

Compilation of Spontaneous Neoplastic Lesions And Survival in Crl:CD[®](SD) BR Rats From Control Groups

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INTRODUCTION:

In the course of data analysis from a carcinogenicity study, statistical tests will occasionally indicate that the incidence of a particular neoplasm is significantly greater in a treated group than in the concurrent control. Since statistical differences can occur as a matter of chance alone, using a positive statistic difference as the sole or definitive evaluation tool could produce a false positive result (3,7). Alternatively, a slight increase in the incidence of a rare neoplasm would be unlikely to achieve statistical significance by the tests typically employed in toxicology studies. In this type of situation, the use of historical control data could justify the biological significance of even a slight increase in the incidence of an uncommon neoplasm (7).

The histopathology and survival data presented in this publication were gathered from twenty four toxicology studies of approximately 104 weeks duration. All studies were conducted in accordance with Good Laboratory Practice regulations of the US Food and Drug Administration or the Environmental Protection Agency and/or the Standard Operating Procedures of the participating laboratory. All studies were performed in the United States, Canada or Japan by contract laboratories, academic institutions or industrial toxicology facilities. All studies were conducted in support of in-house research or marketing permits. The data presented were provided to us by the individual laboratories or gathered from the published literature.

PURPOSE:

The purpose of this compilation is to offer the study director, reviewing toxicologist and/or study pathologist some reported incidences of neoplasms and survival data in Crl:CD[®](SD)BR rats maintained as control animals throughout their lifetime, approximately 104 weeks. This document was prepared for informational purposes only. Diagnoses of the various neoplasms 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. For these reasons, care should be taken in using these data that are not intended as a substitute for historical data collected within an institution.

COMMON STUDY PARAMETERS:

The 24 studies included in this publication were initiated between 1991 and 1997 at six different industrial or contract testing facilities in the United States, Canada and Japan. All studies used Crl:CD[®](SD)BR rats from Charles River Laboratories. Rats in studies 15-19 were from Crl:CD[®](SD)BR IGS (International Genetic Standard) colonies. IGS is a breeding system that CRL implemented in the mid-1990's to stabilize the degree of genetic diversity represented among colonies of Crl:CD[®](SD)BR rats, both horizontally (among colonies worldwide) and longitudinally (over subsequent generations). Rats from other studies were not reported as having originated from IGS colonies, although it is possible that some were, in fact, being operated using the IGS system. CRL has never received any information to indicate that Crl:CD[®](SD)BR rats have a different tumor profile in the IGS system. Additional information regarding the IGS system and on background data for Crl:CD[®](SD)BR IGS rats is available (9-11).

The rats in these studies were from control groups of dietary, gavage, or subcutaneous dosing studies and were approximately 4-8 weeks of age at study initiation. Dietary study control groups received untreated diet while groups from oral dosing studies received 1.0% polyethelene glycol; 0.5% aqueous methylcellulose; 1.0% aqueous carboxymethylcellulose; or deionized water as the vehicle control. The animals from the subcutaneous dosing study received sterile water for injection (USP).

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 were allowed

free access to tap water and one of the following commercial diets; Purina PMI Certified Rodent Chow 5002 , CR-LPF (Oriental Yeast Co., Ltd., Japan) or CRF-1 (Oriental Yeast Co., Ltd., Japan).

DATA SETS PRESENTED:

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)

The overall incidences of all neoplastic lesions observed in any organ are reported and are summarized in Tables 3 and 4. These data also include neoplastic lesions from rats that died or were found moribund and killed prior to terminal sacrifice, but not from rats that 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 5 and 6). These organs/systems include liver; pituitary; thyroid; adrenal; pancreas; mammary gland; and whole body/multiple organ.

SUMMARY TABLE CALCULATIONS FOR NEOPLASTIC LESIONS:

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 23 for males and 24 for females.

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 that 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. 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, they were 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.

SYNOMYMS FOR NEOPLASTIC LESIONS:

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, shown below in CAPITAL LETTERS. 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

Heart:

ENDOCARDIAL SCHWANNOMA, MALIGNANT = neurilemmoma, malignant, endocardial schwannoma, NOS

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
PHEOCHROMOCYTOMA, BENIGN= medulla neoplasm, benign
PHEOCHROMOCYTOMA, MALIGNANT=medulla neoplasm, malignant

Pancreas:

ISLET CELL, ADENOMA= islet, adenoma; adenoma, not otherwise specified
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

LYMPHOMA, MALIGNANT=Lymphoma, lymphocytic; Leukemia, lymphocytic

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Table 1: Summary of Individual Study Information and Survival/Males-104 Weeks

