

Spontaneous Neoplastic Lesions and Survival in Crl:CD[®](SD)BR Rats Maintained on Dietary Restriction

March 1998

Information Prepared by
Mary L. A. Giknis, Ph.D.
Charles B. Clifford, D. V.M., Ph.D.


CHARLES RIVER
LABORATORIES

TABLE OF CONTENTS

INTRODUCTION:	1
PURPOSE:	1
COMMON STUDY PARAMETERS:	1
DATA SETS PRESENTED:	1
SUMMARY TABLE CALCULATIONS:	2
SYNONYMS:	3
ABBREVIATIONS:	4
ACKNOWLEDGEMENTS:	4
REFERENCES:	4
TABLE 1: SUMMARY OF INDIVIDUAL STUDY INFORMATION AND SURVIVAL/MALES	5
TABLE 2: SUMMARY OF INDIVIDUAL STUDY INFORMATION AND SURVIVAL/FEMALES .	5
GRAPH 1: MALE SURVIVAL	6
GRAPH 2: FEMALE SURVIVAL.....	7
TABLE 3: INDIVIDUAL STUDY FOOD CONSUMPTION DATA	8
TABLE 4: NEOPLASMS/MALES.....	9
TABLE 5: NEOPLASMS/FEMALES	15
TABLE 6: INCIDENCE OF NEOPLASMS BY STUDY FOR SELECTED ORGANS/MALES	21
TABLE 7: INCIDENCE OF NEOPLASMS BY STUDY FOR SELECTED ORGANS/FEMALES ...	23

Spontaneous Neoplastic Lesions and Survival in CrI:CD®(SD)BR Rats Maintained on Dietary Restriction

INTRODUCTION:

The use of some form of dietary restriction, also referred to as dietary optimization, is becoming increasingly common in standard toxicology studies as it is thought to result in healthier animals than the traditional *ad libitum* feeding regimen (1, 2, 3, 4, 5). The data presented in these tables were gathered from 26 toxicology studies of approximately 104 weeks duration in which some form of dietary restriction was employed. All studies were performed in the United States or Europe by contract laboratories or industrial toxicology facilities.

PURPOSE:

The purpose of this compilation is to offer the study director, reviewing toxicologist and/or study pathologist some reported incidences of neoplasms in CrI:CD®(SD)BR rats maintained throughout the duration of 104 week studies on a regimen of dietary restriction. Diagnoses in the compilations are intentionally grouped in a manner to provide the user with a range of reported incidences of similar types of lesions. This compilation is not intended in any way to propose a system of standardized nomenclature nor does it separately include each and every reported variant of each lesion.

COMMON STUDY PARAMETERS:

The 26 studies included in this publication were initiated between December 1989 and April 1995 in four different laboratories. All studies used CrI:CD®(SD)BR rats from three different Charles River Laboratories production sites: animals in studies A through F were from France, animals in study V were from Portage, Michigan and animals from the remaining 19 studies were from Raleigh, North Carolina.

The rats in these studies were from control groups of dietary or gavage studies and were approximately 4-8 weeks of age at study initiation. Some groups were untreated while others received 1.0% polyethylene glycol; 0.5% aqueous methylcellulose; 1.0% aqueous carboxymethylcellulose; or deionized water as the vehicle control.

Rats included in this publication were singly housed in stainless steel wire mesh cages with free access to water. The animal rooms were generally maintained at average temperatures of 72 +/- 5 degrees Fahrenheit with an average relative humidity of 30-70%. A 12hr/12hr light/dark cycle was employed in all studies. Since these studies were conducted in different facilities, there was some variation in environmental conditions. However, the overall environmental conditions were not considered by those performing the studies to have had any effect on the quality or integrity of the studies. Rats in studies A through F were fed measured amounts of UAR A04C feed with a physiological fuel value of 3.3 kcal/g and rats in all other studies received measured amounts of Purina PMI Certified Rodent Chow 5002 with a physiological fuel value of 3.4 kcal/g. The amount of feed consumed ranged from 14.5 to 17 grams for females and 20.5 to 24 grams for males. The actual amount of feed consumed per day and its respective calculated physiological fuel value are presented by study in Table 3.

Information on health assessment monitoring, other than that associated with pathological examination conducted in accordance with scheduled or moribund sacrifices, was not available.

DATA SETS PRESENTED:

The overall incidences of all neoplastic lesions observed in any organ are reported and summarized in Tables 4 and 5. These data also include neoplastic lesions from rats which died or were found moribund and killed prior to terminal sacrifice. It does not include information from rats which were killed for an interim sacrifice. Due to the apparent diversity in terminology and the variability among studies in the incidence of particular lesions, the individual study incidences of lesions in selected

organs/systems are also presented (Tables 6 and 7). These organs/systems include liver; pituitary; thyroid; adrenal; pancreas; mammary gland; lymphoreticular system and whole body/multiple organ.

Survival data are presented by study as the actual number surviving to terminal sacrifice and as percent survival at terminal sacrifice (Tables 1 and 2). The survival data are also presented in graphic form (Graphs 1 and 2). Survival data are not included for studies W-Z as they were not available at the time of publication.

SUMMARY TABLE CALCULATIONS:

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

Number of Studies (# Studies)

This is the number of studies in which a particular tissue/organ was examined. In this presentation, the number of studies is always 26.

