Spontaneous Neoplastic Lesions and Selected Non-neoplastic Lesions in the Crl:CD® BR Rat

February, 1992

Information Prepared by

Patricia L. Lang, Ph.D.
Consulting Toxicologist

TABLE OF CONTENTS

Spontaneous Neoplastic Lesions and Selected Non-neoplastic Lesions in the CRL:CD® BR Rat

INTRODUCTION: The data in these tables were gathered from chronic toxicology studies designed for product registration. All studies were performed in the United States or England by contract toxicology laboratories or industrial toxicology facilities.

PURPOSE: The purpose of this compilation is to offer the study director, toxicologist and toxicologic pathologist some reported incidences of neoplasms and some non-neoplastic lesions in the CRL:CD® BR rat. Diagnoses in these tables are, therefore, intentionally grouped in order to provide the user with a range of reported incidences of similar types of lesions. This compilation is not intended to propose a system of standardized nomenclature nor does it separately include each and every reported variant of each neoplasm.

I. COMMON STUDY PARAMETERS

Rats in all studies included in this publication were singly housed in wire mesh cages (except in study EB - where rats were housed in polycarbonate cages), and all received Purina rodent chow, ad libitum. All of the rats were from control groups of dietary or gavage studies; some groups received no vehicle while others received acetone, distilled water, 0.5 percent methyl cellulose or 5 percent gum arabic.

The 36 groups reported here were from studies conducted in seven different contract toxicology laboratories and nine different industrial toxicology labs. The 36 studies used VAF® rats from four different Charles River Laboratories production sites: 14 studies from Portage, Michigan, 16 from Kingston, New York, 2 from Lakeview, New Jersey and 4 from Montreal, Canada. The dates on which the studies began range from April 1984 to February 1989 and are presented at the top of the non-neoplastic lesion tables for each individual group.

ENVIRONMENTAL CONDITIONS

The light cycle for all studies was 12 hours light/12 hours dark except for EG (three month study) which was 10 hours light/14 hours dark.

Since the studies were performed in 16 different laboratories, some variation in the environmental conditions is inherent in the dataset. The information obtained was reported in the text of each original report, and included only average ranges. In general, the range of mean values of the temperature in the animals rooms was from 68°F to 72°F. The range of the mean values for relative humidity was 45 to 55 percent. Relative humidity control was not precise in all facilities, allowing the relative humidity to drop as low as 30 percent in winter months and rise to as high as 75 percent in summer months.

Overall, environmental conditions were not considered by those performing and interpreting the studies to have affected the outcome of the studies or the distribution of lesions.

All rats were of VAP health status. Information on health assessment monitoring other than that associated with pathologic examination conducted in accordance with scheduled or moribund sacrifices was not available. Therefore, the infectious disease status of the animals after the start of the studies is unknown.

II. Data Sets Presented

The incidences of all neoplastic lesions observed in any organ are reported. The incidences of select non-neoplastic lesions in the heart, liver and kidney are also reported. These include cardiomyopathy, chronic myocarditis and myocardial fibrosis; liver foci, telangiectasis, biliary proliferation, cholangiofibrosis, hepatocellular hypertrophy and hyperplasia; kidney mineralization, hyperplasia, hydronephrosis, nephrosis, progressive renal disease, glomerulonephritis, glomerulosclerosis, pyelonephritis, and interstitial nephritis.

Three sets of lesion data, representing three different lengths of time on study are presented in this publication. Table 1 gives the total number of each organ or tissue examined, by sex, for each data set. It also gives the number of groups in which each organ was examined for each sex and data set.

The first set contains 13 control groups of rats which were part of three-month (13 week) studies. Any animals that died prior to terminal sacrifice are not included in this compilation. The rats in this first dataset were approximately 4.5 months of age at necropsy. No neoplastic lesions were found in any rats in the 3 month control groups. Non-neoplastic lesion information is presented in Table 2a and 2b, for males and females, respectively.

The second set of information consists of the incidence of neoplastic and non-neoplastic lesions from 19 control groups of rats sacrificed at either 12 or 13 months of study. These rats are, therefore, about 13.5 to 14.5 months age. The neoplastic (Table 3a and 3b) data is presented in summary form, and the non-neoplastic lesions (Table 4a and 4b) are presented by study group.

The third dataset consists of lesions reported in 19 control groups of rats from two-year studies. These data also include lesions from rats which died or which were found moribund and killed prior to terminal sacrifice. However, it does not include information from rats which were killed for a scheduled interim sacrifice (such as at 1 year). Fifteen of these 19 study groups had 1 year sacrifices; these data are included in the 12-13 month dataset and can be identified by common study code, e. g., AQ. The neoplastic lesion incidences (Table 5a and 5b) are presented in summary form, and the non-neoplastic lesion data (Table 6a and 6b) are presented by study group. Neoplastic lesion data from the following organs are also presented by individual study group because of the variety of diagnostic criteria and terms used by different pathologists: liver (Table 7a and 7b), pituitary (Table 8a and 8b), thyroid (Table 9a and 9b), adrenal (Table l0a and 10b) and endocrine pancreas (Table 11a and llb).

In addition to the lesion incidence data, survival data are presented for each group of rats from the two-year studies. This is presented in three formats. First, the actual numbers of rats/sex which were killed at scheduled scrifices, including the terminal sacrifice, and also those which died on study (DOS) are listed in Table 12. Second, a survival graph (Figure la and lb) presents the mean percent of rats surviving, plus or minus one standard deviation from the mean, at eight week intervals for 104 weeks. The mortality data presented here in Figures la and lb do not include scheduled sacrifices. These data are from 15 of the two-year studies in which there was enough information to transform the data using the Kaplan-Meier procedure (Kaplan, E. and P. Meier, "Non-parametic Estimation from Incomplete Observations", Journal of the American Statistical Association, 23:1958 p. 457). Figures 2a and 2b contain the percent of rats surviving at week 104 according to ascending study start date.

SUMMARY TABLE CALCULATIONS

It was obvious during the compilation process that not all pathologists were employing diagnoses similarly, probably as a result of using different criteria and threshholds for many of the diagnoses. This meant the data could not be assumed to have a normal distribution. More importantly perhaps, it called into question the significance of overall incidences and ranges. For example, in many of the studies, a high incidence of myocardial lesions was reported in male rats at 12-13 months (Table 4a), with one study (AP) reporting 10 of 10 having lesions. Two studies (X and AR), however, found no myocardial lesions in male rats from 12-13 month studies. Thus, there was either tremendous variation in the actual incidence of the lesions, or pathologists were using different criteria for the diagnosis. In either case, any estimate of the overall incidence of myocardial disease must be interpreted with a great deal of caution since, depending on one's criteria, the

"true" incidence in male rats at 12-13 months might be anywhere from 0%, to 100%.

III. EXPLANATION OF TABLES

The following is a description of how each of the parameters in the tables has been calculated.

Number of Tissues Examined (# tissues.)

These columns, one for the males and one for the females, contain the sums of the total numbers of each tissue or organ examined in all control groups combined. Tumors of the lymphoreticular system are listed on the basis of the total number of animals examined, since these tumors are frequently found in multiple organs. Data from only 14 of the studies were included in the lymphoreticular data since data from the remaining five studies were not available in a way that allowed them to be used in this data base. Similarly, tumors found in the oral, abdominal, and thoracic cavities, which could not be attributed to any particular organ, were compared to the total number of animals examined for calculating the overall percent incidence.

Mesotheliomas are included in the two-year tumor summary tables under the organ where they were reported in the contributing study, even though histogenetically they are tumors of the lining of the body cavities. A total of eight mesotheliomas were observed in the males from the two-year studies and none in the females. Six of these mesotheliomas were present in one study in six different organs, but it is unknown if these occurred in a single rat or multiple individuals.

Autolysis of tissue did not routinely exclude samples from inclusion in the database, since many lesions could be diagnosed by the contributing pathologists despite some autolysis. Tissue numbers were adjusted only if the individual study table indicated that some were missing or that the tissues were inadequate for evaluation.

Number of Groups in which the Tissue was Examined (# groups)

This is the number of studies, for each length of time on study, in which each particular tissue was examined. For example, in the 3 Month Studies, skin was examined in 11 studies for both the males and the females.

Study Code (e. g., EG, DX)

Three distinct types of entries are in these columns in addition to the start date for each study. First, in the row horizontal to the name of each organ is the number of samples/tissues of that particular organ examined for each study group. Second, in the row horizontal to each diagnosis is the number of times that particular diagnosis was made in each study group. Third, in the row beneath the row for each diagnosis, and horizontal to the row with the "%" is the percent incidence for each particular diagnosis in each study. If a particular diagnosis was not made in a given study group, there is no entry in this or the previous row. For example, in the 3 Month studies (Table 2a), for the males, in Study FR, the heart was examined in 15 rats. In 5 of these the diagnosis of cardiomyopathy was made, for a percent incidence of 33.3.

Total Number of Lesions (Total # Lesions)

Entries in this column are the total number of occurrences of this lesion in the tissue or organ, or animal (i.e., lymphoreticular system, abdominal cavity) examined. These values are the sums of the number of occurrences in all of the study groups used.

Overall Percent Incidence (Overall Percent)

This column represents the percent incidence of a particular diagnosis in the total number (all studies combined) of that tissue or organ, or animal, e.g., lymphoreticular system, examined. These values were obtained by dividing the total number (# lesions) of a particular lesion by the total number of tissues, organs or animals, examined and then expressing the result as a percent, i.e., multiplying the result by 100. Values are expressed to the second decimal place, since many values are below 0.5% and would otherwise be rounded off to zero. As discussed above, these values must be used with a great deal of caution since, for many of the diagnoses, the criteria used for the diagnosis apparently varied from study to study. What one pathologist considered abnormal, another may have considered within normal limits. Before the true incidence of any lesion can be determined, there will need to be agreement among pathologists on the basic terminology used to classify the lesion.

Number of Groups in which the Tissue was Examined (# Groups)

This is the number of the study groups in which each particular tissue or organ was examined. This number should be considered in conjunction with the number of groups in which a particular diagnosis was made.

Number of Groups Using this Diagnosis (# groups using this diagnosis)

This is the number of studies in which each lesion was reported. For some diagnoses, this is probably an accurate reflection of the number of studies where the lesion occurred; in others it represents the number of studies where the diagnosis was in the lexicon of the study pathologist.

Minimum and Maximum Percent Found (minimum % found, maximum % found)

Due to the variation in diagnostic terminology employed by the different study pathologists, the range is reported as the highest and the lowest percent incidence for each lesion from only the individual study groups where the diagnosis was actually made. For example, in the pituitary glands of male rats on study for 24 months, 79 carcinomas of the pars distalis were diagnosed in 1236 tissues examined, for a 6.39 overall percent incidence in the population. Among the 19 control groups represented, the diagnosis was only made in 10. Among these 10, the percent incidences were 1.0, 1.5,2.0,2.1,2.9,6.1,271,28.3,28.8,and33.3.The Minimum % Found, therefore, in the studies making the diagnosis, was 1.0%, and the Maximum % Found was 33.3%. These two statistics should be considered in conjunction with the Number of Studies Making the Diagnosis.

The individual study percentages comprising the range, Minimum % to Maximum %, were calculated by dividing the number of times each diagnosis was made by the total number of tissues, organs or animals (e.g., lymphoreticular system) in each study. Some tissues can be very difficult to find in the adult animal, such as thymus and male mammary gland, unless an obvious lesion exists which was detected as a gross lesion at necropsy. Incidences must be interpreted with caution for these tissues, since the tissue might not have been examined for all animals, and, therefore, only those animals with lesions in these tissues may have been recorded. In this case, the calculated percent incidence will be higher than the actual incidence.