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12
Study Initiation Date	1994-96*	1994-96*	1992	1994	1996	1992	1992	1993	1992	1994	1996	1996
Total Number on Study	130	115	60	110	54	50	52	50	60	70	70	70
Number Surviving to Termination	56	45	25	25	13	10	13	17	20	12	31	36
% Survival	43.1	39.1	41.7	22.7	24.1	20.0	25.0	34.0	33.3	17.1	44.3	51.4
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104	104	104

Study Identification	13	14	15	16	17	18	19	20	21	22	23
Study Initiation Date	1995	1995	1996	1996	1996	1996	1997	1997	1997	1997	1991
Total Number on Study	70	60	50	50	50	50	60	70	60	60	60
Number Surviving to Termination	19	20	25	26	18	16	30	44	31	22	19
% Survival	27.1	33.3	50.0	52.0	36.0	32.0	50.0	62.9	51.7	36.7	31.7
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104	104

* Studies initiated between 1994 and 1996

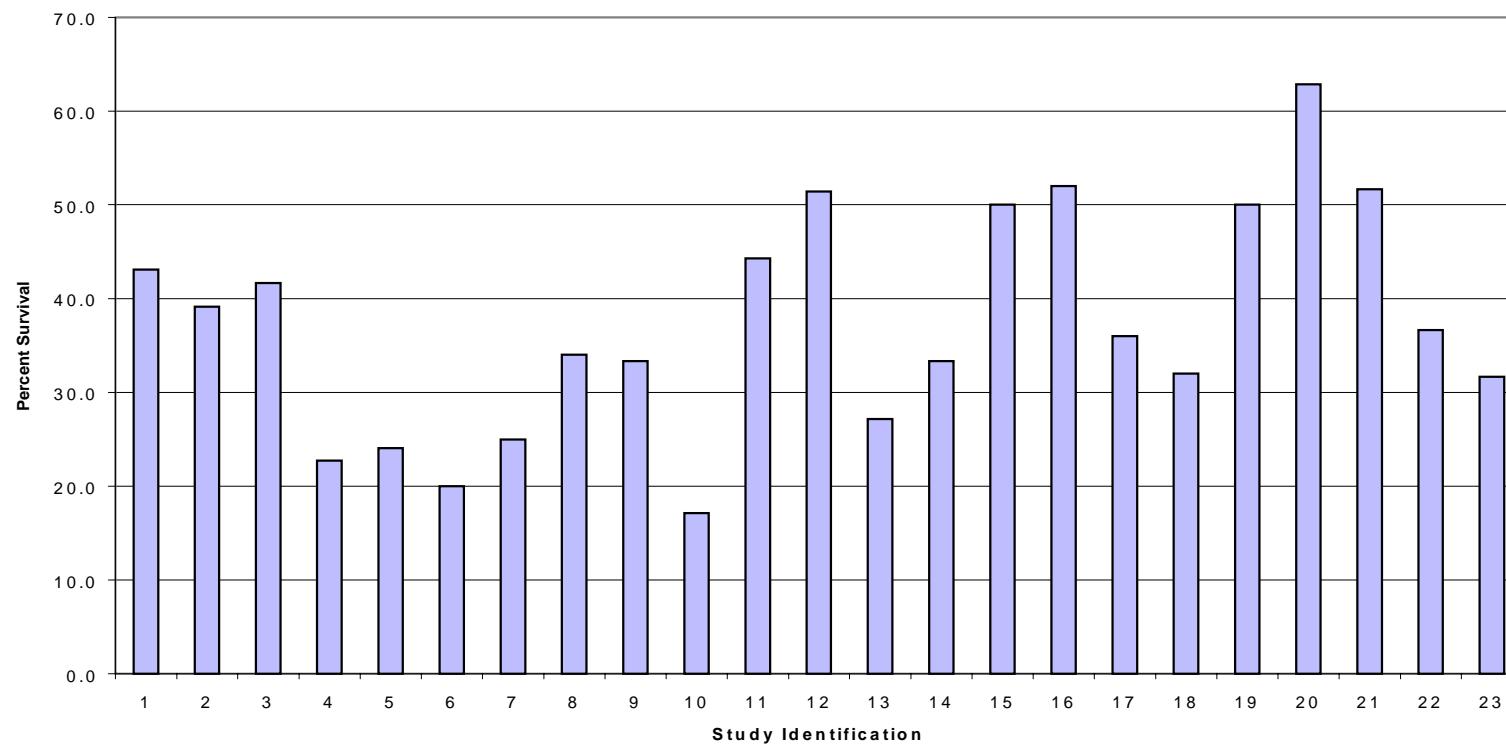
Table 2: Summary of Individual Study Information and Survival/Females-104 Weeks

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12
Study Initiation Date	1994-96*	1994-96*	1992	1994	1996	1992	1992	1993	1992	1994	1996	1996
Total Number on Study	130	115	60	110	54	50	51	49	60	70	70	70
Number Surviving to Termination	44	41	27	41	13	15	15	24	20	14	20	24
% Survival	33.8	35.7	45.0	37.3	24.1	30.0	29.4	49.0	33.3	20.0	28.6	34.3
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104	104	104

