	1	0	0	0	0	0
	LIVER	hdn, median lobe, g1/ 10 x 8 x 4 mm	1	0	0	0	0	0	0
	MAMMARY GLAND	mass, thoracic, g1/ 80 x 70 x 40 mm	0	0	0	0	0	0	1
	OVARIES	cyst(s), bilateral, clear, g1/ 10 mm	0	0	0	1	0	0	0
		cyst(s), bilateral, clear, g1/ 15 x 15 x 15 mm	0	0	0	0	0	0	1
		cyst(s), bilateral, clear, g1/ 8 x 8 x 8 mm	1	1	0	0	0	0	0
		cyst(s), bilateral, clear, g2/ 8 x 8 x 8 mm	0	0	0	1	0	0	0
		cyst(s), left, clear, g1/ 10 x 10 x 10 mm	0	0	0	0	0	0	1
		cyst(s), right, clear, g1/ 10 x 10 x 10 mm	0	1	0	0	0	0	0
		cyst(s), right, clear, g1/ 10 x 8 x 8 mm	0	0	0	0	0	0	1
		cyst(s), right, clear, g1/ 20 x 20 x 20 mm	1	0	0	0	0	0	0
		cyst(s), right, clear, g1/ 30 x 20 x 20 mm	1	0	0	0	0	0	0
		enlarged, left, dark, g1/ 12 x 10 x 10 mm	0	0	0	0	1	0	0
	PITUITARY GLAND	focus, dark, g1/ 1 x 1 mm	0	0	0	1	0	0	0
		focus, dark, g1/ 3 x 2 mm	0	0	0	1	0	0	0
		focus, dark, g1/ 3 x 3 mm	0	0	0	0	0	1	0
		focus, dark, g1/ 4 x 3 mm	0	0	1	0	0	0	0
	SKIN	discoloration(s), caudal (tail), tan, g1/ 12 x 5 mm	0	0	0	0	0	1	0
	STOMACH	nodule, glandular, pale, g1/ 3 x 3 x 1 mm	1	0	0	0	0	0	0

Appendix A. Macroscopic Findings, continued

Sex	Organ	Finding	Control	Tobacco Blend 0.2	Tobacco Blend 2.0	Tobacco Blend 5.0	Tobacco Extract 0.2	Tobacco Extract 2.0	Tobacco Extract 5.0
Female	THYROID GLAND	enlarged, right, tan, g1/ 3x	0	0	0	0	0	1	0
	UTERUS	dilatation, horn, pink, bilateral, g1/ 7 x 7 x 7 mm	0	0	0	0	0	1	0
		dilatation, horn, pink, bilateral, g1/ 8 x 8 x 8 mm	0	0	0	0	1	0	0
		dilatation, horn, pink, bilateral, g1/ 9x 9 x 9 mm	0	0	0	0	0	1	0
		dilatation, horn, pink, right, g1/ 6 x 6 x 6 mm	0	0	0	0	1	0	0
		enlarged, cervix, pale, g1/ 2x	0	0	1	0	0	0	0
		mass, cervix, pale, g2/ 35 x 25 x 25 mm	0	0	0	0	0	0	1
		mass, cervix, tan, g1/ 12 x 10 x 8 mm	0	1	0	0	0	0	0
		mass, cervix, tan, g1/ 15 x 12 x 10 mm	0	0	0	0	0	0	1
	VAGINA	trimming)	0	1	0	0	0	0	0
Male	ADRENAL GLANDS	small, right, g1/ 0.5x	0	0	0	0	0	0	1
	BONE	floor of cranial (cranium) cavity	0	0	0	1	0	0	0
	KIDNEYS	dilatation, right, g2/ 15 x 8 x 8 mm	0	0	0	1	0	0	0
		focus, right, tan, g1/ 1 x 1 mm	0	0	0	1	0	0	0
	LIVER	hdn, median lobe, g1/ 10 x 6 x 4 mm	0	0	0	0	1	0	0
	LN MESENTERIC	enlarged, dark, g1/ 3x	0	0	0	0	0	0	1
	LUNG	discoloration(s), diffuse, red, g1	0	0	0	0	1	0	0
		discoloration(s), diffuse, red, g2	0	0	0	0	1	0	0
	SKIN	crust(s), pedal (foot), brown, g1/ 3 x 3 mm, rear foot	0	1	0	0	0	0	0
		crust(s), pedal (foot), brown, right, g1/ 3 x 2 mm, rear foot	0	0	0	0	0	1	0

Appendix A. Macroscopic Findings, continued

Sex	Organ	Finding	Control	Tobacco Blend 0.2	Tobacco Blend 2.0	Tobacco Blend 5.0	Tobacco Extract 0.2	Tobacco Extract 2.0	Tobacco Extract 5.0
Male	SKIN	crust(s), pedal (foot), dark, bilateral, g1/ 4 x 4 mm, rear foot	0	1	0	0	0	0	0
		discoloration(s), pedal (foot), red, g1/ 3 x 2 mm	0	0	0	0	1	0	0
		nodule, labial (lip), pale, g1/ 2 x 2 x 2 mm	0	0	0	0	1	0	0
		nodule, pedal (foot), pale, left, g1/ left rear foot, 2 x 2x 1 mm	0	1	0	0	0	0	0
		nodules, dorsal, pale, g1/ 5 x 5 x 2 mm	1	0	0	0	0	0	0
		ulcer, dorsal, dark, g1/ 5 x 5 x 2 mm	0	0	0	0	0	0	1
	SPINAL CORD	cervical spinal cord - black discoloration in muscle adjacent to spinal cord 1.4 x 7.0 x 1.5 cm (noted at gross trimming)	0	0	0	0	1	0	0
	TESTES	discoloration(s), left, mottled, g1	0	0	0	0	0	1	0
		small, bilateral, g1/ 0.5x	0	0	0	0	0	0	1
		small, left, g1/ 0.5x	0	0	0	1	0	0	0
	THYMUS	small, g1/ 0.5x	0	1	1	0	0	0	0

Appendix B. Data Set for Tumor Incidence Analysis

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
101	Male	1	365	2	LIVER	Inflammation, grade 1	
101	Male	1	365	2	SPLEEN	Pigment Deposition, grade 1	
102	Male	1	365	2	KIDNEYS	Nephropathy, grade 1	
102	Male	1	365	2	KIDNEYS	Pelvic Dilatation, unilateral, grade 1	
102	Male	1	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
102	Male	1	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
102	Male	1	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
103	Male	1	365	2	LIVER	Pigment; Periportal, grade 2	
103	Male	1	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
104	Male	1	365	2	LIVER	Inflammation, grade 1	
105	Male	1	365	2	HARDERIAN GLANDS	Inflammation, grade 1	
105	Male	1	365	2	KIDNEYS	Nephropathy, grade 1	
105	Male	1	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
106	Male	1	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
106	Male	1	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
107	Male	1	365	2	KIDNEYS	Nephropathy, grade 1	
107	Male	1	365	2	LIVER	Inflammation, grade 1	
107	Male	1	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
108	Male	1	365	2	HEART	Cardiomyopathy, grade 1	
109	Male	1	365	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
109	Male	1	365	2	EPIDIDYMIDES	Hypospermia, grade 4	
109	Male	1	365	2	HEART	Cardiomyopathy, grade 2	
109	Male	1	365	2	KIDNEYS	Nephropathy, grade 1	
109	Male	1	365	2	LIVER	Inflammation, grade 1	
109	Male	1	365	2	NOSE/TURBINATES	Inflammation, grade 1	
109	Male	1	365	2	TESTES	Atrophy, grade 3	
110	Male	1	365	2	LIVER	Inflammation, grade 1	
110	Male	1	365	2	PHARYNX	Increased Mucus; Mucosal Glands, grade 1	
110	Male	1	365	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
111	Male	1	366	2	LIVER	Inflammation, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
111	Male	1	366	2	LIVER	Lipidosis; Periportal, grade 1	
111	Male	1	366	2	SKIN, OTHER	Carcinoma; Sebaceous Gland (malignant neoplasm)	I
112	Male	1	366	2	EYES	Degeneration; Retina, grade 1	
112	Male	1	366	2	HEART	Epicardium; Inflammation; Chronic, grade 1	
112	Male	1	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
112	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
112	Male	1	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
113	Male	1	366	2	HEART	Cardiomyopathy, grade 1	
113	Male	1	366	2	KIDNEYS	Nephropathy, grade 1	
113	Male	1	366	2	LIVER	Inflammation, grade 1	
113	Male	1	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
113	Male	1	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
113	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
114	Male	1	366	2	KIDNEYS	Nephropathy, grade 1	
115	Male	1	366	2	KIDNEYS	Nephropathy, grade 1	
115	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
116	Male	1	366	2	HEART	Cardiomyopathy, grade 1	
116	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
117	Male	1	366	2	HEART	Cardiomyopathy, grade 1	
117	Male	1	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
118	Male	1	366	2	LIVER	Inflammation, grade 1	
118	Male	1	366	2	NOSE/TURBINATES	Inflammation, grade 1	
118	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
118	Male	1	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
119	Male	1	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
119	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
120	Male	1	366	2	EYES	Degeneration; Retina, grade 1	
120	Male	1	366	2	LUNG	Inflammation, grade 1	
120	Male	1	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
301	Male	3	365	2	HEART	Cardiomyopathy, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
301	Male	3	365	2	KIDNEYS	Nephropathy, grade 1	
301	Male	3	365	2	LIVER	Inflammation, grade 1	
301	Male	3	365	2	NOSE/TURBINATES	Cyst(s); Mucosa	
301	Male	3	365	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
301	Male	3	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
302	Male	3	365	2	KIDNEYS	Nephropathy, grade 1	
303	Male	3	365	2	HEART	Cardiomyopathy, grade 1	
303	Male	3	365	2	LIVER	Inflammation, grade 1	
303	Male	3	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
303	Male	3	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
304	Male	3	365	2	HEART	Cardiomyopathy, grade 1	
304	Male	3	365	2	KIDNEYS	Inflammation; Pelvic, unilateral, grade 2	
304	Male	3	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
304	Male	3	365	2	LIVER	Tension Lipidosis, grade 2	
304	Male	3	365	2	LUNG	Osseous Metaplasia	
304	Male	3	365	2	TESTES	Interstitial Fluid, unilateral, grade 2	
305	Male	3	365	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
305	Male	3	365	2	LIVER	Inflammation, grade 1	