Total Number of Organs (Total # Organs)

This number represents the sum of the total number of tissues or organs examined in all control groups from all studies combined. Widespread tumors which showed involvement of multiple organs were listed on the basis of total number of animals examined. Occasionally a tumor would be noticed in a tissue not designated for histological examination by the study protocol. In these instances, the tumor incidence was based on the total number of animals examined as any such tumor or lesion would have been noticed on gross examination of the animal. Autolysis of tissues did not routinely exclude tissues from diagnosis. Tissue numbers were adjusted only if the individual study table indicated that some tissues were missing or inadequate for examination. Some laboratories presented data separately for different regions within an organ (i.e., duodenum, jejunum and ileum) while most presented data by the organ (i.e., small intestine). When data were presented separately by organ region, it was grouped under the organ and calculations were based on the number of organs examined.

Total Number of Lesions (# Lesions)

This represents the total number of occurrences of this lesion in the specified organ in all studies examined.

Percent of Total

These values represent the percent incidence of a particular lesion/diagnosis in the total number (all studies combined) of a particular organ examined. These values were calculated by dividing the total number of lesions by the total number of organs/animals examined and multiplying by 100 to express the values as a percent. Values are expressed to the second decimal place. Some caution is indicated in using this number, since not all pathologists or institutions will include all diagnoses in their lexicon.

Number of Studies Using This Diagnosis

This is the number of studies in which a particular diagnosis was reported. This number may be useful in interpreting the overall incidence (percent of total) of a particular diagnosis, see above.

Minimum and Maximum Percent Found (Minimum and Maximum % Found)

The range reported is the lowest and highest percent incidence for each lesion from the studies where the diagnosis was made. Therefore, if a study did not include a particular diagnosis, it was excluded from these calculations. The minimum and maximum percent found values should be considered in conjunction with the Number of Studies Using the Diagnosis.

The individual study percentages, Minimum % Found and Maximum % Found, were calculated by dividing the number of times each diagnosis was made by the total number of organs examined in each study and then multiplying the resultant value by 100 to express it as a percent. Values are expressed to the second decimal place.

SYNONYMS:

Synonymous terms or diagnoses were frequently encountered in different studies, and were combined under a single, often broad diagnosis, which was considered to be 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. A 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 publication are considered to be consistent with that trend. The synonyms which were included in the various diagnoses are presented in the synonym list which follows. Where possible, terminology is consistent with the classification system proposed by the Society of Toxicologic Pathologists.

Stomach:

NONGLANDULAR MUCOSA/SQUAMOUS CELL PAPILLOMA = papilloma; non-glandular mucosa papilloma; squamous cell papilloma
NONGLANDULAR MUCOSA, CARCINOMA = squamous cell carcinoma

Liver:

BILE DUCT ADENOMA = cholangioma

Prostate:

CARCINOMA/CARCINOMA NOS = adenocarcinoma

Uterus:

ENDOMETRIAL STROMAL POLYP = polyp
ENDOMETRIUM, ADENOCARCINOMA = adenocarcinoma; endometrium, carcinoma
ENDOMETRIAL STROMAL SARCOMA = sarcoma

Skin:

BASAL CELL CARCINOMA = malignant basal cell tumor

Mammary Gland:

ADENOMA = cystadenoma

Adrenal:

CORTEX, CARCINOMA = cortex, adenocarcinoma

Pancreas:

ISLET CELL, ADENOMA = islet, adenoma; adenoma NOS
ISLET CELL, CARCINOMA = islet cell, adenocarcinoma; islet, carcinoma

Pituitary:

ADENOMA = adenoma anterior lobe; adenoma pars distalis
CARCINOMA = carcinoma pars distalis; adenocarcinoma; adenocarcinoma pars distalis

Thyroid:

C-CELL = parafollicular cell
FOLLICULAR CELL CARCINOMA = follicular cell adenocarcinoma

Body:

WHOLE BODY/MULTIPLE ORGAN = primary site undetermined

ABBREVIATIONS:

NOS = not otherwise specified.

ACKNOWLEDGEMENTS:

Our thanks to Joseph Frank, Janice Van Dyke and all of the contributing laboratories without whose help this publication would not have been possible.

REFERENCES:

1. Hart, R.W., Neumann, D. A., and Robertson, R.T. (1995) Dietary Restriction: Implications for the Design and Interpretation of Toxicity and Carcinogenicity Studies. ILSI Press, Washington, D.C.
2. Keenan, K.P., (1996) The Uncontrolled Variable in Risk Assessment: *Ad Libitum* Overfed Rodents - Fat, Facts and Fiction. *Toxicol. Pathol.* 24: 376-383.
3. Keenan, K.P., Laroque, P., Ballam, G.C., Soper, K.A., Dixit, R, Mattson, B.A., Adams, S.P. & Coleman, J.B. (1996) The Effects of Diet, *Ad Libitum* Overfeeding, and Moderate Dietary Restriction on the Rodent Bioassay: The Uncontrolled Variable in Safety Assessment. *Toxicol. Pathol.* 24: 757-768.
4. Masoro, E.J. (1996) Possible Mechanisms Underlying the Antiaging Actions of Caloric Restriction. *Toxicol. Pathol.* 24:738-741.
5. Roe, F.J.C., Lee, P.N., Conybeare, G., Kelly, D., Matter, B. , Prentice, D., and Tobin, G. (1995) The Biosure Study: Influence of Composition of Diet and Food Consumption on Longevity, Degenerative Diseases and Neoplasia in Wistar Rats Studied for up to 30 Months Post Weaning. *Food and Chemical Toxicology* 33.