EXPANDED TABLES FOR SELECTED ORGANS

Because of the apparent diversity in terminology, we decided to present a series of tables separating specific neoplastic diagnoses by study group. In addition, when there was a dramatic difference between study groups in the distribution of malignant versus benign tumors in a given organ (e.s., pituitary pars distalis), the data were presented in expanded fashion. In the case of the pituitary gland, it seemed likely that the criteria used to differentiate a carcinoma from an adenoma differed among pathologists.

Presenting the data by study group allows the readers to interpret the data according to their needs. Organ specific neoplastic lesions summarized in this manner include proliferative lesions of the liver (Tables 7a and 7b), pituitary gland (Tables 8a and 8b), thyroid gland (Tables 9a and 9b), adrenal gland (Tables l0a and 10b), and endocrine pancreas (Tables 11a and l lb).

IV. SYNONYMS

SYNONYMOUS TERMS, NEOPLASMS

In compiling the summary tables for neoplastic lesions, it became clear that sometimes pathologists gave different names to the same tumor. In general, it was felt that the information would be more useful to the reader if identical, or similar, tumors were combined under one heading. For example, the term "inverted papilloma" was included as a synonym under keratoacanthoma. The current trend in toxicologic pathology is to simplify tumor classification (i.e., "lumping" as opposed to "splitting") and the categories of neoplasms used in this series were considered to be consistent with that trend.

For the endocrine pancreas, pituitary, thyroid and parathyroid, the diagnoses used in the summary table are those proposed in the Standardized System of Nomenclature and Diagnostic Criteria published by the Society of Toxicologic Pathologists in Guides for Toxicologic Pathology, 1990, STP/ARP/AFIP, Washington, D.C.. Ovarian tumors were grouped according to the nomenclature suggested by Akihiko Maekawa in Atlas of Tumor Pathology of the Fischer Rat, edited by S. F. Stinson, H. M. Schuller and G. Reznik, 1990, CRC Press, Boca Raton, FL.

The synonyms which were included in the various diagnoses are presented in the synonym list which follows. Synonymous terms or diagnoses were frequently encountered in different studies, and for utilitarian purposes were combined under a single, often broad, diagnosis, which was termed the primary diagnosis. Although some effort was made to use currently acceptable terms, it is beyond the scope of this publication to propose a system of "preferred" diagnoses. For example, in the thyroid gland, follicular adenocarcinoma, adenocarcinoma

and carcinoma were considered synonymous diagnoses under the primary diagnosis of follicular cell carcinoma. The number of lesions reported in each table include all those listed by either the primary diagnoses or the synonymous diagnoses.

Variation in terminology among the studies was even more pronounced, and much more difficult to deal with for the non-neoplastic lesions. Where one pathologist might have used cardiomyopathy as an umbrella diagnosis to include chronic myocarditis and myocardial fibrosis, another may have used the latter diagnoses separately, with some rats having either one or the other of the diagnoses, and still other rats having both diagnoses. Thus, it was impossible to meaningfully combine many of the non-neoplastic diagnoses. Caution is also needed in interpreting overall incidences. For example, with myocardial fibrosis, only a subset of the pathologists used the term, and one cannot be sure that the pathologists who did use the term used similar criteria for the diagnosis.

SYNONYMOUS TERMS: NEOPLASTIC LESIONS

Lymphoreticular system:

FIBROUS HISTIOCYTOMA = fibrous histiocytoma (malignant);
MALIGNANT LYMPHOMA = lymphosarcoma
GRANULOCYTIC LEUKEMIA = myeloid leukemia
LARGE GRANULAR LYMPHOCYTIC LEUKEMIA = monocytic leukemia

Skin:

OSTEOSARCOMA = osteogenic sarcoma
PAPILLOMA (BENIGN) = keratotic papilloma; papilloma (not otherwise specified); squamous cell papilloma
BASAL CELL CARCINOMA = baso-squamous cell carcinoma
BASAL CELL TUMOR = basal cell tumor (benign); basal cell adenoma; basal cell epithelioma
NEUROFIBROSARCOMA = schwannoma (malignant); neurilemmoma
SEBACEOUS GLAND CARCINOMA = sebaceous gland adenocarcinoma; sebaceous squamous cell carcinoma
KERATOACANTHOMA = squamous cell papilloma, inverted

Mammary:

CARCINOMA = adenocarcinoma (malignant); adenocarcinoma (not otherwise specified); adenocarcinoma, acini; adenocarcinoma
ADENOMA = adenoma (benign); adenoma (not otherwise specified); cystadenoma (benign); intraductal papillary adenoma, (benign)

Lung:

BRONCHIOLAR/ALVEOLAR ADENOMA = adenoma (not otherwise specified)
BRONCHIOLAR/ALVEOLAR CARCINOMA = carcinoma (not otherwise specified)

Liver:

NODULAR HEPATOCELLULAR PROLIFERATION = nodular hyperplasia
HEPATOCELLULAR ADENOMA = benign liver tumor; neoplastic nodule
HEPATOCELLULAR CARCINOMA = malignant liver tumor
CHOLANGIOMA = bile duct adenoma

Pancreas:

ISLET CELL ADENOMA = islet cell microadenoma
ACINAR CELL ADENOMA = adenoma (not otherwise specified)

Kidney:

RENAL CELL ADENOMA = cortical adenoma; tubular cell adenoma; adenoma (benign)

Urinary Bladder:

TRANSITIONAL CELL CARCINOMA = urothelium: carcinoma

Testes:

INTERSTITIAL (LEYDIG) CELL TUMOR (BENIGN) = interstitial cell tumor (benign); interstitial cell adenoma (benign); interstitial (Leydig) cell tumor (not otherwise specified; interstitial cell tumor (not otherwise specified)

Prostate:

CARCINOMA (MALIGNANT) = adenocarcinoma

Uterus/Cervix:

ENDOMETRIAL STROMAL POLYP = benign polyp; uterine polyp
ADENOCARCINOMA (MALIGNANT) = adenocarcinoma (not otherwise specified); carcinoma

Ovary:

GRANULOSA, THECA CELL TUMOR = granulosa cell tumor (benign); thecal cell tumor (benign); luteoma

SEX CORD STROMAL TUMOR (BENIGN) = arrhenoblastoma

Pituitary:

CARCINOMA, PARS DISTALIS = adenocarcinoma; adenocarcinoma pars distalis; carcinoma (not otherwise specified); carcinoma (malignant); chromophobe carcinoma

ADENOMA, PARS DISTALIS = adenoma (benign); adenoma (not otherwise specified); chromophobe adenoma; adenoma, anterior lobe

Thyroid:

C-CELL CARCINOMA = medullary carcinoma

FOLLICULAR CELL CARCINOMA = follicular adenocarcinoma; adenocarcinoma; carcinoma

FOLLICULAR CELL ADENOMA = adenoma (benign); follicular adenoma/cystadenoma

C-CELL ADENOMA = follicular cell cystadenoma; adenoma (interstitial cells); medullary adenoma

Adrenal Gland:

CORTICAL CARCINOMA = cortical adenocarcinoma

PHEOCHROMOCYTOMA (BENIGN) = benign medullary neoplasm

PHEOCHROMOCYTOMA (MALIGNANT) = malignant medullary neoplasm

Brain:

ASTROCYTOMA (BENIGN) = astrocytoma (not otherwise specified)

ASTROCYTOMA (MALIGNANT) = glioblastoma multiforme

Abdominal Cavity:

LIPOMA = lipoma, diaphragm; lipoma, mesentary; lipoma, peritoneal cavity

Bone:

NEUROFIBROSARCOMA (M) = neurilemmoma

SYNONYMOUS TERMS: NON-NEOPLASITIC LESIONS

Heart:

CARDIOMYOPATHY = degenerative cardiomyopathy; degeneration; myocardial degeneration/fibrosis

MYOCARDIAL FIBROSIS = fibrosis, focal

Kidney:

HYPERPLASIA, TRANSITIONAL = hyperplasia, pelvic epithelium; hyperplastic pelvic urothelium

MINERALIZATION/CALCIFICATION, PARENCHYMA (Not Otherwise Specified)= mineralization (not otherwise specified); calcification (not otherwise specified)

MINERALIZATION/CALCIFICATION, CORTEX = mineralization, glomerulus

MINERALIZATION/CALCIFICATION, MEDULLA = mineralization/calcium deposits in pelvic urothelium; mineralization deposition, medulla; mineralization calcareous material: pelvis; mineralization, pelvis/distal tubules: tubule mineralization; mineralization, calyces; mineralization, papillary; calculi, tubules

CALCULI (Not Otherwise Specified) = urolith; urolithiasis; microcalculi; mineral deposition

MINERALIZATION, VASCULAR = medial calcification

PROGRESSIVE RENAL DISEASE = nephropathy; chronic nephropathy; chronic interstitial inflammation/chronic nephropathy; senile nephropathy; glomerulonephropathy; glomerulonephrosis; chronic progressive nephritis; chronic nephritis

INTERSTITIAL NEPHRITIS = nephritis suppurative

PYELONEPHRITIS = pyelonephritis suppurative

Liver:

FOCUS OF ALTERED HEPATOCYES, ACIDOPHILIC = hepatocellular alteration, eosinophilic; cytoplasmic alteration, eosinophilic

FOCUS OF ALTERED HEPATOCYES, BASOPHILIC = basophilic hepatocytes; cytoplasmic alteration, basophilic

FOCUS OF ALTERED HEPATOCYTES, CLEAR CELL = clear hepatocytes; cytoplasmic alteration, clear; altered foci, clear cell
FOCUS OF ALTERED HEPATOCYTES, GROUND GLASS = ground glass hepatocytes
FOCUS OF ALTERED HEPATOCYTES, (NOS) = altered hepatocytes; basophilic/vacuolated hepatocytes; eosinophilic/vacuolated hepatocytes; altered focus; hepatocytic cytoplasmic change; hepatocellular cytoplasm, vesiculated/vacuolated
FOCUS OF ALTERED HEPATOCYTES, VACUOLATED = focal fine vacuolation; vacuolar change, focus; hepatocytic vacuolation, multifocal; vacuolization cytoplasmic, multifocal; cytoplasmic, focal
TELANGIECTASIS = angiectasis
BILIARY PROLIFERATION = biliary hyperplasia
HEPATOCELLULAR HYPERTROPHY = hepatocellular enlargement
HEPATOCELLULAR HYPERPLASIA = hepatocellular hypertrophy/hyperplasia

KEY TO ABBREVIATIONS

The following abbreviations are used in conjunction with many of the tables:

NOS = Not otherwise specified
M = Malignant
B = Benign
= All lesions found in one study group.
= Subcutis
\+ = Number of animals examined

ACKNOWLEDGEMENTS

Our thanks to: Ella Davis, who did all of the data extraction, entry, and compilation for this publication.and to Joseph K. Haseman, Ph.D., for his review and helpful comments.