305	Male	3	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
306	Male	3	365	2	KIDNEYS	Nephropathy, grade 1	
306	Male	3	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
306	Male	3	365	2	LIVER	Inflammation, grade 1	
306	Male	3	365	2	LIVER	Lipidosis; Focal, grade 1	
306	Male	3	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
306	Male	3	365	2	THYMUS	Cyst(s)	
306	Male	3	365	2	THYROID GLAND (BOTH LOBES)	Adenoma; C-Cell, unilateral (benign neoplasm)	I
307	Male	3	365	2	LIVER	Tension Lipidosis, grade 1	
307	Male	3	365	2	LUNG	Osseous Metaplasia	
308	Male	3	365	2	HEART	Cardiomyopathy, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
309	Male	3	365	2	HEART	Cardiomyopathy, grade 1	
309	Male	3	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
310	Male	3	365	2	KIDNEYS	Nephropathy, grade 1	
310	Male	3	365	2	LIVER	Hyperplasia; Bile Duct, grade 1	
310	Male	3	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
310	Male	3	365	2	THYMUS	Cyst(s)	
311	Male	3	366	2	EYES	Degeneration; Retina, grade 1	
311	Male	3	366	2	KIDNEYS	Nephropathy, grade 1	
311	Male	3	366	2	LIVER	Inflammation, grade 1	
311	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
311	Male	3	366	2	PROSTATE GLAND	Inflammation, grade 1	
311	Male	3	366	2	SKIN, OTHER	Hyperkeratosis, grade 2	
311	Male	3	366	2	SKIN, OTHER	Inflammation, grade 2	
312	Male	3	366	2	LIVER	Inflammation, grade 1	
312	Male	3	366	2	SKIN, OTHER	Hyperkeratosis, grade 2	
312	Male	3	366	2	SKIN, OTHER	Inflammation, grade 1	
313	Male	3	366	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
313	Male	3	366	2	HEART	Cardiomyopathy, grade 1	
313	Male	3	366	2	KIDNEYS	Nephropathy, grade 1	
313	Male	3	366	2	LIVER	Inflammation, grade 1	
313	Male	3	366	2	LIVER	Tension Lipidosis, grade 2	
313	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
313	Male	3	366	2	PROSTATE GLAND	Inflammation, grade 1	
314	Male	3	366	2	LIVER	Hyperplasia; Bile Duct, grade 1	
314	Male	3	366	2	LIVER	Inflammation, grade 1	
314	Male	3	366	2	LUNG	Inflammation, grade 1	
314	Male	3	366	2	SKIN, OTHER	Fat Infiltration	
315	Male	3	366	2	LIVER	Inflammation, grade 1	
315	Male	3	366	2	LIVER	Lipidosis; Periportal, grade 1	
315	Male	3	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
315	Male	3	366	2	SPLEEN	Pigment Deposition, grade 1	
316	Male	3	366	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
316	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
317	Male	3	366	2	LIVER	Inflammation, grade 1	
317	Male	3	366	2	LIVER	Tension Lipidosis, grade 1	
318	Male	3	366	2	LUNG	Pigmented Macrophages, grade 2	
318	Male	3	366	2	PITUITARY GLAND	Adenoma; Pars Distalis (benign neoplasm)	I
318	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
318	Male	3	366	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
319	Male	3	366	2	LIVER	Tension Lipidosis, grade 1	
319	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
319	Male	3	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral, grade 1	
320	Male	3	366	2	KIDNEYS	Inflammation; Pelvic, grade 1	
320	Male	3	366	2	LIVER	Inflammation, grade 1	
320	Male	3	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
401	Male	4	365	2	LIVER	Inflammation, grade 1	
401	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
401	Male	4	365	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
402	Male	4	365	2	EYES	Degeneration; Retina, grade 1	
402	Male	4	365	2	LUNG	Inflammation, grade 1	
402	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
402	Male	4	365	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
403	Male	4	365	2	HEART	Cardiomyopathy, grade 1	
403	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
404	Male	4	365	2	HEART	Cardiomyopathy, grade 1	
404	Male	4	365	2	LIVER	Inflammation, grade 1	
404	Male	4	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
405	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
405	Male	4	365	2	THYMUS	Atrophy, grade 1	
406	Male	4	365	2	HARDERIAN GLANDS	Inflammation, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
406	Male	4	365	2	KIDNEYS	Nephropathy, grade 1	
406	Male	4	365	2	LIVER	Inflammation, grade 1	
406	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
407	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
408	Male	4	365	2	THYROID GLAND (BOTH LOBES)	Adenoma; C-Cell, unilateral (benign neoplasm)	I
409	Male	4	365	2	LUNG	Inflammation, grade 1	
410	Male	4	365	2	PHARYNX	Foreign Material	
410	Male	4	365	2	PHARYNX	Inflammation, grade 3	
410	Male	4	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
410	Male	4	365	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
411	Male	4	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
412	Male	4	366	2	EYES	Degeneration; Retina, grade 1	
412	Male	4	366	2	KIDNEYS	Nephropathy, grade 1	
412	Male	4	366	2	LIVER	Inflammation, grade 1	
413	Male	4	366	2	INTESTINE-LARGE, COLON	Metazoan Parasite	
413	Male	4	366	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
413	Male	4	366	2	LIVER	Inflammation, grade 1	
413	Male	4	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
413	Male	4	366	2	PITUITARY GLAND	Cyst(s)	
413	Male	4	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
413	Male	4	366	2	SEMINAL VESICLES	Distention, grade 3	
414	Male	4	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
415	Male	4	366	2	KIDNEYS	Cyst(s), unilateral	
415	Male	4	366	2	THYMUS	Cyst(s)	
416	Male	4	366	2	LIVER	Inflammation, grade 1	
416	Male	4	366	2	LUNG	Alveolar Macrophages; Increased, grade 2	
416	Male	4	366	2	LUNG	Inflammation, grade 1	
417	Male	4	366	2	ADRENAL GLANDS	Vacuolation; Cortex, unilateral, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
418	Male	4	366	2	LIVER	Inflammation, grade 1	
418	Male	4	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
419	Male	4	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
420	Male	4	366	2	EPIDIDYMIDES	Aspermia, unilateral	
420	Male	4	366	2	KIDNEYS	Nephropathy, grade 1	
420	Male	4	366	2	LIVER	Tension Lipidosis, grade 2	
420	Male	4	366	2	PANCREAS	Atrophy; Acinar Cell, grade 2	
420	Male	4	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
420	Male	4	366	2	TESTES	Atrophy, unilateral, grade 3	
420	Male	4	366	2	ZYMBAL'S GLANDS	Squamous Papilloma, unilateral (benign neoplasm)	I
501	Male	5	365	2	ADRENAL GLANDS	Vacuolation; Cortex, unilateral, grade 1	
501	Male	5	365	2	EPIDIDYMIDES	Aspermia, unilateral	
501	Male	5	365	2	HEART	Cardiomyopathy, grade 1	
501	Male	5	365	2	PROSTATE GLAND	Inflammation; Chronic, grade 1	
501	Male	5	365	2	TESTES	Atrophy, unilateral, grade 3	
502	Male	5	365	2	HEART	Cardiomyopathy, grade 1	
502	Male	5	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
502	Male	5	365	2	PHARYNX	Inflammation, grade 1	
502	Male	5	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
503	Male	5	365	2	HEART	Cardiomyopathy, grade 1	
503	Male	5	365	2	LIVER	Hyperplasia; Bile Duct, grade 1	
503	Male	5	365	2	LIVER	Inflammation, grade 1	
503	Male	5	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
503	Male	5	365	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
504	Male	5	142	1	BONE	Hemorrhage, grade 2	
504	Male	5	142	1	CAUSE OF DEATH	Malignant Schwannoma	
504	Male	5	142	1	HARDERIAN GLANDS	Malignant Schwannoma; Invasive, unilateral (site of primary neoplasm: SKEL MUSCLE, OTHER)	
504	Male	5	142	1	KIDNEYS	Pelvic Dilatation, unilateral, grade 2	
504	Male	5	142	1	NOSE/TURBINATES	Hemorrhage, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
504	Male	5	142	1	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
504	Male	5	142	1	SKELETAL MUSCLE, OTHER	Malignant Schwannoma (malignant neoplasm, definitely fatal)	F
504	Male	5	142	1	SPLEEN	Lymphoid Depletion, grade 3	
505	Male	5	365	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
505	Male	5	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
506	Male	5	365	2	LIVER	Focus/Foci; Clear Cell, grade 1	
507	Male	5	365	2	KIDNEYS	Nephropathy, grade 1	
507	Male	5	365	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