Table 1: Summary of Individual Study Information and Survival/Males

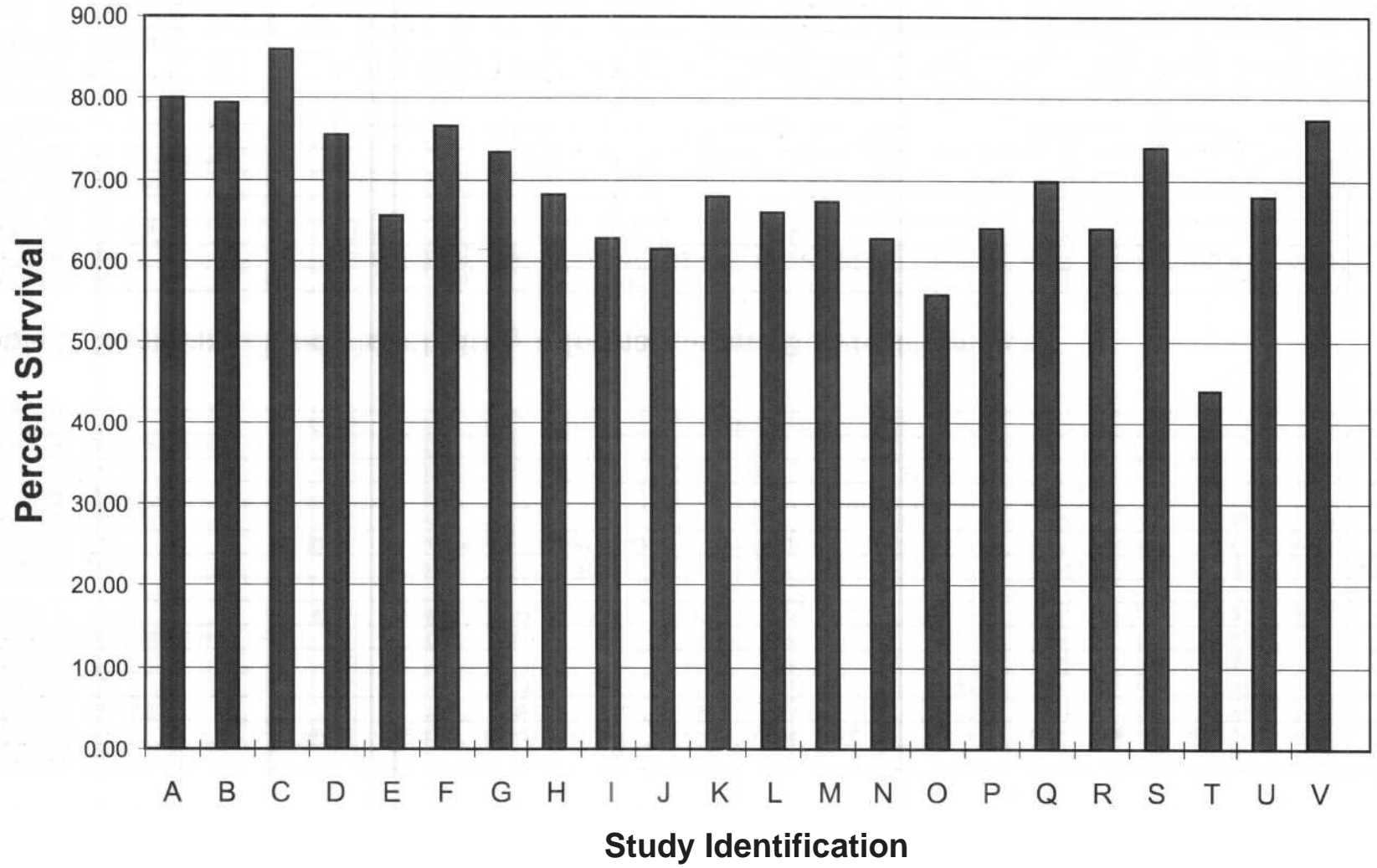
									I	J	K	L	M
										May-93	May-93	Jun-93	Jun-93
									78	78	78	50	49
									13	14	14	10	10
									16	16	11	7	6
									49	48	53	33	33
									62.82	61.54	67.95	66.00	67.35
									W	X	Y	Z	TOTAL
									Feb-92	Feb-92	Nov-93	Nov-93	
									60	60	60	60	1686
													197
													240
													1009

Table 2: Summary of Individual Study Information and Survival/Females

Study Identification	A	B	C	D	E	F	G	H	I	J	K	L	M	
Study Initiation Date	Jun-92	Jun-92	Jun-92	Jun-92	Dec-94	Dec-94	Dec-89	Apr-93	Apr-93	Apr-93	Apr-93	Jun-93	Jun-93	
Total Number Necropsied	126	78	78	78	60	60	60	126	78	78	78	50	50	
Number Found Dead	7	8	3	4	4	6	10	21	6	8	7	13	10	
Number Sacrificed Moribund	20	13	21	19	21	11	14	38	20	25	25	6	9	
Number Surviving to Termination	99	57	54	55	35	43	36	67	52	45	46	31	31	
% Survival	78.57	73.08	69.23	70.51	58.33	71.67	60.00	53.17	66.67	57.69	58.97	62.00	62.00	
									V	W	X	Y	Z	TOTAL
										Feb-92	Feb-92	Nov-93	Nov-93	
									48	60	60	60	60	1691
									14*					164
									8					366
									26					921