TABLE 1
TOTAL TISSUES EXAMINED
BY TIME ON STUDY

Study Length	3 Month		12 Month		24 Month	
	# tissues	# groups	# tissues	# groups	# tissues	# groups
TISSUE	M/F		M/F		M/F	
HEMATOPOETIC SYSTEM						
LYMPH NODES	162/164	13	309/312	19	1240/1235	19
THYMUS	153/153	12	273/283	19	1020/1064	19
SPLEEN	153/155	12	300/302	18	1253/1258	19
BONE MARROW	138/139	11	299/301	18	1152/1151	18
LYMPHORETICULAR TUMORS	163/165+	13	310/312+	19	1040/1039+	15
INTEGUMENTARY SYSTEM						
SKIN	138/150	11/12'	309/312	19	1259/1258	19
MAMMARY GLAND	114/128	9/10'	144/308	11/19'	816/1250	17/19"
MUSCULO-SKELETAL SYSTEM						
SKELETAL MUSCLE	123/125	10	282/282	18	1256/1256	19
BONE	145/145	11	279/281	17	1194/1186	18
RESPIRATORY SYSTEM						
NASAL TURBINATES	25/25	2	70/70	7	445/445	8
TRACHEA	153/155	12	270/272	17	1175/1192	18
LUNG	163/165	13	310/312	19	1260/1263	19
CIRCULATORY SYSTEM						
HEART	153/155	12	310/312	19	1260/1263	19
AORTA	138/140	11	214/215	14	929/930	14
DIGESTIVE SYSTEM						
SALIVARY GLAND	138/139	11	300/302	18	1239/1240	19
ESOPHAGUS	153/155	12	300/302	18	1102/1111	17
STOMACH	1531155	12	310/312	19	1253/1254	19
SMALL INTESTINE	148/150	12	280/282	17	1175/1204	19
LARGE INTESTINE	153/155	12	290/292	18	1200/1236	19
LIVER	163/165	13	310/312	19	1258/1263	19
PANCREAS (EXOCRINE)	163/165	13	310/312	19	1242/1256	19
URINARY SYSTEM						
KIDNEY	163/165	13	310/312	19	1253/1258	19
URINARY BLADDER	163/162	13	310/309	19	1250/1249	19
REPRODUCTIVE SYSTEM						
TESTIS	153/---	12	3101---	19	1260/---	19
PROSTATE	138/---	11	310/---	19	1253/---	19
UTERUS/CERVIX	---/165	13	---/311	19	---/1258	19
OVARY	---/155	12	---/281	17	---/1251	19
ENDOCRINE SYSTEM						
PANCREAS (ENDOCRINE)	163/165	13	310/312	19	1242/1257	19
PITUITARY GLAND	153/165	12/13"	306/310	19	1236/1251	19
THYROID GLAND	162/164	13	308/303	19	1244/1242	19
PARATHYROID GLAND	129/128	11	247/236	17	1173/1133	19
ADRENAL GLAND	153/155	12	308/311	19	1249/1258	19
NERVOUS SYSTEM						
BRAIN	163/165	13	310/312	19	1255/1259	19
NERVES	135/140	11	252/251	16	1067/1067	16
SPECIAL SENSES						
EYE AND ADNEXA	148/150	12	310/312	19	1231/1244	19
HARDERIAN/LACRIMAL GLAND	55/55	4	78/89	6/7*	463/396	7
ABDOMINAL CAVITY	163/165+	13	310/312+	19	1260/1263+	19
THORACIC CAVITY	163/165+	13	310/312+	19	1260/1263+	19
ORAL CAVITY	163/165+	13	310/312+	19	1260/1263+	19

= Male/Female

+ = # Animals examined

TABLE 2a
NON-NEOPLASTIC LESIONS
3 MONTH STUDIES
MALE CD® RATS

STUDY IDENTIFICATION	EG	DX	BI	FL	FQ	EA	FR	FS	FT	FU	FV	CO	**EB**	TOTAL#	OVERALL
STUDY START DATE	Nov-86	Mar-88	Dec-88	Jan-88	May-87	May-88	Jan-86	Dec-85	Apr-88	Jun-87	Feb-89	Apr-88	Nov-88	LESIONS	PERCENT_
#ANIMALS IN GROUP	15	10	10	15	10	15	15	10	15	8	10	20	10		
LOCATION & TUMOR															
HEART	15	10	10	15	-	15	15	10	15	8	10	20	10		
cardiomyopathy							5	2		2		2		**11**	**7.19**
%							33.3	10.0		25.0		10.0			
chronic myocarditis	6								6					**12**	**7.84**
%	40.0								40.0						
LIVER	15	10	10	15	10	15	15	10	15	8	10	20	10		
focus of altered hepatocytes,															
vacuolated	13										1			**14**	**8.59**
%	86.7										10.0				
biliary proliferation							4	1						**5**	**3.07**
%							26.7	20.0							
KIDNEY	15	10	10	15	10	15	15	10	15	8	10	20	10		
mineralization/calcification,															
parenchyma (NOS)	5													**5**	**3.07**
%	33.3														
progressive renal disease	5		5					10					3	**23**	**14.11**
%	33.3		50.0					100.0					30.0		
hydronephrosis	1		1			1			1					**4**	**2.45**
%	6.7		10.0			6.7			6.7						

TABLE 2b
NON-NEOPLASTIC LESIONS
3 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	EG	DX	BI	FL	FQ	EA	FR	FS	FT	FU	FV	CO	EB	TOTAL#	OVERALL
STUDY START DATE	Nov-86	Mar-88	Dec-88	Jan-88	May-87	May-88	Jan-86	Dec-85	Apr-88	Jun-87	Feb-89	Apr-88	Nov-88	LESIONS	PERCENT
#ANIMALS IN GROUP	15	10	10	15	10	15	15	10	15	10	10	20	10		
LOCATION & TUMOR															
HEART	15	10	10	15	-	15	15	10	15	10	10	20	10		
chronic myocarditis									4					4	2.58
%									26.7						
myocardial fibrosis	1													1	0.65
%	6.7														
LIVER	15	10	10	15	10	15	15	10	15	10	10	20	10		
focus of altered hepatocytes,															
vacuolated	14													14	8.48
%	93.3														
biliary proliferation							1	1						2	1.21
%							6.7	10.0							
KIDNEY	15	10	10	15	10	15	15	10	15	10	10	20	10		
mineralization/calcification,															
parenchyma (NOS)	13												1	14	8.48
%	86.7												10.0		
mineralization/calcification,															
medulla								1		1		1		3	1.82
%								10.0		10.0		5.0			
calculi (NOS)							1							1	0.61
%							6.7								
progressive renal disease	13		1					5						19	11.52
%	86.7		10.0					5.0							
hydronephrosis	3		2		3	1					2			11	6.67
%	20.0		20.0		30.0	6.7					20.0				

TABLE 3a
NEOPLASMS
12-13 MONTH STUDIES
MALE CD® RATS

LOCATION & TUMOR	# groups tissue examined	total # lesions	overall total	# groups using this diagnosis	minimum % found	maximum % found
INTEGUMENTARY SYSTEM						
SKIN	19					
papilloma		1	0.32	1	-	5.0
keratoacanthoma		4	1.29	4	5.0	10.0
pilomatrixoma (B)		2	0.65	2	3.7	10.0
myxofibroma (B)		1	0.32	1	-	5.6
sebaceous gland carcinoma		1	0.32	1	-	5.0
CIRCULATORY SYSTEM						
HEART	19					
endocardial sarcoma		1	0.32	1	-	6.7
DIGESTIVE SYSTEM						
LIVER	19					
hepatocellular carcinoma		1	0.32	1	-	5.3
ENDOCRINE SYSTEM						
PANCREAS (ENDOCRINE)	19					
islet cell adenoma		2	0.65	2	4.3	10.0
PITUITARY GLAND	19					
adenoma, pars distalis		37	12.09	14	5.0	40.0
carcinoma, pars distalis		3	0.98	1	-	15.8
THYROID GLAND	19					
follicular cell adenoma		1	0.32	1	-	5.3
C-cell adenoma		2	0.65	2	3.6	6.7
ADRENAL GLAND	19					
cortical adenoma (B)		4	1.30	4	5.0	10.0
pheochromocytoma (B)		2	0.65	2	10.0	10.0
NERVOUS SYSTEM						
BRAIN	19					
ependymoma		1	0.32	1	-	5.6

TABLE 3b
NEOPLASMS
12-13 MONTH STUDIES
FEMALE CD® RATS

LOCATION & TUMOR	# groups tissue examined	total # lesions	overall percent	# groups using this diagnosis	minimum % found	maximum % found
INTEGUMENTARY SYSTEM						
SKIN	19					
fibrosarcoma, tail		1	0.3	1	-	5.0
trichoepithelioma with horn cysts		1	0.3	1	-	5.9
MAMMARY GLAND	19					
adenoma		1	0.3	1	-	6.3
carcinoma (M)		4	1.3	4	5.0	10.0
fibroadenoma		6	1.9	5	3.7	10.0
DIGESTIVE SYSTEM						
LIVER	19					
hepatocellular adenoma		1	0.3	1	-	5.0
REPRODUCTIVE SYSTEM						
UTERUS/CERVIX	19					
endometrial stromal						
polyp		3	1.0	3	5.0	6.7
endometrial stromal sarcoma		1	0.3	1	-	5.0
cervical polyp		1	0.3	1	-	6.7
polyp, vagina		1	0.3	1	-	10.0
ENDOCRINE SYSTEM						
PANCREAS (ENDOCRINE)	19					
islet cell adenoma		1	0.3	1	-	4.0
PITUITARY GLAND	19					
adenoma, pars distalis		72	23.2	19	10.0	50.0
THYROID GLAND	19					
C-cell adenoma		4	1.3	4	5.0	10.0
ADRENAL GLAND	19					
cortical adenoma		3	1.0	2	10.0	10.0
pheochromocytoma (M)		1	0.3	1	-	5.0
NERVOUS SYSTEM						
BRAIN	19					
glioma (B)		1	0.3	1	-	10.0
ABDOMINAL CAVITY	19					
lipoma		1	0.3	1	-	5.0

TABLE 4a
NON-NEOPLASTIC LESIONS
12-13 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	ES	AR	ET	EL	EV	ER	FW	ToTAL#	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Dec-85	Mar-85	Sep-84	Jul-84	Jun-86	Dec-86	May-88	LESIONS	PERCENT
LOCATION & LESION																					
HEART																					
# TISSUES EXAMINED	15	10	10	10	18	10	10	10	20	19	10	20	18	23	19	28	20	20	20		
cardiomyopathy	11	7			6	6				1		12	2		7				6	58	18.71
%	73.3	70.0			33.3	60.0				5.3		60.0	11.1		36.8				30.0		
myocardial fibrosis							4									9		3		16	5.16
%							40.0									32.1		15.0			
chronic myocarditis			2	10			8		9	1	4						12	8		54	17,42
%			20.0	100.0			80.0		45.0	5.3	40.0						60.0	40.0			
LIVER																					
# TISSUES EXAMINED	15	10	10	10	18	10	10	10	20	19	10	20	18	23	19	28	20	20	20		
focus of altered hepatocytes,																					
(NOS)		6	2			1				1			1			25	7	9		52	16.77
%		60.0	20.0			10.0				5.3			5.6			89.3	35.0	45.0			
focus of altered hepatocytes,																					
acidophilic	3														1	5			8	17	5.48
%	20.0														5.3	17.9			40.0		
focus of altered hepatocytes,																					
basophilic	2		1												1	1			3	8	2.58
%	13.3		10.0												5.3	3.6			15.0		
focus of altered hepatocytes,																					
mixed cell												3								3	0.97
%												15.0									
focus of altered hepatocytes,																					
ground glass									5											5	1.61
%									25.0												
focus of altered hepatocytes,																					
clear cell			1			1		1	6			3				1				13	4.19
%			10.0			10.0		10.0	30.0			15.0				3.6					
focus of altered hepatocytes,																					
vacuolated										9				6						15	4.84
%										47.4				26.1							
hepatocellular hypertrophy				1																1	0.32
%				10.0																	
biliary proliferation	12	9	3	2	4	7	7	2	1	3		15	4	4	3	8	2	3	8	97	31.29
%	80.0	90.0	30.0	20.0	22.2	70.0	70.0	20.0	5.0	15.8		75.0	22.2	17.4	15.8	28.6	10.0	15.0	40.0		
cholangiofibrosis	5	9		1			1					10	2			4				32	10.32
%	33.3	90.0		10.0			10.0					50.0	11.1			14.3					
telangiectasis				1		1			2	1							2		1	8	2.58
%				10.0		10.0			10.0	5.3							10.0		5.0		