507	Male	5	365	2	THYROID GLAND (BOTH LOBES)	Follicular Cyst(s), unilateral	
508	Male	5	365	2	KIDNEYS	Nephropathy, grade 1	
508	Male	5	365	2	URINARY BLADDER	Hemorrhage; Mucosa, grade 2	
509	Male	5	365	2	HEART	Cardiomyopathy, grade 1	
510	Male	5	365	2	ADRENAL GLANDS	Vacuolation; Cortex, unilateral, grade 1	
510	Male	5	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
510	Male	5	365	2	LIVER	Inflammation, grade 1	
510	Male	5	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
510	Male	5	365	2	PROSTATE GLAND	Inflammation; Chronic, grade 1	
511	Male	5	366	2	STOMACH	Mucosal Cyst; Glandular	
512	Male	5	366	2	LIVER	Inflammation, grade 1	
512	Male	5	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 3	
513	Male	5	366	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
513	Male	5	366	2	KIDNEYS	Cyst(s), unilateral	
513	Male	5	366	2	KIDNEYS	Nephropathy, grade 1	
514	Male	5	366	2			
515	Male	5	366	2	KIDNEYS	Nephropathy, grade 2	
515	Male	5	366	2	LIVER	Inflammation, grade 1	
515	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
515	Male	5	366	2	STOMACH	Inflammation, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
516	Male	5	366	2	HARDERIAN GLANDS	Inflammation, grade 2	
516	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
516	Male	5	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
517	Male	5	366	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
517	Male	5	366	2	LIVER	Hyperplasia; Bile Duct, grade 1	
517	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
518	Male	5	366	2	HEART	Cardiomyopathy, grade 1	
518	Male	5	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
518	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
519	Male	5	366	2	HEART	Cardiomyopathy, grade 1	
519	Male	5	366	2	KIDNEYS	Inflammation; Pelvic, unilateral, grade 2	
519	Male	5	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 3	
519	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
519	Male	5	366	2	PROSTATE GLAND	Inflammation; Chronic, grade 1	
520	Male	5	366	2	HEART	Cardiomyopathy, grade 1	
520	Male	5	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
601	Male	6	365	2	KIDNEYS	Nephropathy, grade 1	
601	Male	6	365	2	LUNG	Osseous Metaplasia	
602	Male	6	365	2	KIDNEYS	Mineralization; Pelvic, unilateral, grade 1	
602	Male	6	365	2	KIDNEYS	Nephropathy, grade 1	
602	Male	6	365	2	LIVER	Inflammation, grade 1	
603	Male	6	365	2	EPIDIDYMIDES	Aspermia	
603	Male	6	365	2	EYES	Degeneration; Retina, grade 1	
603	Male	6	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
603	Male	6	365	2	SKIN, OTHER	Hyperkeratosis, grade 2	
603	Male	6	365	2	TESTES	Atrophy, grade 4	
603	Male	6	365	2	THYMUS	Cyst(s)	
604	Male	6	365	2	LUNG	Congestion, grade 1	
604	Male	6	365	2	LUNG	Pigmented Macrophages, grade 1	
604	Male	6	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
605	Male	6	365	2	KIDNEYS	Nephropathy, grade 1	
605	Male	6	365	2	PROSTATE GLAND	Inflammation, grade 1	
605	Male	6	365	2	SKIN, OTHER	Epidermal Ulceration, grade 2	
605	Male	6	365	2	SKIN, OTHER	Inflammation, grade 2	
605	Male	6	365	2	THYMUS	Cyst(s)	
606	Male	6	365	2	KIDNEYS	Nephropathy, grade 1	
606	Male	6	365	2	LIVER	Inflammation, grade 1	
606	Male	6	365	2	PANCREAS	Atrophy; Acinar Cell, grade 2	
607	Male	6	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
608	Male	6	365	2			
609	Male	6	365	2	LIVER	Inflammation, grade 1	
609	Male	6	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
609	Male	6	365	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
610	Male	6	365	2			
611	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
612	Male	6	366	2	HEART	Cardiomyopathy, grade 1	
612	Male	6	366	2	LIVER	Inflammation, grade 1	
612	Male	6	366	2	LUNG	Osseous Metaplasia	
612	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
612	Male	6	366	2	SKIN, OTHER	Hyperplasia; Sebaceous Gland, grade 1	
613	Male	6	366	2	EPIDIDYMIDES	Hypospermia, grade 3	
613	Male	6	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
613	Male	6	366	2	LIVER	Inflammation, grade 1	
613	Male	6	366	2	LIVER	Tension Lipidosis, grade 1	
613	Male	6	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
613	Male	6	366	2	TESTES	Atrophy, grade 3	
614	Male	6	366	2	KIDNEYS	Nephropathy, grade 1	
615	Male	6	366	2	LIVER	Hepatodiaphragmatic Nodule	
615	Male	6	366	2	LIVER	Hyperplasia; Bile Duct, grade 1	
615	Male	6	366	2	LIVER	Inflammation, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
615	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
615	Male	6	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
616	Male	6	366	2	LIVER	Inflammation, grade 1	
617	Male	6	366	2	LIVER	Inflammation, grade 1	
617	Male	6	366	2	PITUITARY GLAND	Cyst(s)	
617	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 3	
618	Male	6	366	2	BONE	Osteosarcoma (malignant neoplasm)	I
618	Male	6	366	2	HEART	Cardiomyopathy, grade 1	
618	Male	6	366	2	KIDNEYS	Nephropathy, grade 1	
618	Male	6	366	2	LIVER	Inflammation, grade 1	
618	Male	6	366	2	LUNG	Inflammation, grade 1	
619	Male	6	366	2	LIVER	Inflammation, grade 1	
619	Male	6	366	2	LUNG	Inflammation, grade 1	
619	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
620	Male	6	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
620	Male	6	366	2	PROSTATE GLAND	Inflammation, grade 1	
701	Male	7	365	2	LUNG	Osseous Metaplasia	
701	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
702	Male	7	365	2	EYES	Degeneration; Retina, grade 1	
702	Male	7	365	2	LIVER	Inflammation, grade 1	
702	Male	7	365	2	LUNG	Alveolar Macrophages; Increased, grade 2	
702	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
703	Male	7	365	2	EYES	Degeneration; Retina, grade 1	
703	Male	7	365	2	HEART	Cardiomyopathy, grade 1	
703	Male	7	365	2	KIDNEYS	Nephropathy, grade 1	
703	Male	7	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
703	Male	7	365	2	PANCREAS	Atrophy; Acinar Cell, grade 2	
703	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 3	
704	Male	7	365	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
704	Male	7	365	2	HEART	Cardiomyopathy, grade 2	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
704	Male	7	365	2	KIDNEYS	Nephropathy, grade 1	
704	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 2	
704	Male	7	365	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
705	Male	7	365	2	LIVER	Inflammation, grade 1	
705	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
706	Male	7	365	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
706	Male	7	365	2	KIDNEYS	Nephropathy, grade 1	
706	Male	7	365	2	LUNG	Inflammation, grade 1	
707	Male	7	365	2	LIVER	Inflammation, grade 1	
707	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
707	Male	7	365	2	THYROID GLAND (BOTH LOBES)	Follicular Cyst(s), unilateral	
708	Male	7	365	2	HEART	Cardiomyopathy, grade 1	
708	Male	7	365	2	KIDNEYS	Nephropathy, grade 1	
708	Male	7	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
708	Male	7	365	2	LIVER	Inflammation, grade 1	
708	Male	7	365	2	LIVER	Tension Lipidosis, grade 1	
708	Male	7	365	2	LYMPH NODE, MESENTERIC	Angiomatous Hyperplasia, grade 2	
708	Male	7	365	2	LYMPH NODE, MESENTERIC	Hemangiosarcoma (malignant neoplasm)	I
708	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
708	Male	7	365	2	PROSTATE GLAND	Inflammation, grade 2	
709	Male	7	365	2	KIDNEYS	Nephropathy, grade 1	
710	Male	7	365	2	LIVER	Inflammation, grade 1	
710	Male	7	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
711	Male	7	366	2	LIVER	Inflammation, grade 1	
712	Male	7	366	2	EYES	Degeneration; Retina, grade 1	
712	Male	7	366	2	LIVER	Inflammation, grade 1	
712	Male	7	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
712	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
712	Male	7	366	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
713	Male	7	366	2	LIVER	Inflammation, grade 1	
713	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
714	Male	7	366	2	LIVER	Inflammation, grade 1	
714	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
714	Male	7	366	2	SPLEEN	Pigment Deposition, grade 1	