* = Number includes one accidental death

Graph 1: Male Survival



Graph 2: Female Survival

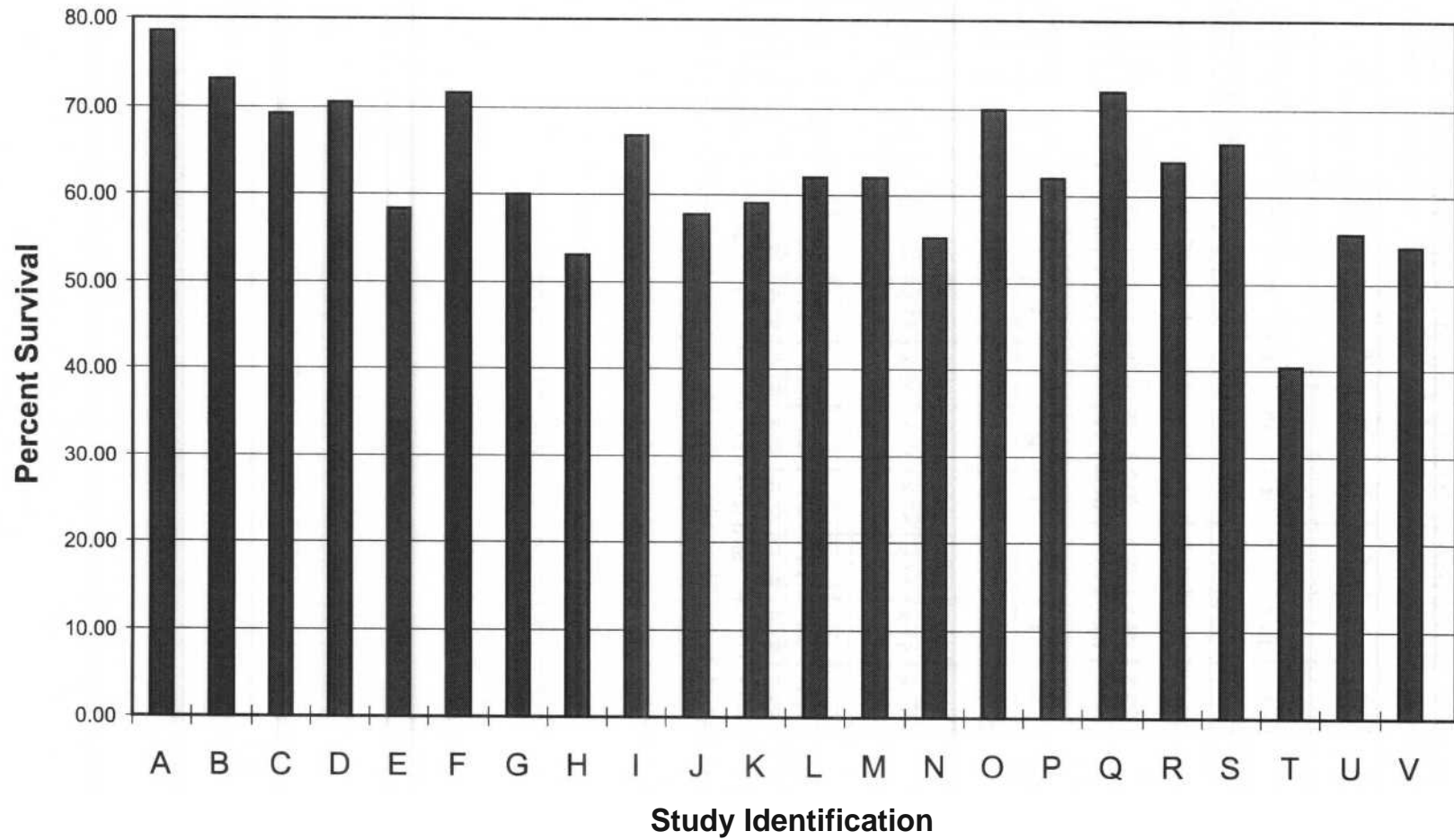


Table 3: Individual Study Food Consumption Data

Study Identification	A	B	C	D	E	F	G	H	I	J	K	L	M
Females													
g/day	14.5	14.5	14.5	14.5	17	16.1	16	17	17	17	17	17	17
kcal/day	47.9	47.9	47.9	47.9	56.1	53.1	54.4	57.8	57.8	57.8	57.8	57.8	57.8
Males													
g/day	20.5	20.5	20.5	20.5	24	24.2	21.5	24	24	24	24	24	24
kcal/day	67.7	67.7	67.7	67.7	79.2	79.9	73.1	81.6	81.6	81.6	81.6	81.6	81.6

Study Identification	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
Females													
g/day	17	17	17	17	17	17	17	16	18	16	16	16	16
kcal/day	57.8	57.8	57.8	57.8	57.8	57.8	57.8	54.4	61.2	54.4	54.4	54.4	54.4
Males													
g/day	24	24	24	24	24	24	24	22	23	21	21	21	21
kcal/day	81.6	81.6	81.6	81.6	81.6	81.6	81.6	74.8	78.2	71.4	71.4	71.4	71.4

Rats in studies A-F received UAR A04C feed with a physiological fuel value of 3.3 kcal/gram; all other rats received Purina PMI Certified Rodent Chow 5002 with a physiological fuel value of 3.4 kcal/gram.