TABLE 4a (Continued)
NON-NEOPLASTIC LESIONS
12-13 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	ES	AR	ET	EL	EV	ER	FW	TOTAL k	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Dec-85	Mar-85	Sep-84	Jul-84	Jun-86	Dec-86	May-88	LESIONS	PERCENT
LOCATION & LESION																					
KIDNEY																					
# TISSUES EXAMINED	15	10	10	10	18	10	10	10	20	19	10	20	18	23	19	28	20	20	20		
progressive renal disease	10	10	8	9	15	9	7	8	20	19	6	18	9	3	15	26	17	10	16	235	75.81
%	66.7	100.0	80.0	90.0	83.3	90.0	70.0	80.0	100.0	100.0	60.0	90.0	50.0	13.0	78.9	92.9	85.0	50.0	80.0		
interstitial nephritis				1			1													2	**0.65**
%				10.0			10.0														
pyelonephritis						1												1		2	0.65
%						10.0												5.0			
hyperplasia, transitional		1		3		1				1					1	1			1	9	2.90
%		10.0		30.0		10.0				5.3					5.3	3.6			5.0		
mineralization/calcification,																					
parenchyma (NOS)								1	1										1	3	0.97
%								10.0	5.0										5.0		
mineralization/calcification,																					
cortex																3				3	0.97
%																10.7					
mineralization/calcification,																					
medulla		2								4		1				6				13	4.19
%		20.0								21.1		5.0				21.4					
mineralization/calcification,																					
urothelium						1														1	0.32
%						10.0															
calculi (NOS)	2														1		4			7	2.26
%	13.3														5.3		20.0				
calculi, tubules				1																1	0.32
%				10.0																	
calculi,pelvis				2						2		5		4				1		14	4.52
%				20.0						10.5		25.0		17.4				5.0			
mineralization, vascular																1				1	0.32
%																3.6					

TABLE 4b
NON-NEOPLASTIC LESIONS
12-13 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	ES	AR	ET	EL	EV	ER	FW	TOTAL #	**OVERALL**
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Dec-85	Mar-85	Sep-84	Jul-84	Jun-86	Dec-86	May-88	lesions	percent
LOCATION & LESION																					
HEART																					
# TISSUES EXAMINED	15	10	10	10	20	10	10	10	19	17	10	20	18	25	19	29	20	20	20		
cardiomyopathy	9	2				1						8	3		5				2	30	9.62
%	60.0	20.0				10.0						40.0	16.7		26.3				10.0		
myocardial fibrosis							1									7		1		9	2.88
%							10.0									24.1		5.0			
chronic myocarditis			1	10			2	1	4		1						2			21	6.73
%			10.0	100.0			20.0	10.0	21.1		10.0						10.0				
LIVER																					
# TISSUES EXAMINED	15	10	10	10	20	10	10	10	19	17	10	20	18	25	19	29	20	20	20		
focus of altered hepatocytes, (NOS)		1	3							2			1			21	2	1		31	9.94
%		10.0	30.0							11.8			5.6			72.4	10.0	5.0			
focus of altered hepatocytes, acidophilic	1		3	2								2				3			3	14	4.49
%	6.7		30.0	20.0								10.0				10.3			15.0		
focus of altered hepatocytes, basophilic			1									1			1	5			4	12	3.85
%			10.0									5.0			5.3	17.2			20.0		
focus of altered hepatocytes, mixed cell												3								3	0.96
%												15.0									
focus of altered hepatocytes, clear cell			1	2	1				2											**6**	1.92
%			10.0	20.0	5.0				10.5												
focus of altered hepatocytes, vacuolated										4				1						5	1.60
%										23.5				4.0							
hepatocellular hypertrophy																			2	2	0.64
%																			10.0		
hepatocellular hyperplasia																		1		1	0.32
%																		5.0			
biliary proliferation	11	4	2	1	6	1	3	2				8	7	2	2	5	4	1	5	64	20.51
%	73.3	40.0	20.0	10.0	30.0	10.0	30.0	20.0				40.0	38.9	8.0	10.5	17.2	20.0	5.0	25.0		
cholangiofibrosis	2	4							1			5	1							13	4.17
%	13.3	40.0							5.3			25.0	5.6								
telangiectasis									1	1								1		3	0.96
%									5.3	5.9								5.0			

TABLE 4b **(Continued)**
NON-NEOPLASTIC LESIONS
12-13 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	DO	FF	X	FH	EQ	EU	EW	ES	AR	El'	EL	EV	ER	FW	TOTAL#	**OVERALL**
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Dec-85	Mar-85	Sep-84	Jul-84	Jun-86	Dec-86	May-88	lesions	percent
LOCATION & LESION																					
KIDNEY																					
#TISSUES EXAMINED	15	10	10	10	20	10	10	10	19	17	10	20	18	25	19	29	20	20	20		
progressive renal disease	2	2	4	5	9	4		5	7	12	5	13	4	5	8	13	9	2	2	111	35.58
%	13.3	20.0	40.0	50.0	45.0	40.0		50.0	36.8	70.6	50.0	65.0	22.2	20.0	42.1	44.8	45.0	10.0	10.0		
interstitial nephritis														3						3	0.96
%														12.0							
pyelonephritis														1					2	3	0.96
%														4.0					10.0		
hyperplasia, tubular		3																		3	0.96
%		30.0																			
hyperplasia, transitional		2	1	1		6	1			3		1			7	5		2	2	31	9.94
%		20.0	10.0	10.0		60.0	10.0			17.6		5.0			36.8	17.2		10.0	10.0		
hydronephrosis						3								3					4	10	3.21
%						30.0								12.0					20.0		
mineralization/calcification,																					
parenchyma (NOS)	1								1											2	**0.64**
%	6.7								5.3												
mineralization/calcification,																					
cortex					1											5				6	1.92
%					5.0											17.2					
mineralization/calcification,																					
medulla		4	2		5					15		5	7			3				41	13.14
%		40.0	20.0		25.0					88.2		25.0	38.9			10.3					
mineralization/calcification,																					
urothelium			4			6										16				26	8.33
%			40.0			60.0										55.2					
calculi (NOS)	12																7	2		21	6.73
%	80.0																35.0	10.0			
calculi, tubules				3			1													**4**	1.28
%				30.0			10.0														
calculi, pelvis			5	4			1			13		9		9	8	15		7	6	77	24.68
%			50.1)	40.0			10.0			76.5		45.0		36.0	42.1	51.7		35.0	30.0		

TABLE 5a
NEOPLASMS
24 MONTH STUDIES
MALE CD® RATS

LOCATION & TUMOR	# groups in which organ examined	total # lesions	percent of total	# groups using this diagnosis	minimum % found	maximum %found
HEMATOPOIETIC SYSTEM						
LYMPH NODES	19					
hemangioma (B)		5	0.40	4	1.4	2.9
hemangiosarcoma		3	0.24	3	1.3	1.6
THYMUS	19					
thymoma		4	0.39	3	2.1	3.2
thymic carcinoma		1	0.10	1	-	2.0
SPLEEN	19					
hemangiosarcoma		4	0.32	3	1.1	4.1
LYMPHORETICULAR TUMORS	15					
malignant lymphoma		1	0.10	1	-	L3
malignant lymphoma,						
lymphocytic		5	0.48	4	1.4	2.9
malignant lymphoma,						
histiocytic		3	0.29	2	2.0	2.8
histiocytic sarcoma		17	1.63	6	1.4	7.1
granulocytic leukemia		4	0.38	4	1.0	2.0
large granular						
lymphocyte leukemia		2	0.19	2	1.0	1.4
SKIN/SUBCUTIS	19					
squamous keratosis (B)		2	0.16	1	-	3.3
papilloma (B)		26	2.07	12	1.4	8.6
keratoacanthoma		70/1*	5.64	17	1.4	14.0
squamous cell carcinoma		8/1	0.71	7	1.1	4.0
basal cell tumor (B)		8/4	0.95	6	2.0	5.6
basal cell carcinoma		8/1	0.71	6	1.4	43
trichoepithelioma		211	0.24	2	1.4	2.9
pilomatrixoma (B)		6	0.48	2	4.3	5.0
sebaceous gland adenoma		5	0.40	2	1.4	6.5
sebaceous gland carcinoma		2/1	0.24	3	1.0	1.4
preputial gland						
squamous cell carcinoma		1	0.08	1	-	1.6
zymbals gland tumor		4	0.32	2	2.0	6.0
zymbals gland carcinoma		5	0.40	4	1.1	3.9
adenoma		1	0.08	1	-	1.4
carcinoma		1/1	0.16	2	1.4	1.4
carcinosarcoma		1	0.08	1	-	2.0
fibroma		22/16	3.02	11	1.4	10.0
fibrosarcoma		10/6	1.27	10	1.0	4.1
osteogenic sarcoma		0/1	0.08	1	-	1.4
leiomyosarcoma		1	0.08	1	-	1.4
neurofibrosarcoma		2/2	0.32	3	1.4	4.0
sarcoma		3	0.24	2	2.0	4.0
lipoma		8/7	1.19	11	1.3	4.0
liposarcoma		1/1	0.16	2	1.0	1.9
hemangioma (B)		2/1	0.24	3	1.4	2.0
hemangiosarcoma		1/1	0.16	2	1.4	1.6
fibrous histiocytoma (M)		1	0.08	1	-	1.6
hemangiopericytoma		0/1	0.08	1		1.4

TABLE 5a (Continued)
NEOPLASMS
24 MONTH STUDIES
MALE CD® RATS

LOCATION & TUMOR	# groups in which organ examined	total # lesions	percent of total	# groups using this diagnosis	minimum % found	maximum % found
MAMMARY GLAND	17					
fibroadenoma		16	1.96	**12**	1.6	25.0
adenoma		3	0.37	3	1.0	2.8
fibroma		1	0.12	1	-	2.7
carcinoma (M)		8	0.98	6	1.6	4.7
MUSCULO-SKELETAL SYSTEM						
SKELETAL MUSCLE	19					
fibrosarcoma		2	0.16	2	1.0	1.4
sarcoma		1	0.08	1	-	1.4
BONE	18					
osteoma		1	0.08	1	-	1.3
RESPIRATORY SYSTEM						
NASAL TURBINATES	8					
fibrosarcoma		1	0.22	1	-	2.0
hemangiosarcoma		1	0.22	1	-	1.6
LUNG	19					
bronchiolar/alveolar						
adenoma		6	0.48	5	1.3	4.0
bronchiolar/alveolar						
carcinoma		1	0.08	1	-	2.0
carcinosarcoma		1	0.08	1	-	2.0
fibrosarcoma		1	0.08	1	-	1.4
CIRCULATORY SYSTEM						
HEART	19					
atriocaval mesothelioma (M)		1	0.08	1	-	1.0
DIGESTIVE SYSTEM						
SALIVARY GLAND	19					
carcinoma (M)		2	0.16	2	1.3	1.4
STOMACH	19					
squamous papilloma,						
nonglandular mucosa		3	0.24	2	2.0	2.8
carcinoma (M)		1	0.08	1	-	1.4
mesothelioma		1	0.08	1	-	1.0
SMALL INTESTINE	19					
adenocarcinoma (M)		1	0.09	1	-	1.5
LARGE INTESTINE	19					
adenoma (B)		1	0.08	1	-	1.9
adenocarcinoma		1	0.08	1	-	1.7
fibroma (B)		1	0.08	1	-	2.1
sarcoma (NOS), cecum		1	0.08	1	-	1.9