714	Male	7	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
715	Male	7	366	2	EYES	Degeneration; Retina, grade 1	
715	Male	7	366	2	KIDNEYS	Nephropathy, grade 1	
715	Male	7	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
716	Male	7	366	2	EPIDIDYIMIDES	Hypospermia, unilateral, grade 4	
716	Male	7	366	2	KIDNEYS	Nephropathy, grade 1	
716	Male	7	366	2	LIVER	Inflammation, grade 1	
716	Male	7	366	2	TESTES	Atrophy, unilateral, grade 4	
716	Male	7	366	2	TESTES	Interstitial Cell Adenoma, unilateral (benign neoplasm)	I
717	Male	7	366	2	KIDNEYS	Nephropathy, grade 1	
717	Male	7	366	2	LIVER	Inflammation, grade 1	
717	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, grade 2	
717	Male	7	366	2	PROSTATE GLAND	Inflammation, grade 1	
718	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
718	Male	7	366	2	THYMUS	Cyst(s)	
719	Male	7	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
719	Male	7	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
720	Male	7	366	2	EYES	Degeneration; Retina, grade 1	
720	Male	7	366	2	KIDNEYS	Nephropathy, grade 1	
720	Male	7	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
720	Male	7	366	2	PITUITARY GLAND	Adenoma; Pars Distalis (benign neoplasm)	I
801	Male	8	365	2	KIDNEYS	Nephropathy, grade 1	
801	Male	8	365	2	LUNG	Pigmented Macrophages, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
801	Male	8	365	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
801	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
802	Male	8	365	2	LIVER	Inflammation, grade 1	
802	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
802	Male	8	365	2	PROSTATE GLAND	Inflammation, grade 2	
803	Male	8	365	2	HARDERIAN GLANDS	Inflammation, grade 1	
803	Male	8	365	2	KIDNEYS	Nephropathy, grade 1	
803	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 2	
804	Male	8	365	2	EPIDIDYMIDES	Aspermia	
804	Male	8	365	2	HEART	Cardiomyopathy, grade 1	
804	Male	8	365	2	KIDNEYS	Nephropathy, grade 2	
804	Male	8	365	2	LIVER	Hyperplasia; Bile Duct, grade 1	
804	Male	8	365	2	LIVER	Inflammation, grade 1	
804	Male	8	365	2	LUNG	Osseous Metaplasia	
804	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
804	Male	8	365	2	TESTES	Atrophy, grade 3	
805	Male	8	365	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
805	Male	8	365	2	HEART	Valve; Inflammation, grade 1	
805	Male	8	365	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
805	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
806	Male	8	365	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
806	Male	8	365	2	LIVER	Inflammation, grade 1	
806	Male	8	365	2	LIVER	Pigment; Periportal, grade 2	
806	Male	8	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
806	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
806	Male	8	365	2	PROSTATE GLAND	Inflammation; Chronic, grade 1	
807	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
808	Male	8	365	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
808	Male	8	365	2	INTESTINE-SMALL, JEJUNUM	Inflammation, grade 3	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
808	Male	8	365	2	INTESTINE-SMALL, JEJUNUM	Ulcer, grade 3	
808	Male	8	365	2	KIDNEYS	Nephropathy, grade 1	
808	Male	8	365	2	LUNG	Alveolar Macrophages; Increased, grade 1	
808	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
809	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
810	Male	8	365	2	ADRENAL GLANDS	Vacuolation; Cortex, unilateral, grade 1	
810	Male	8	365	2	EPIDIDYMIDES	Aspermia	
810	Male	8	365	2	HEART	Cardiomyopathy, grade 1	
810	Male	8	365	2	PREPUTIAL GLANDS	Inflammation, grade 1	
810	Male	8	365	2	TESTES	Atrophy, grade 3	
811	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
811	Male	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
812	Male	8	366	2	KIDNEYS	Nephropathy, grade 1	
812	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
813	Male	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
814	Male	8	366	2	LYMPH NODE, MESENTERIC	Hemangiosarcoma (malignant neoplasm)	I
814	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
815	Male	8	366	2	KIDNEYS	Nephropathy, grade 1	
815	Male	8	366	2	LIVER	Inflammation, grade 1	
815	Male	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
815	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 3	
815	Male	8	366	2	SKIN, OTHER	Epidermal Ulceration, grade 3	
815	Male	8	366	2	SKIN, OTHER	Hyperplasia; Epithelial, grade 2	
816	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
816	Male	8	366	2	SPLEEN	Pigment Deposition, grade 1	
817	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
818	Male	8	366	2	KIDNEYS	Nephropathy, grade 1	
818	Male	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
819	Male	8	366	2	LIVER	Inflammation, grade 1	
819	Male	8	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
819	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, unilateral, grade 1	
820	Male	8	366	2	KIDNEYS	Nephropathy, grade 1	
820	Male	8	366	2	LIVER	Hyperplasia; Bile Duct, grade 1	
820	Male	8	366	2	PREPUTIAL GLANDS	Inflammation, grade 1	
820	Male	8	366	2	TESTES	Atrophy, grade 2	
820	Male	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1101	Female	1	366	2	INTESTINE-LARGE, RECTUM	Metazoan Parasites	
1101	Female	1	366	2	LIVER	Cyst; Multilocular; Bile	
1101	Female	1	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1101	Female	1	366	2	OVARIES	Decreased Corpora Lutea	
1101	Female	1	366	2	SPLEEN	Pigment Deposition, grade 1	
1102	Female	1	366	2	CLITORAL GLANDS	Inflammation, grade 3	
1102	Female	1	366	2	EYES	Degeneration; Retina, grade 2	
1102	Female	1	366	2	THYMUS	Cyst(s)	
1102	Female	1	366	2	UTERUS	Dilatation, grade 3	
1103	Female	1	366	2	LIVER	Inflammation, grade 1	
1103	Female	1	366	2	OVARIES	Decreased Corpora Lutea	
1103	Female	1	366	2	UTERUS	Stromal Polyp (benign neoplasm)	I
1104	Female	1	366	2	LIVER	Inflammation, grade 1	
1105	Female	1	366	2	KIDNEYS	Nephropathy, grade 1	
1105	Female	1	366	2	OVARIES	Cyst(s); Parovarian, unilateral	
1105	Female	1	366	2	THYMUS	Cyst(s)	
1105	Female	1	366	2	UTERUS	Dilatation, grade 3	
1105	Female	1	366	2	VAGINA	Mucification	
1106	Female	1	366	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1106	Female	1	366	2	CLITORAL GLANDS	Inflammation, grade 2	
1106	Female	1	366	2	HEART	Cardiomyopathy, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1106	Female	1	366	2	LIVER	Inflammation, grade 1	
1106	Female	1	366	2	LUNG	Inflammation, grade 1	
1106	Female	1	366	2	SALIVARY GLAND	Atrophy, unilateral, grade 1	
1106	Female	1	366	2	SALIVARY GLAND	Inflammation, unilateral, grade 1	
1107	Female	1	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1107	Female	1	366	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1107	Female	1	366	2	OVARIES	Decreased Corpora Lutea	
1107	Female	1	366	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
1107	Female	1	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
1107	Female	1	366	2	STOMACH	Mucosal Cyst; Non-Glandular	
1108	Female	1	366	2	LIVER	Inflammation, grade 1	
1108	Female	1	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1108	Female	1	366	2	UTERUS	Dilatation, grade 2	
1109	Female	1	366	2	SPLEEN	Pigment Deposition, grade 2	
1109	Female	1	366	2	TONGUE	Inflammation; Chronic, grade 1	
1110	Female	1	366	2	HEART	Cardiomyopathy, grade 1	
1110	Female	1	366	2	INTESTINE-LARGE, RECTUM	Metazoan Parasites	
1110	Female	1	366	2	OVARIES	Decreased Corpora Lutea	
1110	Female	1	366	2	SPLEEN	Pigment Deposition, grade 1	
1111	Female	1	367	2			
1112	Female	1	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1112	Female	1	367	2	OVARIES	Decreased Corpora Lutea	
1112	Female	1	367	2	STOMACH	Erosion; Glandular, grade 1	
1112	Female	1	367	2	STOMACH	Inflammation, grade 1	
1112	Female	1	367	2	THYROID GLAND (BOTH LOBES)	Hyperplasia; Follicular Cell, unilateral, grade 1	
1113	Female	1	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1113	Female	1	367	2	HARDERIAN GLANDS	Inflammation, grade 1	