Table 4: Neoplasms/Males

LOCATION AND TUMOR	# STUDIES	TOTAL	PERCENT OF TOTAL	# STUDIES USING THIS DIAGNOSIS	MINIMUM % FOUND	MAXIMUM % FOUND
		# ORGANS # LESIONS				
ORAL CAVITY	26	1686				
Hard Palate, Squamous Cell Carcinoma		1	0.06	1	1.67	1.67
Squamous Cell Carcinoma		1	0.06	1	1.67	1.67
SALIVARY GLAND	26	1686				
Adenoma		1	0.06	1	2.00	2.00
Adenocarcinoma		1	0.06	1	2.00	2.00
Hemangiosarcoma		1	0.06	1	1.28	1.28
STOMACH	26	1686				
Non-glandular Mucosa/Squamous Cell Papilloma		6	0.36	5	0.79	4.00
Leiomyosarcoma		4	0.24	4	1.28	2.00
Sarcoma		1	0.06	1	1.67	1.67
SMALL INTESTINE	26	1684				
Adenocarcinoma		7	0.42	6	0.79	2.56
Leiomyoma		1	0.06	1	2.00	2.00
Leiomyosarcoma		3	0.18	3	1.28	2.00
LARGE INTESTINE	26	1682				
Adenoma		1	0.06	1	1.67	1.67
Adenocarcinoma		1	0.06	1	1.28	1.28
Cecum, Leiomyoma		1	0.06	1	2.00	2.00
Polyp		1	0.06	1	0.79	0.79
LIVER	26	1686				
Hepatocellular Adenoma		34	2.02	20	0.79	8.00
Hepatocellular Carcinoma		59	3.50	23	0.79	12.00
Bile Duct, Adenoma		4	0.24	4	0.79	1.96
Hemangioma		1	0.06	1	1.28	1.28
PERITONEUM	26	1686				
Fibrosarcoma		1	0.06	1	1.28	1.28

LOCATION AND TUMOR	# STUDIES	TOTAL	PERCENT OF TOTAL	# STUDIES USING THIS DIAGNOSIS	MINIMUM % FOUND	MAXIMUM % FOUND
		# ORGANS # LESIONS				
PERITONEUM (cont.)						
Osteogenic Sarcoma		1	0.06	1	2.00	2.00
Paraganglioma		1	0.06	1	2.00	2.00
NASAL CAVITY						
Sarcoma, NOS	26	1686				
		1	0.06	1	1.67	1.67
LUNG						
	26	1686				
Adenoma/Bronchoalveolar Adenoma		6	0.36	6	0.79	2.00
Adenocarcinoma		3	0.18	2	2.00	2.56
Hemangiosarcoma		1	0.06	1	1.28	1.28
KIDNEY						
	26	1686				
Adenoma/Tubular Adenoma		4	0.24	4	1.28	2.00
Transitional Cell Carcinoma		1	0.06	1	1.28	1.28
Lipoma		2	0.12	2	1.28	1.96
Liposarcoma		5	0.30	4	0.79	4.08
Mesenchymal Tumor, Malignant		1	0.06	1	1.67	1.67
URINARY BLADDER						
	26	1685				
Papilloma		2	0.12	2	2.00	2.04
Transitional Cell Carcinoma		1	0.06	1	2.00	2.00
Leiomyoma		1	0.06	1	1.96	1.96
TESTIS						
	26	1685				
Interstitial Cell Tumor, Benign		66	3.92	22	1.28	8.47
Hemangioma		1	0.06	1	2.00	2.00
Mesothelioma, Benign		3	0.18	3	0.79	2.00
Mesothelioma, Malignant		2	0.12	2	1.67	1.67
Tunica Vaginalis, Mesothelioma, Malignant		1	0.06	1	2.00	2.00
SEMINAL VESICLE						
	26	1686				
Adenocarcinoma		1	0.06	1	1.28	1.28

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
PROSTATE	26	1686				
Adenoma		3	0.18	2	1.67	3.33
Carcinoma/Carcinoma NOS		4	0.24	3	1.96	3.33
SKIN	26	1685				
Basal Cell Tumor, Benign		12	0.71	10	0.79	5.00
Basal Cell Carcinoma		1	0.06	1	1.69	1.69
Keratoacanthoma, Benign		35	2.08	16	1.28	8.47
Papilloma/Squamous Cell Papilloma		31	1.84	18	0.79	6.90
Squamous Cell Carcinoma		6	0.36	5	0.79	2.56
Tricoepithelioma, Benign		4	0.24	4	1.28	2.00
Sebaceous Adenoma		2	0.12	2	1.28	1.96
Fibroma		62	3.68	24	1.28	10.00
Fibrosarcoma		24	1.42	15	0.79	4.00
Sarcoma		1	0.06	1	0.79	0.79
Hemangioma		1	0.06	1	1.67	1.67
Hemangiosarcoma		2	0.12	2	0.79	1.72
Mast Cell Sarcoma		1	0.06	1	2.00	2.00
Lipoma		14	0.83	9	1.28	6.12
Histiocytic Sarcoma		2	0.12	2	1.67	2.00
Fibrous Histiocytoma		4	0.24	2	3.33	4.08
Neurofibrosarcoma, Malignant		1	0.06	1	0.79	0.79
Schwannoma, Malignant		1	0.06	1	1.67	1.67
MAMMARY GLAND	26	1637				
Adenoma		3	0.18	3	1.28	1.96
Adenocarcinoma		3	0.18	3	0.79	2.00
Fibroma		2	0.12	2	1.28	1.67
Fibroadenoma		14	0.86	10	1.28	4.44
ADRENAL	26	1686				
Cortex, Adenoma		20	1.19	16	0.79	4.08
Cortex, Carcinoma		5	0.30	5	1.28	2.00
Pheochromocytoma, Benign		95	5.63	24	1.67	16.67
Pheochromocytoma, Malignant		17	1.01	10	1.67	5.00
Ganglioneuroma, Benign		2	0.12	1	1.59	1.59