TABLE 5a (Continued)
NEOPLASMS
24 MONTH STUDIES
MALE CD® RATS

LOCATION & **TUMOR**	# groups in which organ examined	total if lesions	percent of total	# groups using this diagnosis	minimum % found	maximum % found
LIVER	19					
nodular hepatocellular proliferation		9	0.72	2	8.0	10.2
hepatocellular adenoma		53	4.21	18	1.3	18.2
hepatocellular carcinoma		33	2.62	12	1.1	9.1
cholangioma		1	0.08	1	-	1.4
cholangiocellular carcinoma		2	0.16	2	1.0	2.0
carcinosarcoma		1	0.08	1	-	2.0
PANCREAS (EXOCRINE)	19					
acinar cell adenoma		7	0.56	7	1.3	2.0
sarcoma (NOS)		1	0.08	1	-	1.8
URINARY SYSTEM						
KIDNEY	19					
renal cell adenoma		3	0.24	3	1.4	2.1
renal adenocarcinoma		4	0.32	4	1.0	2.0
transitional cell carcinoma		2	0.16	2	1.4	2.0
hemangiosarcoma		1	0.08	1	-	2.1
lipoma		1	0.08	1	-	1.3
liposarcoma		1	0.08	1	-	2.1
lipomatous tumour (M)		1	0.08	1	-	1.0
mixed cell tumor (M)		3	0.24	2	2.0	3.0
mixed mesenchymal tumor (NOS)		1	0.08	1	-	1.4
URINARY BLADDER	19					
transitional cell papilloma		1	0.08	1	-	1.0
transitional cell carcinoma		3	0.24	3	1.4	1.5
mesothelioma		1	0.08	1	-	1.0
REPRODUCTIVE SYSTEM						
TESTIS	19					
interstitial (leydig) cell tumor (B)		59	4.68	18	1.4	10.0
interstitial cell tumor (M)		1	0.08	1	-	1.4
mesothelioma (M)		2	0.16	2	1.0	1.4
PROSTATE	19					
carcinoma (M)		3	0.24	3	1.0	1.8
lipoma		1	0.08	1	-	1.4
mesothelioma (M)		1	0.08	1	-	1.0
ENDOCRINE SYSTEM						
PANCREAS (ENDOCRINE)	19					
islet cell adenoma		103	8.29	17	2.9	24.0
islet cell carcinoma		25	2.01	10	1.6	8.2
mesothelioma		1	0.08	1	-	1.0
PITUITARY GLAND	19					
adenoma, pars intermedia		4	0.32	2	1.0	4.9
adenoma, pars distalis		750	60.68	19	37.1	81.3
carcinoma,						
pars distalis		79	6.39	10	1.0	33.3
craniopharyngioma		1	0.08	1	-	1.9
hemangioma		1	0.08	1	-	1.9

TABLE 5a (Continued)
NEOPLASMS
24 MONTH STUDIES
MALE CD' RATS

LOCATION & TUMOR	# groups in which organ examined	total # lesions	percent of total	# groups using this diagnosis	minimum % found	maximum % found
THYROID GLAND	19					
follicular cell adenoma		69	5.55	17	1.1	25.7
follicular cell carcinoma		16	1.29	12	1.0	6.0
C-cell adenoma		79	6.35	17	1.0	17.4
C-cell carcinoma		29	2.33	13	1.1	7.0
PARATHYROID GLAND	19					
adenoma (B)		15	1.28	11	1.4	7.4
adenocarcinoma		1	0.09	1	-	2.7
ADRENAL GLAND	19					
cortical adenoma (B)		36	2.88	15	1.4	16.4
cortical carcinoma		5	0.40	5	1.4	2.0
pheochromocytoma (B)		188	15.05	19	4.0	30.0
pheochromocytoma (M)		24	1.92	12	1.6	8.6
ganglioneuroma		2	0.16	2	1.7	2.0
NERVOUS SYSTEM						
BRAIN	19					
glioma (B)		1	0.08	1	-	1.4
glioma (M)		4	0.32	2	3.3	4.0
astrocytoma (B)		5	0.40	3	2.0	4.3
astrocytoma (M)		11	0.88	6	1.0	5.7
astrocytoma (M), spinal cord		3	0.24	2	2.0	2.0
granular cell tumor (B)		2	0.16	2	1.4	2.0
granular cell tumor (M)		2	0.16	2	1.3	1.4
adenocarcinoma		4	0.32	2	2.1	6.1
sarcoma, spinal chord		1	0.08	1	-	2.0
PERIPHERAL NERVES	16					
neurofibroma (M)		1	0.09	1	-	1.8
neurinoma, thorax		1	0.09	1	-	1.0
BODY CAVITIES						
ABDOMINAL CAVITY	19					
lipoma		2	0.16	2	1.4	1.8
liposarcoma		2	0.16	2	1.1	1.4
fibrosarcoma, mesentery		1	0.08	1	-	1.4
hemangioma, mesentery		1	0.08	1	-	1.4
fibrous histiocytoma (M), mesentery-omentum		1	0.08	1	-	2.0
mesothelioma (B), abdomen		1	0.08	1	-	1.4
carcinoma (M), seminal vesicle		1	0.08	1	-	1.4
THORACIC CAVITY	19					
liposarcoma		2	0.16	1	-	2.2
hibernoma		1	0.08	1	-	1.1
ORAL CAVITY	19					
fibrosarcoma, gingiva		1	0.08	1	-	1.4
squamous cell carcinoma, mouth		1	0.08	1	2.0	2.0

TABLE 5b
NEOPLASMS
24 MONTH STUDIES
FEMALE CD® RATS

	k groups in which	total k	percent	k groups using this	minimum	maximum
LOCATION & TUMOR	tissue examined	lesions	of total	**diagnosis**	**% found**	**% found**
HEMATOPOIETIC SYSTEM						
LYMPH NODES	19					
hemangioma		1	**0.08**	1	-	1.7
THYMUS	19					
thymoma		2	0.19	2	1.5	2.3
squamous cell carcinoma		2	0.19	2	1.9	2.4
hemangiosarcoma		1	0.09	1	--	1.9
liposarcoma		1	0.09	1	--	1.3
LYMPHORETICULAR TUMORS	15					
malignant lymphoma		3	0.29	3	1.0	1.6
malignant lymphoma,						
lymphocytic		4	0.38	2	2.0	4.2
malignant lymphoma,						
histiocytic		1	0.10	1	--	1.4
histiocytic sarcoma		16	1.54	8	1.1	5.7
large granular						
lymphocyte leukemia		3	0.29	3	1.1	1.8
sarcoma, non-specific		1	0.10	1	--	1.4
INTEGUMENTARY SYSTEM						
SKIN/SUBCUTIS	19					
papilloma		2	0.16	2	1.1	1.6
keratoacanthoma		5	0.40	3	1.3	3.0
squamous cell carcinoma		6	0.48	6	1.3	1.9
basal cell tumor		1*	0.08	1	--	1.4
basal cell carcinoma		1	0.08	1	--	1.4
pilomatrixoma		3	0.24	1	--	4.3
sebaceous carcinoma		1	0.08	1	--	1.4
zymbal's gland tumor		3	0.24	2	2.0	4.1
fibroma		9/5*	1.11	9	1.0	2.0
zymbal's gland carcinoma		4/2	0.48	4	1.6	4.0
carcinoma		1	0.08	1	--	1.0
fibrosarcoma		4/2	0.48	6	1.1	1.7
neurofibrosarcoma		3	0.24	3	1.4	2.0
sarcoma		2	0.16	1	--	4.1
lipoma		6/4	0.79	7	1.4	4.0
liposarcoma		2	0.16	2	1.4	2.0
hemangiosarcoma		1	0.08	1	--	2.0
fibrous histiocytoma (M)		1	0.08	1	--	2.0
hemangiopericytoma		1	0.08	1	--	1.4
MAMMARY GLAND	19					
lipoma		1	0.08	1	--	1.9
adenoma		50	4.00	16	1.4	12.9
carcinoma (M)		221	17.68	19	7.1	31.4
fibroma		1	0.08	1	--	2.0
fibroadenoma		393	31.44	19	13.7	49.0
cystadenoma (B)		3	0.24	1	--	3.4
intraductal papillary adenoma. (B)		1	0.08	1	--	1.0

TABLE 5b (Continued)
NEOPLASMS
24 MONTH STUDIES
FEMALE CD® RATS

LOCATION & TUMOR	# groups in which tissue examined	total # lesions	percent of total	# groups using this diagnosis	minimum % found	maximum % found
MUSCULOSKELETAL SYSTEM						
SKELETAL MUSCLE	19					
rhabdomyosarcoma		2	0.16	2	1.3	1.4
lipoma		1	0.08	1	--	1.0
BONE	18					
osteosarcoma		2	0.17	2	1.0	1.4
neurofibrosarcoma (M)		1	0.08	1	--	1.4
RESPIRATORY SYSTEM						
NASAL TURBINATES	8					
squamous cell carcinoma		1	0.22	1	--	2.0
basosquamous tumor,						
lateral sinuses		1	0.22	1	--	1.0
LUNG	19					
bronchiolar/alveolar carcinoma		1	0.08	1	--	2.0
adenocarcinoma		3	0.24	2	2.0	4.0
CIRCULATORY SYSTEM						
HEART	19					
endocardial sarcoma		1	0.08	1	--	2.0
DIGESTIVE SYSTEM						
STOMACH	19					
sarcoma		1	0.08	1	--	2.0
SMALL INTESTINE	19					
leiomyosarcoma		1	0.08	1	--	1.7
leiomyoma		1	0.08	1	--	1.5
LIVER	19					
nodular hepatocellular proliferation		9	0.71	2	8.0	10.0
hepatocellular adenoma		28	2.22	16	1.0	5.5
hepatocellular carcinoma		5	0.40	4	1.0	4.0
cholangioma		2	0.16	2	1.1	1.4
PANCREAS (EXOCRINE)	19					
acinar cell adenoma		1	0.08	1	--	1.0
URINARY SYSTEM						
KIDNEY	19					
renal cell adenoma		1	0.08	1	--	1.4
renal cell carcinoma		3	0.24	2	2.0	3.6
lipomatous tumor		2	0.16	2	1.0	1.4
liposarcoma		1	0.08	1	--	1.6
transitional cell carcinoma		1	0.08	1	--	1.4

TABLE 5b (Continued)
NEOPLASMS
24 MONTH STUDIES
FEMALE CD® RATS

LOCATION & TUMOR	# groups in which tissue examined	total X lesions	percent of total	k groups using this diagnosis	minimum % found	maximum % found
URINARY BLADDER	19					
polyp		1	0.08	1	--	1.4
transitional cell papilloma		1	0.08	1	–	1.4
transitional cell carcinoma		1	0.08	1	--	1.4
REPRODUCTIVE SYSTEM						
UTERUS/CERVIX	19					
adenocarcinoma (M)		4	0.32	4	1.0	1.4
endometrial stromal						
polyp		51	4.05	15	1.1	10.0
fibroma		1	0.08	1	--	1.4
leiomyoma		3	0.24	1	--	5.5
endometrial stromal sarcoma		3	0.24	3	1.4	1.6
leiomyosarcoma		2	0.16	1	--	3.6
hemangiosarcoma		1	0.08	1	--	1.4
sarcoma (NOS)		1	0.08	1	--	1.4
fibroma, cervix		1	0.08	1	--	1.4
leiomyosarcoma, cervix		1	0.08	1	-	1.4
squamous cell carcinoma,						
vagina/cervix		2	0.16	2	1.4	1.6
squamous cell carcinoma,						
vagina		4	0.32	3	1.4	2.9
stromal polyp, vagina		3	0.24	3	1.4	1.6
fibroma, vagina		4	0.32	4	1.4	2.0
hemangioma, vagina		1	0.08	1	--	1.4
OVARY	19					
granulosa/theca cell tumor		13	1.04	9	1.4	3.2
papillary adenoma		1	0.08	1	1.4	1.4
tubular adenoma		1	0.08	1	1.0	1.0
sex cord stromal tumor (B)		3	0.24	3	1.0	2.0
ENDOCRINE SYSTEM						
PANCREAS (ENDOCRINE)	19					
islet cell adenoma		48	3.82	17	1.4	8.6
islet cell carcinoma		18	1.43	8	1.4	8.2
PITUITARY GLAND	19					
microadenoma, pars intermedia		1	0.08	1	--	1.0
adenoma, pars distalis		902	72.10	19	31.4	88.8
carcinoma, pars distalis		131	10.47	14	1.3	57.1
THYROID GLAND	19					
follicular cell adenoma		32	2.58	15	1.0	14.5
follicular cell carcinoma		13	1.05	9	1.0	5.8
C-cell adenoma		91	7.33	19	1.0	17.1
medullary carcinoma		42	3.38	11	2.1	13.1
PARATHYROID GLAND	19					
adenoma (B)		6	0.53	5	1.6	4.0