1113	Female	1	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1113	Female	1	367	2	UTERUS	Cyst(s); Endometrial	
1114	Female	1	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1114	Female	1	367	2	KIDNEYS	Mineralization; Tubular, grade 1	
1114	Female	1	367	2	LIVER	Inflammation, grade 1	
1114	Female	1	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1114	Female	1	367	2	LUNG	Inflammation, grade 1	
1114	Female	1	367	2	OVARIES	Cystic Bursa	
1114	Female	1	367	2	OVARIES	Decreased Corpora Lutea	
1114	Female	1	367	2	THYMUS	Cyst(s)	
1115	Female	1	367	2	KIDNEYS	Mineralization; Pelvic, unilateral, grade 1	
1115	Female	1	367	2	SPLEEN	Pigment Deposition, grade 1	
1115	Female	1	367	2	THYMUS	Cyst(s)	
1116	Female	1	367	2	UTERUS	Dilatation, grade 1	
1117	Female	1	367	2	ADRENAL GLANDS	Pigment Deposition, unilateral, grade 1	
1117	Female	1	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1117	Female	1	367	2	LIVER	Inflammation, grade 1	
1117	Female	1	367	2	SPLEEN	Pigment Deposition, grade 1	
1118	Female	1	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1118	Female	1	367	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1118	Female	1	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1118	Female	1	367	2	OVARIES	Cyst(s); Parovarian, unilateral	
1118	Female	1	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1119	Female	1	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1119	Female	1	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1119	Female	1	367	2	OVARIES	Persistent Corpora Lutea	
1119	Female	1	367	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
1119	Female	1	367	2	THYROID GLAND (BOTH LOBES)	Hyperplasia; C-Cell, unilateral, grade 2	
1119	Female	1	367	2	VAGINA	Mucification	
1120	Female	1	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1120	Female	1	367	2	OVARIES	Decreased Corpora Lutea	
1120	Female	1	367	2	SPLEEN	Pigment Deposition, grade 1	
1120	Female	1	367	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 2	
1301	Female	3	367	2	KIDNEYS	Hyperplasia; Urothelium, grade 2	
1301	Female	3	367	2	KIDNEYS	Inflammation; Pelvic, grade 2	
1301	Female	3	367	2	KIDNEYS	Pelvic Dilatation, grade 2	
1301	Female	3	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1301	Female	3	367	2	LIVER	Lipidosis; Focal, grade 1	
1301	Female	3	367	2	OVARIES	Persistent Corpora Lutea	
1301	Female	3	367	2	SPLEEN	Pigment Deposition, grade 1	
1301	Female	3	367	2	URETERS	Dilatation, unilateral, grade 4	
1301	Female	3	367	2	URETERS	Hyperplasia; Urothelium, unilateral, grade 4	
1301	Female	3	367	2	URETERS	Inflammation, unilateral, grade 2	
1301	Female	3	367	2	URINARY BLADDER	Calculi	
1301	Female	3	367	2	URINARY BLADDER	Hyperplasia; Urothelium, grade 3	
1301	Female	3	367	2	URINARY BLADDER	Inflammation, grade 2	
1301	Female	3	367	2	VAGINA	Mucification	
1302	Female	3	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1302	Female	3	367	2	LIVER	Inflammation, grade 1	
1302	Female	3	367	2	SPLEEN	Pigment Deposition, grade 1	
1302	Female	3	367	2	UTERUS	Cyst(s); Endometrial	
1302	Female	3	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1303	Female	3	367	2	LIVER	Pigment; Periportal, grade 1	
1303	Female	3	367	2	OVARIES	Decreased Corpora Lutea	
1303	Female	3	367	2	SPLEEN	Pigment Deposition, grade 1	
1303	Female	3	367	2	UTERUS	Cyst(s); Endometrial, unilateral	
1304	Female	3	367	2	UTERUS	Cyst(s); Endometrial, unilateral	
1304	Female	3	367	2	UTERUS	Dilatation, grade 2	
1305	Female	3	367	2	LIVER	Inflammation, grade 1	
1305	Female	3	367	2	OVARIES	Insufficient Tissue, unilateral	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1305	Female	3	367	2	THYMUS	Cyst(s)	
1306	Female	3	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1306	Female	3	367	2	LIVER	Inflammation, grade 1	
1306	Female	3	367	2	SPLEEN	Pigment Deposition, grade 1	
1307	Female	3	367	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
1307	Female	3	367	2	EYES	Degeneration; Retina, grade 1	
1307	Female	3	367	2	UTERUS	Dilatation, grade 2	
1308	Female	3	367	2	ADRENAL GLANDS	Degeneration; Cortex, unilateral, grade 2	
1308	Female	3	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1308	Female	3	367	2	OVARIES	Decreased Corpora Lutea, unilateral	
1308	Female	3	367	2	UTERUS	Dilatation, grade 2	
1309	Female	3	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1309	Female	3	367	2	LIVER	Inflammation, grade 1	
1309	Female	3	367	2	THYMUS	Cyst(s)	
1310	Female	3	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1310	Female	3	367	2	KIDNEYS	Mineralization; Tubular, grade 1	
1310	Female	3	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1310	Female	3	367	2	OVARIES	Decreased Corpora Lutea	
1310	Female	3	367	2	SPLEEN	Pigment Deposition, grade 1	
1310	Female	3	367	2	UTERUS	Cyst(s); Endometrial	
1310	Female	3	367	2	UTERUS	Fibrosis; Cervix, grade 4	
1310	Female	3	367	2	VAGINA	Stromal Polyp (benign neoplasm)	I
1311	Female	3	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1311	Female	3	368	2	LIVER	Inflammation, grade 1	
1311	Female	3	368	2	OVARIES	Cystic Bursa	
1311	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1311	Female	3	368	2	SPLEEN	Pigment Deposition, grade 2	
1312	Female	3	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1312	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1312	Female	3	368	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1313	Female	3	368	2	OVARIES	Cyst(s), unilateral	
1313	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1313	Female	3	368	2	SPLEEN	Pigment Deposition, grade 1	
1314	Female	3	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1314	Female	3	368	2	EYES	Degeneration; Retina, grade 1	
1314	Female	3	368	2	KIDNEYS	Nephropathy, grade 1	
1314	Female	3	368	2	LIVER	Pigment; Periportal, grade 4	
1314	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1315	Female	3	368	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1315	Female	3	368	2	LIVER	Inflammation, grade 1	
1315	Female	3	368	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
1315	Female	3	368	2	SPLEEN	Pigment Deposition, grade 1	
1316	Female	3	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1316	Female	3	368	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1316	Female	3	368	2	LIVER	Inflammation, grade 1	
1316	Female	3	368	2	PITUITARY GLAND	Cyst(s)	
1316	Female	3	368	2	SPLEEN	Pigment Deposition, grade 1	
1316	Female	3	368	2	THYMUS	Cyst(s)	
1317	Female	3	368	2	LIVER	Inflammation, grade 1	
1317	Female	3	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1317	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1317	Female	3	368	2	SPLEEN	Pigment Deposition, grade 1	
1318	Female	3	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1318	Female	3	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1318	Female	3	368	2	KIDNEYS	Mineralization; Pelvic, unilateral, grade 2	
1318	Female	3	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1318	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1318	Female	3	368	2	SPLEEN	Pigment Deposition, grade 2	
1319	Female	3	368	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1319	Female	3	368	2	SPLEEN	Pigment Deposition, grade 2	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1320	Female	3	368	2	ADRENAL GLANDS	Angiectasis; Cortex, unilateral, grade 1	
1320	Female	3	368	2	KIDNEYS	Mineralization; Pelvic, unilateral, grade 1	
1320	Female	3	368	2	LIVER	Inflammation, grade 1	
1320	Female	3	368	2	OVARIES	Decreased Corpora Lutea	
1320	Female	3	368	2	SPLEEN	Pigment Deposition, grade 2	
1320	Female	3	368	2	THYMUS	Cyst(s)	
1320	Female	3	368	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1401	Female	4	367	2	LIVER	Inflammation, grade 1	
1402	Female	4	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1402	Female	4	367	2	LIVER	Inflammation, grade 1	
1402	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1402	Female	4	367	2	THYMUS	Cyst(s)	
1403	Female	4	367	2	KIDNEYS	Nephropathy, grade 1	
1403	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1403	Female	4	367	2	THYMUS	Cyst(s)	