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
PANCREAS	26	1686				
Acinar Cell, Adenoma		7	0.42	6	1.28	3.92
Islet Cell, Adenoma		164	9.73	26	1.67	32.00
Islet Cell, Carcinoma		27	2.02	15	1.28	10.00
Histiocytic Sarcoma		1	0.06	1	1.67	1.67
PITUITARY	26	1683				
Adenoma		608	36.13	26	14.00	62.00
Carcinoma		7	0.42	5	0.79	3.45
Pars Intermedia, Adenoma		5	0.30	4	1.67	3.33
Craniopharyngioma		1	0.06	1	2.00	2.00
THYROID	26	1686				
C-Cell, Adenoma		145	8.60	25	1.67	23.53
C-Cell, Carcinoma		38	2.25	18	0.79	14.00
Follicular Cell, Adenoma		10	0.59	10	0.79	2.00
Follicular Cell, Carcinoma		8	0.47	7	0.79	4.00
PARATHYROID	26	1679				
Adenoma		22	1.31	14	0.79	3.85
BRAIN		1686				
Astrocytoma, Benign	26	15	0.89	8	1.67	4.00
Astrocytoma, Malignant		6	0.36	6	1.67	2.00
Glioma, Malignant		7	0.42	5	1.28	2.56
Granular Cell Tumor, Benign		16	0.95	13	1.28	4.00
Granular Cell Tumor, Malignant		1	0.06	1	1.28	1.28
Meningioma, Malignant		1	0.06	1	1.72	1.72
Meningeal Sarcoma		1	0.06	1	2.00	2.00
Reticulosis, Malignant		1	0.06	1	2.04	2.04
SPINAL CORD	26	1682				
Glioma, Malignant		1	0.06	1	2.00	2.00
Schwannoma, Benign		1	0.06	1	1.72	1.72

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
PERIPHERAL NERVE	26	1686				
Schwannoma, Malignant		2	0.12	2	1.67	2.00
SKELETAL MUSCLE	26	1686				
Fibrosarcoma		3	0.18	2	2.00	4.00
Hemangioma		1	0.06	1	2.00	2.00
Hemangiosarcoma		1	0.06	1	2.00	2.00
Rhabdomyosarcoma		3	0.18	3	0.79	2.00
Histiocytic Sarcoma		1	0.06	1	1.67	1.67
BONE	26	1686				
Chordoma, Benign		1	0.06	1	2.00	2.00
Osteoma, Benign		1	0.06	1	2.00	2.00
Osteosarcoma		3	0.18	3	0.79	2.00
HEART	26	1686				
Mesothelioma, Benign		1	0.06	1	1.67	1.67
Mesothelioma, Malignant		3	0.18	3	0.79	1.28
Schwannoma, Malignant		4	0.24	4	1.28	2.00
BLOOD VESSEL	26	1686				
Aorta, Paraganglioma, Benign		2	0.12	2	1.67	1.72
BONE MARROW	26	1686				
Hemangioma		1	0.06	1	1.28	1.28
Mast Cell Sarcoma, Malignant		1	0.06	1	1.28	1.28
SPLEEN	26	1685				
Hemangioma		1	0.06	1	1.28	1.28
Hemangiosarcoma		5	0.30	4	1.28	2.00
Sarcoma		1	0.06	1	1.28	1.28
THYMUS	26	1644				
Thymoma, Benign		4	0.24	4	2.00	2.00
Thymoma, Malignant		3	0.18	3	0.79	2.00

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
THYMUS (cont.)						
Lymphoma		2	0.12	2	0.79	1.28
Fibrosarcoma		1	0.06	1	1.28	1.28
LYMPHORETICULAR SYSTEM	26	1681				
Lymph Node, Hemangioma		6	0.36	5	1.59	2.04
Lymph Node, Hemangiosarcoma		3	0.18	3	0.79	1.75
WHOLE BODY/MULTIPLE ORGAN	26	1686				
Lymphoma		41	2.43	20	1.28	8.33
Leukemia/Myeloid Leukemia		7	0.42	7	0.79	2.00
Histiocytic Sarcoma		38	2.25	22	0.79	8.00
Reticulum Cell Sarcoma		1	0.06	1	1.28	1.28
EYE	26	1686				
Conjunctiva, Schwannoma, Benign		1	0.06	1	1.96	1.96
Melanoma, Malignant		1	0.06	1	1.67	1.67
Iris, Melanoma		1	0.06	1	1.28	1.28
Schwannoma, Benign		1	0.06	1	0.79	0.79
EAR	26	1686				
Zymbal's Gland, Adenoma		2	0.12	2	1.28	2.00
Zymbal's Gland, Carcinoma		7	0.42	7	0.79	2.00
Pinna, Fibrosarcoma		1	0.06	1	2.00	2.00
Pinna, Schwannoma, Benign		3	0.18	3	0.79	1.72

Table 5: Neoplasms/Females

LOCATION AND TUMOR	# STUDIES	TOTAL	PERCENT OF TOTAL	# STUDIES USING THIS DIAGNOSIS	MINIMUM % FOUND	MAXIMUM % FOUND
		# ORGANS # LESIONS				
ORAL CAVITY	26	1691				
Lip, Papilloma		1	0.06	1	2.00	2.00
Squamous Cell Carcinoma		3	0.18	3	1.67	1.67
STOMACH	26	1691				
Non-glandular Mucosa, Carcinoma		3	0.18	3	1.28	2.00
Non-glandular Mucosa, Keratoacanthoma, Benign		1	0.06	1	2.00	2.00
Leiomyosarcoma		1	0.06	1	1.67	1.67
Lipoma		1	0.06	1	0.79	0.79
SMALL INTESTINE	26	1680				
Adenocarcinoma		2	0.12	2	1.28	1.67
Leiomyoma		5	0.30	5	0.79	1.92
Leiomyosarcoma		1	0.06	1	1.28	1.28
LARGE INTESTINE	26	1682				
Adenoma		1	0.06	1	2.00	2.00
Leiomyosarcoma		2	0.12	2	1.92	2.00
LIVER	26	1691				
Hepatocellular Adenoma		37	2.19	20	1.28	2.00
Hepatocellular Carcinoma		12	0.71	9	0.79	2.56
Bile Duct, Adenoma		2	0.12	2	1.28	1.67
Histiocytic Sarcoma		1	0.06	1	2.00	2.00
PERITONEUM	26	1691				
Hemangiopericytoma, Benign		1	0.06	1	2.00	2.00
Hemangiosarcoma		1	0.06	1	1.28	1.28
NASAL CAVITY	26	1691				
Squamous Cell Carcinoma		1	0.06	1	1.67	1.67