TABLE 5b (Continued)
NEOPLASMS
24 MONTH STUDIES
FEMALE CD® RATS

LOCATION & TUMOR	# groups in which tissue examined	total # lesions	percent of total	# groups using this diagnosis	minimum % found	maximum % found
ADRENAL GLAND	19					
cortical adenoma		76	6.04	19	1.0	21.6
cortical adenocarcinoma		8	0.64	7	1.0	2.9
pheochromocytoma (B)		49	3.90	16	1.0	14.5
pheochromocytoma (M)		7	0.56	6	1.4	4.0
NERVOUS SYSTEM						
BRAIN	19					
glioma (B)		1	0.08	1	--	1.4
glioma (M)		4	0.32	2	2.9	3.3
astrocytoma (B)		2	0.16	2	1.4	2.0
astrocytoma (M)		1	0.08	1	--	1.0
astrocytoma (M),						
spinal cord		1	0.08	1	--	1.3
granular cell tumor (B)		2	0.16	1	--	3.2
PERIPHERAL NERVES	16					
neurofibroma (M)		1	0.09	1	--	1.7
SPECIAL SENSES						
EYE AND ADNEXA	19					
fibroma, iris (B)		1	0.08	1	--	1.4
fibroma, conjunctiva (B)		1	0.08	1	--	2.0
BODY CAVITIES						
ABDOMINAL CAVITY	19					
lipoma		6	0.48	5	1.4	3.6
liposarcoma		1	0.08	1	--	1.4
fibrous histiocytoma,						
mesentary-omentum		1	0.08	1	--	2.0
THORACIC CAVITY	19					
undifferentiated sarcoma		1	0.08	1	--	2.0
ORAL CAVITY	19					
sarcoma, lip		1	0.08	1	--	2.0
carcinoma, mouth		1	0.08	1	--	2.0
tooth/jaw: malignant mixed						
tumor		1	0.22	1	--	1.4

TABLE 6a
NON-NEOPLASTIC LESIONS
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	130	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	FI	EV	ER	TOTAL#	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Jul-86	Apr-85	Apr-85	Dec-85	Nov-86	Mar-85	Sep-84	LESIONS	PERCENT
LOCATION & LESION																					
HEART																					
# TISSUES EXAMINED	90	50	70	50	72	62	51	55	70	71	80	70	100	50	49	70	60	69	70		
cardiomyopathy	40	47			45	61				1		63		6	8	58				329	26.13
%	44.4	94.0			62.5	98.4				1.4		90.0		12.0	16.3	82.9					
myocardial fibrosis			35				43						49				45			172	13.66
%			50.0				84.3						49.0				75.0				
chronic myocarditis			15	49			5	49	1	58	58						45	43	63	386	30.66
%			21.4	98.0			9.8	89.1	1.4	81.7	72.5						75.0	62.3	90.0		
LIVER																					
#TISSUES EXAMINED	90	49	70	50	72	62	51	55	70	71	80	70	100	50	50	69	60	70	70		
focus of altered hepatocytes, (NOS)		15	37			10				2	8						43	13	13	141	11.20
%		30.6	52.9			16.1				2.8	10.0						71.7	18.6	18.6		
focus of altered hepatocytes, acidophilic			19	3	7		2	5	2			10	13	1	1	10	7			80	6.35
%			27.1	6.0	9.7		3.9	9.1	2.9			14.3	13.0	2.0	2.0	14.5	11.7				
focus of altered hepatocytes, basophilic	2		18	3	4	3			1			20	20		1	11	13			96	7.63
%	2.2		25.7	6.0	5.6	4.8			1.4			28.6	20.0		2.0	15.9	21.7				
focus of altered hepatocytes, mixed cell	3					4						30								37	2.94
%	3.3					6.5						42.9									
focus of altered hepatocytes, ground glass													28							28	2.22
%													28.0								
focus of altered hepatocytes, clear cell			2	1		4		6				5		1	1					20	1.59
%			2.9	2.0		6.5		10.9				7.1		2.0	2.0						
focus of altered hepatocytes, vacuolated								9												9	0.71
%								16.4													
hepatocellular hypertrophy		2	2	2						2	1	7				2				18	1.43
%		4.1	2.9	4.0						2.8	1.3	10.0				2.9					
hepatocellular hyperplasia		2	2					1	1	1	2								22	31	2.46
%		4.1	2.9					1.8	1.4	1.4	2.5								31.4		
biliary proliferation	34	42	47	10	33	37	34	38	23	14	9	51	28	2	1	44	30	30	17	524	41.62
%	37.8	85.7	67.1	20.0	45.8	59.7	66.7	69.1	32.9	19.7	11.3	72.9	28.0	4.0	2.0	63.8	50.0	42.9	24.3		
cholangiofibrosis		42	36	13			22		6			34		17	21		19			210	16.68
%		85.7	51.4	26.0			43.1		8.6			48.6		34.0	42.0		31.7				
telangiectasis	5			5		1	13	7	16	2	5	4		15	13	3		21	7	117	9.29
%	5.6			10.0		1.6	25.5	12.7	22.9	2.8	6.3	5.7		30.0	26.0	4.3		30.0	10.0		

TABLE 6a (Continued)
NON-NEOPLASTIC LESIONS
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	F1	FM	FN	ET	FI	EV	ER	TOTAL lt	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Jul-86	Apr-85	Apr-85	Dec-85	Nov-86	Mar-85	Sep-84	LESIONS	PERCENT
LOCATION & LESION																					
KIDNEY																					
# TISSUES EXAMINED	90	48	70	50	72	62	51	55	70	71	80	70	100	48	50	67	59	70	70		
progressive renal disease	80	40	68	47	66	55	45	50	63	70	66	67	69	48	45	61	58	66	54	1118	89.23
%	88.9	83.3	97.1	94.0	91.7	88.7	88.2	90.9	90.0	98.6	82.5	95.7	69.0	100.0	90.0	91.0	98.3	94.3	77.1		
glomerulosclerosis							6													6	0.48
%							11.8														
glomerulonephritis													1							1	0.08
%													1.0								
interstitial nephritis				1		1														2	0.16
%				2.0		1.6															
pyelonephritis	3					5	2		1	13		1	2	1					1	29	2.31
%	3.3					8.1	3.9		1.4	18.3		1.4	2.0	2.1					1.4		
hyperplasia, tubular	1	1				1					1						5			**9**	0.72
%	1.1	2.1				1.6					1.3						8.5				
hyperplasia, transitional		28	6	6		21	4			2		4	4			10	12			97	7.74
%		58.3	8.6	12.0		33.9	7.8			2.8		5.7	4.0			14.9	20.3				
hyperplasia (NOS)								1											5	6	**0.48**
%								1.8											7.1		
hydronephrosis						111		2	1				2							15	1.20
%						16.1		3.6	1.4				2.0								
hypertrophic cortical tubules													2							2	0.16
%													2.0								
mineralization/calcification,																					
parenchyma (NOS)	4	2				1			8			3		1						19	1.52
%	4.4	4.2				1.6			11.4			4.3		2.1							
mineralization/calcification,																					
cortex			12		5								1				10			28	2.23
%			17.1		6.9								1.0				16.9				
mineralization/calcification,																					
medulla		3	3		8		1			8		3				4	13			43	3.43
%		6.3	4.3		11.1		2.0			11.3		4.3				6.0	22.0				
mineralization/calcification,																					
urothelium			10			21											13			44	3.51
			14.3			33.9											22.0				
calculi (NOS)	4							8						1	3	13		8		37	2.95
%	4.4							14.5						2.1	6.0	19.4		11.4			
calculi, tubules				17																17	1.36
%				34.0																	
calculi, pelvis			8	3			7			6		34	23				9		10	100	7.98
%			11.4	6.0			13.7			8.5		48.6	23.0				15.3		14.3		
mineralization, vascular			2					2									2	3		9	0.72
%			2.9					3.6									3.4	4.3			

TABLE 6b
NON-NEOPLASTIC LESIONS
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER	TOTAL#	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Jul-86	Apr-85	Apr-85	Dec-85	Nov-86	Mar-85	Sep-84	LESIONS	PERCENT
LOCATION & LESION																					
HEART																					
# TISSUES EXAMINED	90	50	70	50	70	62	51	55	71	73	80	70	100	50	50	71	60	70	70		
cardiomyopathy	23	28			18	36				1	1	58		2	7	42				216	17.10
%	25.6	56.0			25.7	58.1				1.4	1.3	82.9		4.0	14.0	59.2					
myocardial fibrosis			29				25	29			1		35				22		1	142	11.24
%			41.4				49.0	52.7			1.3		35.0				36.7		1.4		
chronic myocarditis			14	48			11			51	46						22	21	52	265	20.98
%			20.0	96.0			21.6			69.9	57.5						36.7	30.0	74.3		
LIVER																					
# TISSUES EXAMINED	90	50	70	50	70	62	51	55	71	73	80	70	100	50	50	71	60	70	70		
focus of altered hepatocytes, (NOS)		5	38			5				4	7						35	12	19	125	9.90
%		10.0	54.3			8.1				5.5	8.8						58.3	17.1	27.1		
focus of altered hepatocytes, acidophilic	1		13	4	7	4	1					11	15	4	2	3	4			69	5.46
%	1.1		18.6	8.0	10.0	6.5	2.0					15.7	15.0	8.0	4.0	4.2	6.7				
focus of altered hepatocytes, hasophilic	3		29	11	20		2	3	8			28	44			29	23			200	15.84
%	3.3		41.4	22.0	28.6		3.9	5.5	11.3			40.0	44.0			40.8	38.3				
focus of altered hepatocytes, mixed cell	9											37								46	3.64
%	10.0											52.9									
focus of altered hepatocytes, ground glass													20							20	1.58
%													20.0								
focus of altered hepatocytes, clear cell			1		4	1		12	1			4	1	3						27	2.14
%			1.4		5.7	1.6		21.8	1.4			5.7	1.0	6.0							
focus of altered hepatocytes, vacuolated								11												11	0.87
%								20.0													
hepatocellular hyperplasia		2						1	2	2						1		1	**18**	27	2.14
%		4.0						1.8	2.8	2.7						1.4		1.4	25.7		
hepatocellular hypertrophy		2		3				1		1	1	4				5			5	22	1.74
%		4.0		6.0				1.8		1.4	1.3	5.7				7.0			7.1		
biliary proliferation	16	33	43	16	25	22	26	32	12	4	5	35	5			36	21	24	7	362	28.66
%	17.8	66.0	61.4	32.0	35.7	35.5	51.0	58.2	16.9	5.5	6.3	50.0	5.0			50.7	35.0	34.3	10.0		
cholangiofibrosis		33	19	9			9		5			22	1	11	12		IS			136	10.77
%		66.0	27.1	18.0			17.6		7.0			31.4	1.0	22.0	24.0		25.0				
telangiectasis	9			8		1	10	1	9	10	7	3	1	2	1	3		2	7	74	5.86
%	10.0			16.0		1.6	19.6	1.8	12.7	13.7	8.8	4.3	1.0	4.0	2.0	4.2		2.9	10.0		