1404	Female	4	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1404	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1404	Female	4	367	2	SPLEEN	Pigment Deposition, grade 2	
1404	Female	4	367	2	UTERUS	Cyst(s); Endometrial, unilateral	
1405	Female	4	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1405	Female	4	367	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1405	Female	4	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1405	Female	4	367	2	UTERUS	Dilatation, grade 3	
1406	Female	4	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1406	Female	4	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1406	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1407	Female	4	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 2	
1407	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1407	Female	4	367	2	SPLEEN	Pigment Deposition, grade 1	
1407	Female	4	367	2	THYMUS	Cyst(s)	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1407	Female	4	367	2	UTERUS	Endometrial Hyperplasia; Cystic, unilateral, grade 2	
1408	Female	4	367	2	LIVER	Inflammation, grade 1	
1408	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1408	Female	4	367	2	UTERUS	Dilatation, unilateral, grade 1	
1409	Female	4	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1409	Female	4	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1409	Female	4	367	2	KIDNEYS	Nephropathy, grade 1	
1409	Female	4	367	2	THYMUS	Cyst(s)	
1410	Female	4	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1410	Female	4	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1410	Female	4	367	2	LUNG	Pigmented Macrophages, grade 1	
1410	Female	4	367	2	OVARIES	Decreased Corpora Lutea	
1410	Female	4	367	2	THYMUS	Cyst(s)	
1411	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1411	Female	4	368	2	SPLEEN	Pigment Deposition, grade 2	
1411	Female	4	368	2	THYMUS	Cyst(s)	
1411	Female	4	368	2	UTERUS	Fibrosis; Cervix, grade 3	
1411	Female	4	368	2	UTERUS	Hyperplasia; Epithelial, grade 2	
1411	Female	4	368	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1412	Female	4	368	2	UTERUS	Dilatation, grade 2	
1412	Female	4	368	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 1	
1413	Female	4	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1413	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1414	Female	4	368	2	CLITORAL GLANDS	Inflammation, grade 1	
1414	Female	4	368	2	LIVER	Inflammation, grade 1	
1414	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1414	Female	4	368	2	THYMUS	Cyst(s)	
1415	Female	4	368	2	KIDNEYS	Nephropathy, grade 1	
1415	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1415	Female	4	368	2	SPLEEN	Pigment Deposition, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1415	Female	4	368	2	THYMUS	Cyst(s)	
1416	Female	4	368	2	KIDNEYS	Nephropathy, grade 1	
1416	Female	4	368	2	LUNG	Inflammation, grade 1	
1416	Female	4	368	2	OVARIES	Persistent Corpora Lutea	
1416	Female	4	368	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 1	
1416	Female	4	368	2	VAGINA	Mucification	
1417	Female	4	368	2	ADRENAL GLANDS	Angiectasis; Cortex, unilateral, grade 2	
1417	Female	4	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1417	Female	4	368	2	LIVER	Inflammation, grade 1	
1417	Female	4	368	2	MAMMARY GLAND	Lactation, grade 1	
1417	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1417	Female	4	368	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 1	
1418	Female	4	368	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1418	Female	4	368	2	INTESTINE-LARGE, RECTUM	Metazoan Parasites	
1418	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1418	Female	4	368	2	SPLEEN	Pigment Deposition, grade 1	
1419	Female	4	368	2	EYES	Degeneration; Retina, grade 1	
1419	Female	4	368	2	LIVER	Inflammation, grade 1	
1419	Female	4	368	2	MAMMARY GLAND	Hyperplasia, grade 1	
1419	Female	4	368	2	OVARIES	Decreased Corpora Lutea	
1419	Female	4	368	2	PITUITARY GLAND	Adenoma; Pars Distalis (benign neoplasm)	I
1419	Female	4	368	2	SPLEEN	Pigment Deposition, grade 1	
1420	Female	4	368	2	UTERUS	Dilatation, unilateral, grade 2	
1501	Female	5	366	2	CLITORAL GLANDS	Inflammation, grade 1	
1501	Female	5	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1501	Female	5	366	2	LUNG	Inflammation, grade 1	
1501	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1502	Female	5	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1502	Female	5	366	2	LUNG	Pigmented Macrophages, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1502	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1502	Female	5	366	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
1503	Female	5	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1503	Female	5	366	2	KIDNEYS	Mineralization; Pelvic, grade 1	
1503	Female	5	366	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1503	Female	5	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1503	Female	5	366	2	PITUITARY GLAND	Adenoma; Pars Distalis (benign neoplasm)	
1504	Female	5	366	2	OVARIES	Cyst(s); Parovarian	
1504	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1504	Female	5	366	2	SKIN, OTHER	Adenoma; Sebaceous Gland (benign neoplasm)	
1504	Female	5	366	2	THYROID GLAND (BOTH LOBES)	Hyperplasia; C-Cell, unilateral, grade 2	
1505	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1505	Female	5	366	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 2	
1506	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1507	Female	5	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1507	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1508	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1508	Female	5	366	2	THYMUS	Cyst(s)	
1509	Female	5	366	2	HEART	Cardiomyopathy, grade 1	
1509	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1509	Female	5	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
1510	Female	5	366	2	LIVER	Inflammation, grade 1	
1510	Female	5	366	2	OVARIES	Decreased Corpora Lutea	
1510	Female	5	366	2	UTERUS	Dilatation, grade 3	
1511	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1511	Female	5	367	2	SPLEEN	Pigment Deposition, grade 1	
1512	Female	5	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1512	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1513	Female	5	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1513	Female	5	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1513	Female	5	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1513	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1513	Female	5	367	2	THYROID GLAND (BOTH LOBES)	Hyperplasia; C-Cell, unilateral, grade 2	
1513	Female	5	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1514	Female	5	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1514	Female	5	367	2	HARDERIAN GLANDS	Inflammation, grade 2	
1514	Female	5	367	2	LIVER	Angiectasis; Focal, grade 1	
1514	Female	5	367	2	MAMMARY GLAND	Adenocarcinoma (malignant neoplasm)	I
1514	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1514	Female	5	367	2	UTERUS	Cyst(s); Endometrial	
1514	Female	5	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1515	Female	5	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1515	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1516	Female	5	297	1	CAUSE OF DEATH	Undetermined	
1516	Female	5	297	1	OVARIES	Cyst(s); Parovarian	
1516	Female	5	297	1	ZYMBAL'S GLANDS	Dilated Duct(s)	
1517	Female	5	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1517	Female	5	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1518	Female	5	367	2	OVARIES	Decreased Corpora Lutea	
1518	Female	5	367	2	SPLEEN	Pigment Deposition, grade 1	
1519	Female	5	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1519	Female	5	367	2	OVARIES	Atrophy, unilateral, grade 2	
1519	Female	5	367	2	OVARIES	Decreased Corpora Lutea, unilateral	
1519	Female	5	367	2	OVARIES	Pigment Deposition, unilateral, grade 2	
1519	Female	5	367	2	SPLEEN	Pigment Deposition, grade 1	