Study Identification	13	14	15	16	17	18	19	20	21	22	23	24
Study Initiation Date	1995	1995	1996	1996	1996	1996	1997	1997	1997	1997	1991	1994-96*
Total Number on Study	70	60	50	50	50	50	60	70	60	60	60	200
Number Surviving to Termination	21	17	25	24	19	17	29	43	21	19	27	68
% Survival	30.0	28.3	50.0	48.0	38.0	34.0	48.3	61.4	35.0	31.7	45.0	34.0
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104	104	104

* Studies initiated between 1994 and 1996

Graph 1: Male Survival-104 Weeks



Graph 2: Female Survival-104 Weeks

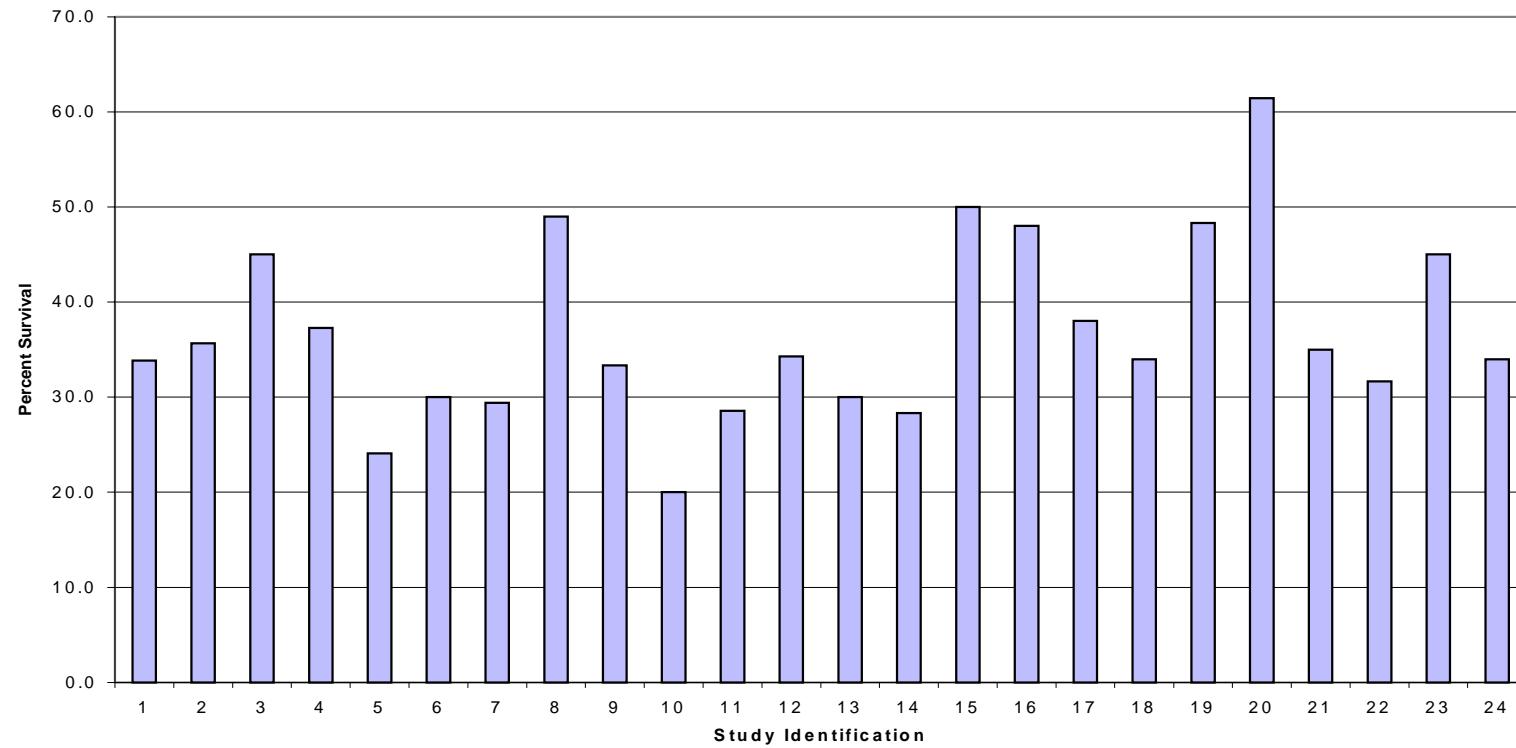


Table 3: Neoplasms/Males-104 Weeks

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
ORAL CAVITY	23	1531				
Fibrosarcoma		1	0.07	1	0.91	0.91
Keratoacanthoma		1	0.07	1	2.00	2.00
Odontoma, Benign		1	0.07	1	1.67	1.67
SALIVARY GLAND	23	1531				
Adenoma		1	0.07	1	1.43	1.43
Mesothelioma		1	0.07	1	1.67	1.67
Schwannoma, Benign		1	0.07	1	1.43	1.43
ESOPHAGUS	23	1531				
Anaplastic Carcinoma		1	0.07	1	0.87	0.87
STOMACH	23	1531				
Adenocarcinoma		1	0.07	1	2.00	2.00
SMALL INTESTINE	23	1531				
Adenocarcinoma		4	0.26	4	1.43	2.00
Leiomyoma		1	0.07	1	1.43	1.43
LARGE INTESTINE/CECUM/ANUS	23	1531				
Adenocarcinoma		1	0.07	1	0.77	0.77
Leiomyoma		1	0.07	1	0.77	0.77
Leiomyosarcoma		1	0.07	1	1.43	1.43
LIVER	23	1531				
Anaplastic Carcinoma		1	0.07	1	0.87	0.87
Hepatocellular Adenoma		37	2.42	17	1.43	8.00
Hepatocellular Carcinoma		32	2.09	16	0.77	6.67
GALL BLADDER	23	1531				
MESENTERY	23	1531				

Table 3: Neoplasms/Males (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
Anaplastic Carcinoma		1	0.07	1	0.87	0.87
Fibroma		1	0.07	1	1.43	1.43
Hemangiosarcoma		1	0.07	1	2.00	2.00
Leiomyosarcoma		1	0.07	1	1.43	1.43
Lipoma		1	0.07	1	0.87	0.87
Liposarcoma		1	0.07	1	1.92	1.92
Mesothelioma		2	0.13	2	0.77	1.43