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
KIDNEY	26	1691				
Adenoma/Tubular Adenoma		6	0.35	6	1.28	2.04
Adenocarcinoma/Tubular Adenocarcinoma		2	0.12	2	1.67	2.00
Hemangioma		1	0.06	1	0.79	0.79
Transitional Cell Carcinoma		1	0.06	1	1.67	1.67
Lipoma		2	0.12	2	1.28	1.67
Liposarcoma		2	0.12	1	2.56	2.56
Mesenchymal Tumor		1	0.06	1	1.92	1.92
Osteosarcoma		1	0.06	1	1.67	1.67
URINARY BLADDER	26	1690				
Papilloma		2	0.12	2	1.67	2.00
Transitional Cell Carcinoma		1	0.06	1	1.92	1.92
Leiomyosarcoma		1	0.06	1	1.28	1.28
OVARY	26	1689				
Tubular Adenoma		6	0.36	3	1.28	3.17
Granulosa Cell Tumor, Benign		10	0.59	7	0.79	4.00
Hemangiosarcoma		1	0.06	1	1.28	1.28
Stromal Sarcoma		1	0.06	1	1.28	1.28
Sarcoma		2	0.12	2	0.79	1.28
Theca Cell Tumor, Benign		9	0.53	8	1.28	2.56
Theca Cell Tumor, Malignant		1	0.06	1	1.28	1.28
Luteoma		1	0.06	1	1.92	1.92
Sertoliform Adenoma		8	0.47	4	1.67	6.90
UTERUS	26	1691				
Endometrium, Adenoma		1	0.06	1	1.28	1.28
Endometrium, Adenocarcinoma		19	1.12	11	1.28	5.00
Endometrial Stromal Polyp		102	6.03	25	1.67	12.82
Endometrial Stromal Sarcoma		10	0.59	9	0.79	3.85
Fibroma		2	0.12	2	1.28	1.67
Hemangioma		1	0.06	1	1.28	1.28
Leiomyoma		6	0.35	5	1.28	2.00
Leiomyosarcoma		5	0.30	4	0.79	2.56
Schwannoma, Malignant		1	0.06	1	1.92	1.92

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
CERVIX	26	1691				
Squamous Papilloma		1	0.06	1	0.79	0.79
Squamous Cell Carcinoma		1	0.06	1	1.92	1.92
Fibroma		1	0.06	1	1.92	1.92
VAGINA	26	1691				
Papilloma		1	0.06	1	1.28	1.28
Polyp		3	0.18	3	1.67	2.00
Squamous Cell Carcinoma		4	0.24	4	1.28	2.08
Fibroma		1	0.06	1	1.28	1.28
Sarcoma		2	0.12	2	1.28	1.28
CLITORAL GLAND	26	1691				
Clitoral Gland, Adenoma		1	0.06	1	1.28	1.28
Clitoral Gland, Carcinoma		1	0.06	1	1.28	1.28
SKIN	26	1691				
Basal Cell Tumor, Benign		2	0.12	2	1.28	1.67
Basal Cell Carcinoma		2	0.12	2	1.28	1.92
Keratoacanthoma, Benign		5	0.30	4	1.67	3.33
Papilloma/Squamous Cell Papilloma		3	0.18	3	0.79	2.00
Squamous Cell Carcinoma		10	0.59	9	0.79	2.56
Tricoepithelioma, Benign		2	0.12	2	0.79	1.92
Sebaceous Adenocarcinoma		2	0.12	2	1.28	1.67
Fibroma		9	0.53	7	1.28	2.38
Fibrosarcoma		13	0.77	11	0.79	3.33
Sarcoma		2	0.12	2	1.28	1.92
Hemangioma		1	0.06	1	0.79	0.79
Hemangiosarcoma		1	0.06	1	0.79	0.79
Liposarcoma		1	0.06	1	2.00	2.00
Histiocytic Sarcoma		1	0.06	1	1.92	1.92
Fibrous Histiocytoma		1	0.06	1	1.67	1.67
Schwannoma, Malignant		1	0.06	1	1.92	1.92
Lymphoma, Malignant, Dermal		1	0.06	1	1.67	1.67
MAMMARY GLAND	26	1689				
Adenoma		105	6.22	24	2.00	16.00
Adenocarcinoma		287	16.99	26	6.67	43.33