1520	Female	5	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1520	Female	5	367	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1520	Female	5	367	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1520	Female	5	367	2	UTERUS	Dilatation, grade 2	
1601	Female	6	367	2	EYES	Degeneration; Retina, grade 1	
1601	Female	6	367	2	MAMMARY GLAND	Hyperplasia, grade 1	
1601	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1602	Female	6	367	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
1602	Female	6	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 2	
1602	Female	6	367	2	LIVER	Hyperplasia; Bile Duct, grade 1	
1602	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1602	Female	6	367	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
1602	Female	6	367	2	SPLEEN	Increased Extramedullary Hematopoiesis, grade 1	
1602	Female	6	367	2	SPLEEN	Pigment Deposition, grade 2	
1602	Female	6	367	2	THYMUS	Cyst(s)	
1603	Female	6	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1603	Female	6	367	2	LIVER	Inflammation, grade 1	
1603	Female	6	367	2	SPLEEN	Pigment Deposition, grade 1	
1603	Female	6	367	2	UTERUS	Endometrial Hyperplasia; Cystic, unilateral, grade 2	
1604	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1604	Female	6	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1605	Female	6	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1605	Female	6	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1605	Female	6	367	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1605	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1605	Female	6	367	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 3	
1605	Female	6	367	2	SPLEEN	Pigment Deposition, grade 1	
1605	Female	6	367	2	THYMUS	Cyst(s)	
1605	Female	6	367	2	UTERUS	Dilatation, grade 1	
1606	Female	6	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1606	Female	6	367	2	EYES	Degeneration; Retina, grade 1	
1606	Female	6	367	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1606	Female	6	367	2	OVARIES	Cyst(s), unilateral	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1606	Female	6	367	2	UTERUS	Dilatation, grade 2	
1607	Female	6	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1607	Female	6	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1607	Female	6	367	2	KIDNEYS	Mineralization; Pelvic, grade 1	
1607	Female	6	367	2	LIVER	Inflammation, grade 1	
1607	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1607	Female	6	367	2	THYMUS	Cyst(s)	
1607	Female	6	367	2	VAGINA	Metazoan Parasite	
1608	Female	6	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1608	Female	6	367	2	EYES	Degeneration; Retina, grade 1	
1608	Female	6	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1608	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1608	Female	6	367	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
1609	Female	6	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1609	Female	6	367	2	ADRENAL GLANDS	One Medulla Examined	
1609	Female	6	367	2	MAMMARY GLAND	Galactocele(s)	
1609	Female	6	367	2	OVARIES	Decreased Corpora Lutea	
1609	Female	6	367	2	THYMUS	Cyst(s)	
1609	Female	6	367	2	UTERUS	Cyst(s); Endometrial, unilateral	
1610	Female	6	367	2	HEART	Cardiomyopathy, grade 2	
1610	Female	6	367	2	THYMUS	Cyst(s)	
1610	Female	6	367	2	VAGINA	Mucification	
1611	Female	6	368	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
1611	Female	6	368	2	LIVER	Inflammation, grade 1	
1611	Female	6	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1612	Female	6	368	2	UTERUS	Dilatation, unilateral, grade 4	
1612	Female	6	368	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1613	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1613	Female	6	368	2	SPLEEN	Increased Extramedullary Hematopoiesis, grade 1	
1614	Female	6	368	2	OVARIES	Hematocyst(s), unilateral	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1615	Female	6	368	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
1615	Female	6	368	2	ADRENAL GLANDS	Vacuolation; Cortex, unilateral, grade 1	
1615	Female	6	368	2	CLITORAL GLANDS	Inflammation, grade 1	
1615	Female	6	368	2	SPLEEN	Pigment Deposition, grade 1	
1616	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1616	Female	6	368	2	SPLEEN	Pigment Deposition, grade 1	
1617	Female	6	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1617	Female	6	368	2	LIVER	Inflammation, grade 1	
1617	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1617	Female	6	368	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
1618	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1618	Female	6	368	2	UTERUS	Dilatation, grade 4	
1619	Female	6	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1619	Female	6	368	2	LIVER	Inflammation, grade 1	
1619	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1620	Female	6	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 2	
1620	Female	6	368	2	LIVER	Inflammation, grade 1	
1620	Female	6	368	2	OVARIES	Decreased Corpora Lutea	
1620	Female	6	368	2	SPLEEN	Pigment Deposition, grade 1	
1701	Female	7	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 3	
1701	Female	7	367	2	LIVER	Inflammation, grade 1	
1701	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1702	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, unilateral, grade 1	
1702	Female	7	367	2	LIVER	Inflammation, grade 1	
1702	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1702	Female	7	367	2	SPLEEN	Pigment Deposition, grade 1	
1702	Female	7	367	2	THYMUS	Cyst(s)	
1703	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, unilateral, grade 1	
1703	Female	7	367	2	ADRENAL GLANDS	Three Adrenals Submitted in Wet	
1703	Female	7	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1703	Female	7	367	2	KIDNEYS	Cyst(s), unilateral	
1703	Female	7	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 2	
1703	Female	7	367	2	OVARIES	Decreased Corpora Lutea, unilateral	
1703	Female	7	367	2	UTERUS	Cyst(s); Endometrial	
1704	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1704	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1705	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1705	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1706	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 2	
1706	Female	7	367	2	LIVER	Inflammation, grade 1	
1706	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1706	Female	7	367	2	THYMUS	Cyst(s)	
1707	Female	7	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1707	Female	7	367	2	LIVER	Inflammation, grade 1	
1707	Female	7	367	2	SPLEEN	Pigment Deposition, grade 1	
1708	Female	7	367	2	THYMUS	Cyst(s)	
1709	Female	7	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1709	Female	7	367	2	INTESTINE-LARGE, RECTUM	Metazoan Parasites	
1709	Female	7	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1709	Female	7	367	2	OVARIES	Decreased Corpora Lutea	
1709	Female	7	367	2	STOMACH	Mineralization; Mucosa, grade 1	
1709	Female	7	367	2	THYMUS	Cyst(s)	
1710	Female	7	367	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1710	Female	7	367	2	CLITORAL GLANDS	Inflammation, grade 2	
1710	Female	7	367	2	EYES	Degeneration; Retina, grade 1	
1710	Female	7	367	2	LIVER	Hyperplasia; Bile Duct, grade 1	
1710	Female	7	367	2	LIVER	Inflammation, grade 1	
1710	Female	7	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1711	Female	7	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1711	Female	7	368	2	LIVER	Inflammation, grade 1	
1711	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1711	Female	7	368	2	THYMUS	Cyst(s)	
1711	Female	7	368	2	THYROID GLAND (BOTH LOBES)	Carcinoma; Follicular Cell, unilateral (malignant neoplasm)	I
1711	Female	7	368	2	UTERUS	Cyst(s); Endometrial	
1711	Female	7	368	2	UTERUS	Endometrial Hyperplasia; Cystic, grade 2	
1712	Female	7	368	2	BONE (STERNUM)	Fibrolipoma (benign neoplasm)	I
1712	Female	7	368	2	HEART	Cardiomyopathy, grade 1	
1712	Female	7	368	2	LIVER	Inflammation, grade 1	