TABLE 6b (Continued)
NON-NEOPLASTIC LESIONS
24 MONTH STUDIES
FEMALE CD' RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER	TOTAL#	OVERALL
STUDY START DATE	Mar-85	May-84	Jun-84	Apr-84	Jun-84	Sep-86	Jul-84	Nov-85	Sep-85	Nov-84	Jun-85	Apr-86	Jul-86	Apr-85	Apr-85	Dec-85	Nov-86	Mar-85	Sep-84	LESIONS	PERCENT
LOCATION & LESION																					
KIDNEY																					
k TISSUES EXAMINED	90	50	70	49	70	62	51	55	70	73	80	70	100	49	49	70	60	70	70		
progressive renal disease	66	22	55	42	55	34	29	36	41	65	43	57	41	28	16	60	45	42	30	807	64.15
%	73.3	44.0	78.6	85.7	78.6	54.8	56.9	65.5	58.6	89.0	53.8	81.4	41.0	57.1	32.7	85.7	75.0	60.0	42.9		
nephrosis						1														1	0.08
%						1.6															
glomerulosclerosis							2													2	0.16
%							3.9														
glomerulonephritis													1							1	0.08
%													1.0								
interstitial nephritis				1				1												2	0.16
%				2.0				1.8													
pyelonephritis	1	3			3	2			1			1						1		12	0.95
%	1.1	6.0			4.3	3.2			1.4			1.4						1.4			
hyperplasia, tubular		11								2										13	1.03
%		22.0								2.7											
hyperplasia, transitional	2	21	12	6		53				6		2				34	10			146	11.61
%	2.2	42.0	17.1	12.2		85.5				8.2		2.9				48.6	16.7				
hyperplasia (NOS)																			12	12	0.95
%																			17.1		
hydronephrosis						11		7	1		4		1							24	1.91
%						17.7		12.7	1.4		5.0		1.0								
mineralization/calcification,																					
parenchyma (NOS)		4				1		2	45		12	1			1					66	5.25
%		8.0				1.6		3.6	64.3		15.0	1.4			2.0						
mineralization/calcification,																					
cortex			14	1													5			20	1.59
%			20.0	2.0													8.3				
ni ineralization/calcification,																					
medulla		24	11		40		2			58		5	1			2	11			154	12.24
%		48.0	15.7		57.1		3.9			79.5		7.1	1.0			2.9	18.3				
mineralization/calcification,																					
urothelium			44			53							1				35			133	10.57
%			62.9			85.5							1.0				58.3				
calculi (NOS)	5							33						14	17			39		108	8.59
%	5.6							60.0						28.6	34.7			55.7			
calculi, tubules				38																38	3.02
%				77.6																	
calculi,pelvis			35	8			43			46		61	34			41	23		36	327	25.99
%			50.0	16.3			84.3			63.0		87.1	34.0			58.6	38.3		51.4		
mineralization, vascular		1																		1	0.08
%		2.0																			

TABLE 7a
LIVER NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	FI	EV	ER
# TISSUES EXAMINED	90	49	70	50	72	62	51	55	70	71	80	70	100	50	49	69	60	70	70
nodular hepatocellular proliferation														4	5				
%														8.0	10.2				
hepatocellular adenoma	4	8	2	2	4	1	1	10	1	4	1	4		1	1	2	1	4	2
%	4.4	16.3	2.9	4.0	5.6	1.6	2.0	18.2	1.4	5.6	1.3	5.7		2.0	2.0	2.9	1.7	5.7	2.9
hepatocellular carcinoma	1	2	4			1	4	5		2		1		3	3			1	6
%	1.1	4.1	5.7			1.6	7.8	9.1		2.8		1.4		6.0	6.1			1.4	8.6
cholangioma																		1	
%																		1.4	
cholangiocellular carcinoma		1											1						
%		2.0											1.0						
carcinosarcoma															1				
%															2.0				

TABLE 7b
LIVER NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER
# TISSUES EXAMINED	90	50	70	50	70	62	51	55	71	73	80	70	100	50	50	71	60	70	70
nodular hepatocellular proliferation														4	5				
%														8.0	10.0				
hepatocellular adenoma		1	3	2	1	1	1	3			3	3	1	1	1	3	1	2	1
%		2.0	4.3	4.0	1.4	1.6	2.0	5.5			3.8	4.3	1.0	2.0	2.0	4.2	1.7	2.9	1.4
hepatocellular carcinoma							1						1	2				1	
%							2.0						1.0	4.0				1.4	
cholangioma	1																		1
%	1.1																		1.4

TABLE 8a
PITUITARY NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER
# TISSUES EXAMINED	88	48	69	46	72	61	50	52	70	69	79	70	99	48	49	67	59	70	70
adenoma, pars intermedia						3							1						
%						4.9							**1.0**						
adenoma, pars distalis	49	34	36	22	54	42	35	24	44	27	50	26	63	39	37	41	28	56	43
%	55.7	70.8	52.2	47.8	75.0	68.9	70.0	46.2	62.9	39.1	63.3	37.1	63.6	81.3	75.5	61.2	47.5	80.0	61.4
carcinoma, pars distalis				13			1	15		23		19	1	1	3	1			2
%				28.3			2.0	28.8		33.3		27.1	1.0	2.1	6.1	1.5			2.9
craniopharyngioma								1											
%								1.9											
hemangioma								1											
%								1.9											

TABLE 8b
PITUITARY NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	**ER**
# TISSUES EXAMINED	90	50	68	49	70	62	51	53	71	70	80	70	98	50	50	71	59	70	69
microadenoma, pars intermedia													1						
%													1.0						
adenoma, pars distalis	68	39	52	16	61	51	30	30	47	32	71	22	81	41	44	50	46	62	59
%	75.6	78.0	76.5	32.7	87.1	82.3	58.8	56.6	66.2	45.7	88.8	31.4	82.7	82.0	88.0	70.4	78.0	88.6	85.5
carcinoma, pars distalis	3		8	28		2	8	16		22	1	30	5		1		3	2	2
%	3.3		11.8	57.1		3.2	15.7	30.2		31.4	1.3	42.9	5.1		2.0		5.1	2.9	2.9

TABLE 9a
THYROID NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER
# TISSUES EXAMINED	89	48	69	50	72	62	50	55	66	71	80	70	100	49	50	66	58	69	70
follicular cell adenoma	1	2	2	2	3	5	6	5	2	1	4	2	7	4		3		2	18
%	1.1	4.2	2.9	4.0	4.2	8.1	12.0	9.1	3.0	1.4	5.0	2.9	7.0	8.2		4.5		2.9	25.7
follicular cell carcinoma	2		1	3		1	1				1	2	1	1	1		1	1	
%	2.2		1.4	6.0		1.6	2.0				1.3	2.9	1.0	2.0	2.0		1.7	1.4	
C-cell adenoma	8	1	12	1	2	2	6	9	3	5	2	6	1	3		7	5	6	
%	9.0	2.1	17.4	2.0	2.8	3.2	12.0	16.4	4.5	7.0	2.5	6.7	1.0	6.1		10.6	8.6	8.7	
C-cell carcinoma	1	2	4				3	1		5	2	2	5	1	1	1		1	
%	1.1	4.2	5.8				6.0	1.8		7.0	2.5	2.9	5.0	2.0	2.0	1.5		1.4	

TABLE 9b
THYROID NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER
# TISSUES EXAMINED	90	48	70	50	70	62	51	55	66	72	80	70	99	48	50	67	56	69	69
follicular cell adenoma		1	2	1	1		2	3	2	1		1	1	1	3	1	2		10
%		2.1	2.9	2.0	1.4		3.9	5.5	3.0	1.4		1.4	1.0	2.1	6.0	1.5	3.6		14.5
follicular cell carcinoma			1	1		1	2			1			1				1	1	4
%			1.4	2.0		1.6	3.9			1.4			1.0				1.8	1.4	5.8
C-cell adenoma	6	7	12	1	2	5	4	7	5	5	2	7	1	3	6	5	2	5	6
%	6.7	14.6	17.1	2.0	2.9	8.1	7.8	12.7	7.6	6.9	2.5	10.0	1.0	6.3	12.0	7.5	3.6	7.2	8.7
medullary carcinoma		1	3	2			5			4	2	3	13	1		5		3	
%		2.1	4.3	4.0			9.8			5.6	2.5	4.3	13.1	2.1		7.5		4.3	

TABLE 10a
ADRENAL NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	**EQ**	EU	EW	FJ	FM	FN	**ET**	Fl	EV	**ER**
# TISSUES EXAMINED	90	50	70	50	72	62	51	55	69	70	79	70	100	50	49	64	60	69	69
cortical adenoma (B)	2	2	2		2	2	1	9		1		1		5	3	1	2	2	1
%	2.2	4.0	2.9		2.8	3.2	2.0	16.4		1.4		1.4		10.0	6.1	1.6	3.3	2.9	1.4
cortical carcinoma		1				1	1										1	1	
%		2.0				1.6	2.0										1.7	1.4	
pheochromocytoma (B)	8	3	4	7	5	13	15	14	6	12	15	16	4	15	14	7	3	16	11
%	8.9	6.0	5.7	14.0	6.9	21.0	29.4	25.5	8.7	17.1	19.0	22.9	4.0	30.0	28.6	10.9	5.0	23.2	15.9
pheochromocytoma (M)			6	1		1	1	1		4				2	1	1	2	2	2
%			8.6	2.0		1.6	2.0	1.8		5.7				4.0	2.0	1.6	3.3	2.9	2.9
ganglioneuroma				1													1		
%				2.0													1.7		

TABLE 10b
ADRENAL NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	ER
# TISSUES EXAMINED	90	50	70	50	69	62	51	55	69	71	80	70	100	50	50	71	60	70	70
cortical adenoma	2	2	5	2	3	1	11	6	1	5	8	1	1	7	10	4	3	2	2
%	2.2	4.0	7.1	4.0	4.3	1.6	21.6	10.9	1.4	7.0	10.0	1.4	1.0	14.0	20.0	5.6	5.0	2.9	2.9
cortical adenocarcinoma			2				1				1	1	1		1			1	
%			2.9				2.0				1.3	1.4	1.0		2.0			1.4	
pheochromocytoma (B)	1	1	2			5	1	8		1	4	6	1	1	5	1	1	4	7
%	1.1	2.0	2.9			8.1	2.0	14.5		1.4	5.0	8.6	1.0	2.0	10.0	1.4	1.7	5.7	10.0
pheochromocytoma (M)				2		1	1			1		1			1				
%				4.0		1.6	2.0			1.4		1.4			2.0				

TABLE 11 a
PANCREAS (ENDOCRINE) NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
MALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	**ER**
# TISSUES EXAMINED	89	48	69	50	72	62	51	55	69	71	80	69	100	48	49	64	58	70	68
islet cell adenoma	10	9	3	3	5	6	6	8	5		5	2	24	4	5		4	2	2
%	11.2	18.8	4.3	6.0	6.9	9.7	11.8	14.5	7.2		6.3	2.9	24.0	8.3	10.2		6.9	2.9	2.9
islet cell carcinoma			2	1		3	3	1		5				1	4	1		4	
%			2.9	2.0		4.8	5.9	1.8		7.0				2.1	8.2	1.6		5.7	
mesothelioma													1						
%													1.0						