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
MAMMARY GLAND (cont.)						
Fibroma		4	0.24	4	0.79	1.67
Fibrosarcoma		1	0.06	1	0.79	0.79
Fibroadenoma		541	32.03	26	17.95	52.54
Mixed Mammary Tumor, Malignant		3	0.18	3	0.79	1.28
Carcinosarcoma		4	0.24	3	2.00	4.00
ADRENAL						
	26	1691				
Cortex, Adenoma		36	2.13	19	0.79	4.70
Cortex, Carcinoma		8	0.47	8	0.79	2.04
Pheochromocytoma, Benign		18	1.06	11	1.28	6.67
Pheochromocytoma, Malignant		3	0.18	1	5.00	5.00
PANCREAS						
	26	1690				
Acinar Cell Adenoma		1	0.06	1	1.28	1.28
Islet Cell, Adenoma		35	2.07	22	0.79	7.69
Islet Cell, Carcinoma		8	0.47	5	2.00	5.00
PITUITARY						
	26	1691				
Adenoma		1052	62.21	26	22.00	82.00
Carcinoma		28	1.66	13	0.79	5.00
THYROID						
	26	1689				
C-Cell, Adenoma		118	6.99	24	2.56	16.00
C-Cell, Carcinoma		29	1.72	16	0.79	12.00
Follicular Cell, Adenoma		3	0.18	3	2.00	2.04
Follicular Cell, Carcinoma		4	0.24	3	0.79	3.33
PARATHYROID						
	26	1681				
Adenoma		8	0.48	6	0.79	3.33
BRAIN						
	26	1691				
Astrocytoma, Benign		4	0.24	3	0.79	3.33
Astrocytoma, Malignant		6	0.35	4	1.67	3.85
Glioma, Malignant		2	0.12	1	2.56	2.56
Granular Cell Tumor, Benign		14	0.83	12	0.79	3.33

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
BRAIN (cont.)						
Meningioma, Benign		1	0.06	1	1.67	1.67
Reticulosis, Malignant		1	0.06	1	2.08	2.08
NERVE						
	26	1691				
Schwannoma, Malignant		1	0.06	1	0.79	0.79
SKELETAL MUSCLE						
	26	1691				
Fibroma		1	0.06	1	1.28	1.28
Leiomyosarcoma		1	0.06	1	1.67	1.67
Sarcoma		1	0.06	1	1.28	1.28
BONE						
	26	1691				
Osteosarcoma		3	0.18	3	0.79	1.28
HEART						
	26	1690				
Schwannoma, Benign		1	0.06	1	0.79	0.79
SPLEEN						
	26	1690				
Mesothelioma, Benign		1	0.06	1	1.67	1.67
THYMUS						
	26	1660				
Thymoma, Benign		4	0.24	4	1.85	2.04
Thymoma, Malignant		1	0.06	1	2.00	2.00
Lymphoma		2	0.12	1	3.33	3.33
LYMPHORETICULAR SYSTEM						
	26	1689				
Lymph Node, Hemangioma		1	0.06	1	1.92	1.92
Lymph Node, Lymphangioma		1	0.06	1	1.69	1.69
Histiocytic Sarcoma		2	0.12	1	4.17	4.17
WHOLE BODY/MULTIPLE ORGAN						
	26	1691				
Lymphoma, Malignant		21	1.24	15	1.28	5.00
Leukemia		2	0.12	2	1.28	1.67

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
WHOLE BODY/MULTIPLE ORGAN						
Histiocytic Sarcoma		14	0.83	10	1.28	3.85
Sarcoma		1	0.06	1	1.28	1.28
Adenocarcinoma		1	0.06	1	0.79	0.79
EYE	26	1690				
Harderian Gland, Adenoma		1	0.06	1	1.67	1.67
Eyelid, Fibrosarcoma		1	0.06	1	2.00	2.00
EAR	26	1691				
Pinna, Fibrosarcoma		1	0.06	1	2.00	2.00
Pinna, Melanoma		1	0.06	1	1.28	1.28
Pinna, Schwannoma, Malignant		1	0.06	1	1.28	1.28
Zymbal's Gland, Carcinoma		3	0.18	3	1.67	1.92

Table 7: Incidence of Neoplasms by Study for Selected Organs/Females

Study Identification	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
LIVER	126	78	78	78	60	60	60	126	78	78	78	50	50	49	50	50	50	50	50	52	52	48	60	60	60	60
Hepatocellular Adenoma	4	1	1	1			1	4	1			4	3	2	3	1	2	1	2		2	1		1	1	1
Hepatocellular Carcinoma	3	1	2	1				1						1						1	1		1			
Bile Duct, Adenoma		1																								1
Histiocytic Sarcoma													1													
PITUITARY	126	78	78	78	60	60	60	126	78	78	78	50	50	49	50	50	50	50	50	52	52	48	60	60	60	60
Adenoma	55	25	34	37	30	29	47	87	58	54	62	36	33	41	41	40	36	15	11	35	36	37	42	45	42	44
Carcinoma	4	3	2		2	3	3	1				1	2							2		1			2	2
THYROID	126	78	78	78	60	60	60	126	78	78	78	50	50	49	50	50	50	50	50	52	52	48	58	60	60	60
C-Cell, Adenoma	4	2	2	5			2	10	8	6	6	8	5	5	5	3	5	6	2	3	9	4	8	6	2	2
C-Cell, Carcinoma	1			1		1	2	2	1	1	3	2			2	1		2	6				1	2		1
Follicular Cell, Adenoma														1			1		1							
Follicular Cell, Carcinoma	1		1			2																				
ADRENAL	126	78	78	78	60	60	60	126	78	78	78	50	50	49	50	50	50	50	50	52	52	48	60	60	60	60
Cortex, Adenoma	3	1	3	2		3	1	1		1	2	3	1	2	2		2				1	3	3	1	1	
Cortex, Carcinoma				1	1		1	1	1					1										1	1	
Pheochromocytoma, Benign		2	1						3	1	2		1	1			1				1		1			4
Pheochromocytoma, Malignant							3																			
PANCREAS	126	78	78	78	60	60	60	126	78	78	78	50	50	49	50	50	50	50	50	52	52	48	60	59	60	60
Acinar Cell Adenoma				1																						
Islet Cell, Adenoma	1	2	1	1	3	3	1	1	1	1	1		1	2	2	1	1	1		3	4	2	1	1		
Islet Cell, Carcinoma									2									1	1							3