1712	Female	7	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1712	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1712	Female	7	368	2	SPLEEN	Pigment Deposition, grade 1	
1712	Female	7	368	2	UTERUS	Dilatation, grade 4	
1713	Female	7	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1713	Female	7	368	2	CLITORAL GLANDS	Inflammation, grade 1	
1713	Female	7	368	2	KIDNEYS	Nephropathy, grade 1	
1713	Female	7	368	2	LIVER	Inflammation, grade 1	
1713	Female	7	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1714	Female	7	368	2	CLITORAL GLANDS	Inflammation, grade 1	
1714	Female	7	368	2	KIDNEYS	Nephropathy, grade 1	
1714	Female	7	368	2	LIVER	Inflammation, grade 1	
1714	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1714	Female	7	368	2	SKIN, OTHER	Hyperkeratosis, grade 2	
1714	Female	7	368	2	SPLEEN	Increased Extramedullary Hematopoiesis, grade 1	
1714	Female	7	368	2	THYMUS	Cyst(s)	
1714	Female	7	368	2	UTERUS	Dilatation, grade 3	
1715	Female	7	368	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1715	Female	7	368	2	MAMMARY GLAND	Inflammation, grade 3	
1715	Female	7	368	2	SPLEEN	Pigment Deposition, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1715	Female	7	368	2	UTERUS	Dilatation, grade 3	
1716	Female	7	368	2	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	
1716	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1717	Female	7	368	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1717	Female	7	368	2	LUNG	Inflammation, grade 1	
1717	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1717	Female	7	368	2	STOMACH	Mineralization; Mucosa, grade 1	
1717	Female	7	368	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1718	Female	7	368	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1718	Female	7	368	2	LIVER	Inflammation, grade 1	
1718	Female	7	368	2	UTERUS	Dilatation, grade 4	
1719	Female	7	368	2	ADRENAL GLANDS	Hyperplasia; Cortex, unilateral, grade 1	
1719	Female	7	368	2	OVARIES	Decreased Corpora Lutea	
1719	Female	7	368	2	PANCREAS	Atrophy; Acinar Cell, grade 1	
1719	Female	7	368	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
1719	Female	7	368	2	STOMACH	Mineralization; Mucosa, grade 1	
1720	Female	7	368	2	KIDNEYS	Nephropathy, grade 1	
1720	Female	7	368	2	PITUITARY GLAND	Angiectasis, grade 3	
1720	Female	7	368	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 2	
1720	Female	7	368	2	UTERUS	Dilatation, grade 2	
1801	Female	8	366	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1801	Female	8	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1801	Female	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1801	Female	8	366	2	OVARIES	Decreased Corpora Lutea	
1801	Female	8	366	2	UTERUS	Dilatation, grade 1	
1801	Female	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1802	Female	8	351	1	CAUSE OF DEATH	Fibroadenoma	
1802	Female	8	351	1	LIVER	Focus/Foci; Basophilic Cell, grade 2	
1802	Female	8	351	1	LIVER	Focus/Foci; Eosinophilic Cell, grade 1	
1802	Female	8	351	1	MAMMARY GLAND	Fibroadenoma (benign neoplasm, probably fatal)	F

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1802	Female	8	351	1	OVARIES	Decreased Corpora Lutea	
1803	Female	8	366	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1803	Female	8	366	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1803	Female	8	366	2	LIVER	Inflammation, grade 1	
1803	Female	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1803	Female	8	366	2	OVARIES	Cyst(s); Parovarian, unilateral	
1803	Female	8	366	2	OVARIES	Decreased Corpora Lutea, unilateral	
1803	Female	8	366	2	THYMUS	Cyst(s)	
1803	Female	8	366	2	UTERUS	Dilatation, grade 4	
1803	Female	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1804	Female	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1804	Female	8	366	2	OVARIES	Decreased Corpora Lutea	
1805	Female	8	366	2	HARDERIAN GLANDS	Inflammation, unilateral, grade 1	
1805	Female	8	366	2	KIDNEYS	Mineralization; Tubular, unilateral, grade 1	
1805	Female	8	366	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1805	Female	8	366	2	OVARIES	Persistent Corpora Lutea	
1805	Female	8	366	2	VAGINA	Mucification	
1806	Female	8	366	2	ADRENAL GLANDS	Hypertrophy; Cortex, unilateral, grade 1	
1806	Female	8	366	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1806	Female	8	366	2	LIVER	Inflammation, grade 1	
1806	Female	8	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 1	
1806	Female	8	366	2	SPLEEN	Pigment Deposition, grade 1	
1807	Female	8	366	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1807	Female	8	366	2	HEART	Cardiomyopathy, grade 1	
1807	Female	8	366	2	KIDNEYS	Nephropathy, grade 1	
1807	Female	8	366	2	OVARIES	Decreased Corpora Lutea	
1807	Female	8	366	2	PITUITARY GLAND	Hyperplasia; Pars Distalis, grade 3	
1807	Female	8	366	2	THYMUS	Cyst(s)	
1808	Female	8	366	2	SPLEEN	Pigment Deposition, grade 2	
1809	Female	8	353	1	ADRENAL GLANDS	Angiectasis; Cortex, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1809	Female	8	353	1	CAUSE OF DEATH	Stromal Sarcoma	
1809	Female	8	353	1	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1809	Female	8	353	1	OVARIES	Decreased Corpora Lutea	
1809	Female	8	353	1	SPLEEN	Increased Extramedullary Hematopoiesis, grade 1	
1809	Female	8	353	1	THYMUS	Cyst(s)	
1809	Female	8	353	1	UTERUS	Stromal Sarcoma; Cervix (malignant neoplasm, definitely fatal)	F
1809	Female	8	353	1	VAGINA	Prolapse	
1810	Female	8	366	2	OVARIES	Decreased Corpora Lutea	
1810	Female	8	366	2	SPLEEN	Pigment Deposition, grade 2	
1810	Female	8	366	2	THYMUS	Cyst(s)	
1810	Female	8	366	2	ZYMBAL'S GLANDS	Dilated Duct(s)	
1811	Female	8	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1811	Female	8	367	2	MAMMARY GLAND	Hyperplasia, grade 1	
1811	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1811	Female	8	367	2	SPLEEN	Pigment Deposition, grade 1	
1811	Female	8	367	2	UTERUS	Stromal Polyp (benign neoplasm)	I
1812	Female	8	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	
1812	Female	8	367	2	OVARIES	Cystic Bursa	
1812	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1813	Female	8	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1813	Female	8	367	2	HEART	Cardiomyopathy, grade 1	
1813	Female	8	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1813	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1813	Female	8	367	2	SPLEEN	Pigment Deposition, grade 2	
1813	Female	8	367	2	UTERUS	Stromal Polyp; Cervix (benign neoplasm)	I
1813	Female	8	367	2	ZYMBAL'S GLANDS	Dilated Duct(s), unilateral	
1814	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1814	Female	8	367	2	UTERUS	Dilatation, grade 4	
1815	Female	8	367	2	CLITORAL GLANDS	Inflammation, unilateral, grade 1	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice

Appendix B. Data Set for Tumor Incidence Analysis (continued)

Animal	Sex	Dose Group	Death Day	Death Status+	Tissue	Diagnosis	Rel. To Death
1815	Female	8	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1815	Female	8	367	2	SPLEEN	Pigment Deposition, grade 2	
1816	Female	8	367	2	EYES	Degeneration; Retina, unilateral, grade 1	
1816	Female	8	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1816	Female	8	367	2	OVARIES	Persistent Corpora Lutea	
1816	Female	8	367	2	VAGINA	Mucification	
1817	Female	8	367	2	LIVER	Inflammation, grade 1	
1817	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1818	Female	8	367	2	CLITORAL GLANDS	Inflammation, grade 1	
1818	Female	8	367	2	LIVER	Focus/Foci; Basophilic Cell, grade 1	
1818	Female	8	367	2	LUNG	Alveolar Macrophages; Increased, grade 1	
1818	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1818	Female	8	367	2	SPLEEN	Pigment Deposition, grade 1	
1819	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1820	Female	8	367	2	CLITORAL GLANDS	Inflammation, grade 3	
1820	Female	8	367	2	LIVER	Inflammation, grade 1	
1820	Female	8	367	2	OVARIES	Decreased Corpora Lutea	
1820	Female	8	367	2	SPLEEN	Pigment Deposition, grade 2	
1820	Female	8	367	2	THYMUS	Cyst(s)	

+ Death Status 1= Natural death or moribund sacrifice, 2= Terminal Sacrifice