TABLE 11 b
PANCREAS (ENDOCRINE) NEOPLASMS BY STUDY GROUP
24 MONTH STUDIES
FEMALE CD® RATS

STUDY CODE	AQ	Y	AN	AP	AY	BO	FF	X	FH	EQ	EU	EW	FJ	FM	FN	ET	Fl	EV	**ER**
# TISSUES EXAMINED	90	50	70	49	70	61	51	55	70	73	80	70	99	50	49	70	60	70	70
islet cell adenoma	3	1	6	3	1	4	1	2	3	3	3	3	4	2		3	5		1
%	3.3	2.0	8.6	6.1	1.4	6.6	2.0	3.6	4.3	4.1	3.8	4.3	4.0	4.0		4.3	8.3		1.4
islet cell carcinoma		1				3	1	1		6				1		4		1	
%		2.0				4.9	2.0	1.8		8.2				2.0		5.7		1.4	

TABLE 12
MALE AND FEMALE CD® RATS
SURVIVAL DATA FOR 24 MONTH STUDIES
SCHEDULED SACRIFICES

STUDY			MALE			
CODE	3 MONTH	6 MONTH	12 MONTH	18 MONTH	24 MONTH	**DOS****
AQ+			15		44	46
Y			10		11	39
AN			10		20	50
AP			10		29	21
AY			9		21	50
BO			10		21	41
FF+		10*	10	9*	24	27
X			10		25	30
FH			20		26	44
EQ+			19		34	37
EU			10		33	47
EW			20		40	30
FJ+			0		56	44
FM			0		21	29
FN			0		17	33
ET			20		41	29
Fl			0		20	40
EV	10		20		24	46
ER			10		30	50
			FEMALE			
	3 MONTH	6 MONTH	12 MONTH	18 MONTH	24 MONTH	DOS**
AQ+			15		30	60
Y			10		11	39
AN			10		31	39
AP			10		28	24
AY			10		40	30
HO			10		22	40
FF+		10*	10	9*	28	23
X			10		29	26
FH			19		26	45
EQ+			17		44	29
EU			10		27	53
EW			20		32	38
FJ+					30	70
FM					18	32
FN					24	26
ET			19		44	27
Fl					18	42
EV	10		18		15	57
ER			19		22	49

*data not included in this publication
+data not included in survival curve (Figures 1 and 2)
**died on study

FIGURE 1a
MEAN SURVIVAL RATES
MALE CD® RATS

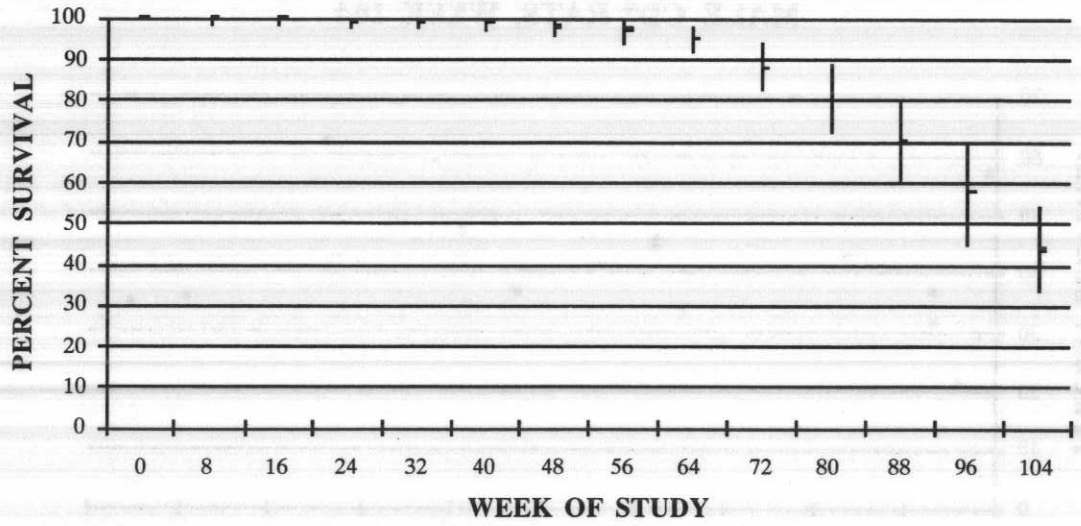

FIGURE 1B
MEAN SURVIVAL RATES
FEMALE CD® RATS

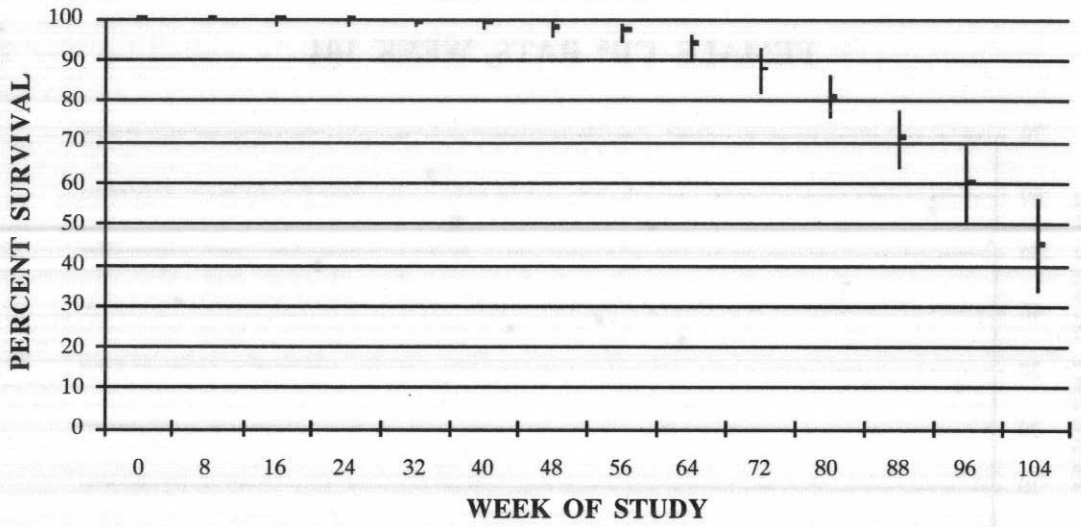

FIGURE 1: MEAN SURVIVAL RATES, MALE (FIGURE 1a) AND FEMALE (FIGURE 1b) CD RATS.

These two tables contain mean survival rates of CD rats in fifteen of the studies from which the neoplastic and non-neoplastic lesion information was obtained. Insufficient data were present for the other four study groups. Data were transformed using the Kaplan-Meier procedure. The plot represents the mean percent survival (indicated on the ordinate) plus and minus one standard deviation from the mean at each eight week interval (indicated on the abscissa).

Although these are accurate representations of the experiences of the 15 study groups, considerable caution must be taken in using these data for predictive purposes, for several reasons. First, the most recent study was completed more than three years ago. Second, the set of Charles River facilities supplying rats for chronic studies has changed in the last 5 years. For example, none of the studies discussed here used rats from Raleigh, North Carolina, which is currently a source of rats for many 2-year studies. Third, the variation among studies (see Table 12 and Figures 2a and 2b) suggests that factors other than the innate longevity potential of the rats may be important. The combination of these factors in any given facility may be more important in determining lifespan than any "average" value of the experiences of others.

FIGURE 2a
PERCENT SURVIVAL AT 104 WEEKS
MALE CD® RATS

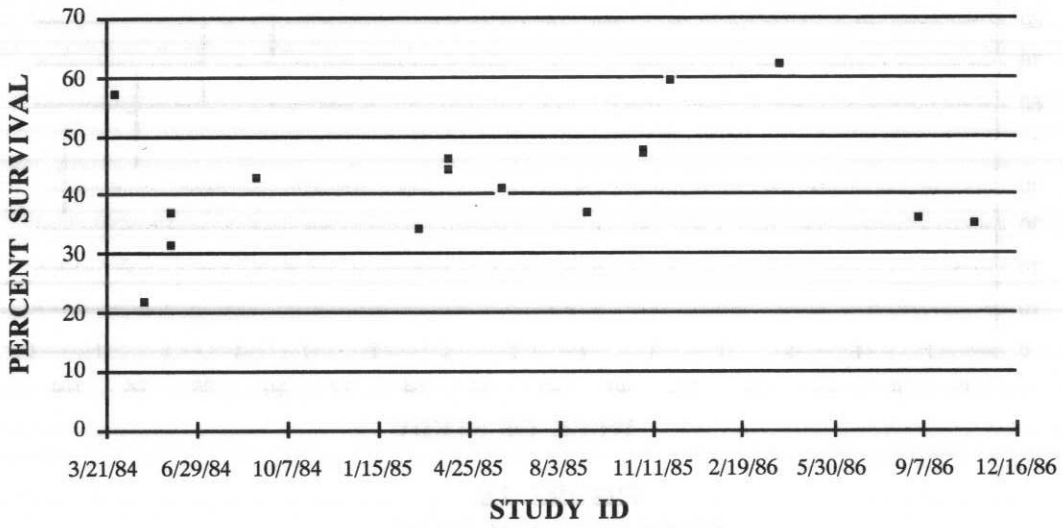

FIGURE 2b
PERCENT SURVIVAL AT 104 WEEKS
FEMALE CD® RATS

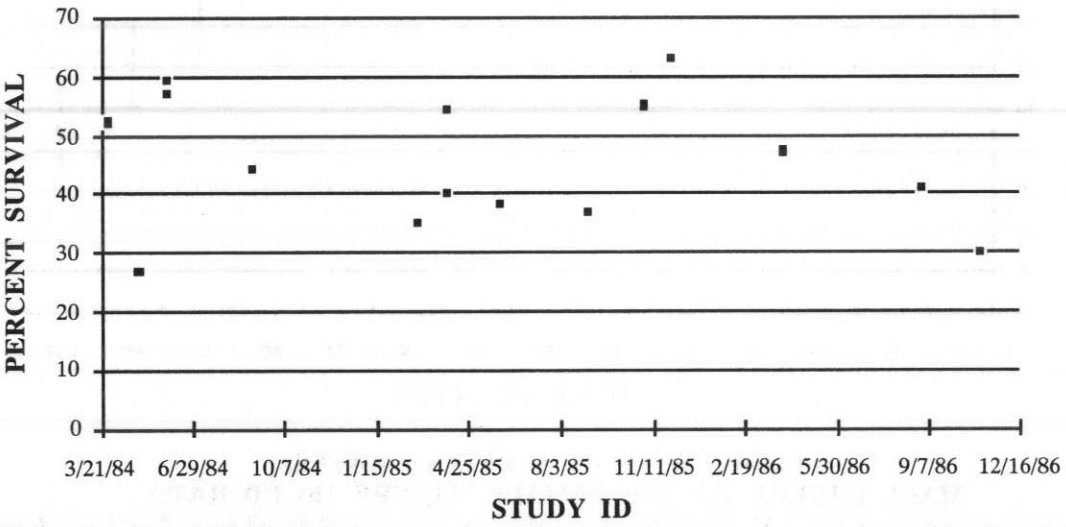

FIGURE 2: PERCENT SURVIVAL AT 24 MONTHS, MALE (FIGURE 2a) AND FEMALE (FIGURE 2b) CD RATS.

The percent survival at 104 weeks of study is presented by study group. This number was calculated using the Kaplan-Meir procedure and incorporated data from moribund sacrifices, scheduled sacrifices, and accidental deaths. Each point represents a single study group. The x-axis represents the time of study start date and is linear.