NASAL CAVITY	23	1531				
Schwannoma, Malignant		1	0.07	1	2.00	2.00
LUNG	23	1531				
Adenoma, Alveolar/Bronchiolar		2	0.13	2	1.43	2.00
Adenocarcinoma, Alveolar/Bronchiolar		2	0.13	2	1.43	2.00
Papilloma		1	0.07	1	1.67	1.67
KIDNEY	23	1531				
Adenoma/Tubular Adenoma		8	0.52	6	1.43	4.00
Adenocarcinoma/Tubular Adenocarcinoma		5	0.33	4	1.67	4.00
Lipoma		10	0.65	10	1.43	2.00
Liposarcoma		3	0.20	3	1.67	2.00
Mesenchymal Tumor, Malignant		4	0.26	3	0.77	1.85
Nephroblastoma, Malignant		1	0.07	1	1.43	1.43
Transitional Cell Carcinoma		1	0.07	1	1.67	1.67
URINARY BLADDER	23	1531				
Anaplastic Carcinoma		1	0.07	1	0.87	0.87
Urothelial Papilloma		4	0.26	3	1.43	3.33
Urothelial Carcinoma		2	0.13	2	1.67	2.00
TESTIS	23	1531				
Granuloma, Spermatic		1	0.07	1	1.67	1.67
Interstitial Cell Tumor, Benign		36	2.35	14	1.43	7.14
Interstitial Cell Tumor, Malignant		5	0.33	3	1.67	3.33
Mesothelioma, Malignant		1	0.07	1	1.43	1.43
Sertoli Cell Tumor, Benign		0	0.00	0	0.00	0.00
SEMINAL VESICLE	23	1531				
Adenoma		1	0.07	1	1.43	1.43

Table 3: Neoplasms/Males (cont'd.)

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
Anaplastic Carcinoma		1	0.07	1	0.87	0.87
PROSTATE	23	1531				
Adenoma		6	0.39	5	1.67	3.33
PREPUTIAL GLAND	23	1531				
Adenoma		1	0.07	1	1.67	1.67
Squamous Cell Carcinoma		2	0.13	2	0.77	1.85
EPIDIDYMYIS	23	1531				
Leiomyosarcoma		1	0.07	1	1.67	1.67
SKIN	23	1531				
Basal Cell Tumor, Benign		8	0.52	6	0.77	4.00
Basal Cell Carcinoma		6	0.39	5	0.77	1.82
Fibroma		67	4.38	20	1.67	10.77
Squamous Cell Carcinoma		8	0.52	6	0.91	4.00
Fibrosarcoma		24	1.57	14	0.87	5.00
Hemangioma		3	0.20	1	5.77	5.77
Hemangiosarcoma		2	0.13	2	1.43	2.00
Keratoacanthoma		35	2.29	14	1.43	10.00
Lipoma		38	2.48	15	0.91	6.96
Liposarcoma		2	0.13	2	1.43	2.00
Myxoma		3	0.20	3	1.67	2.00
Myxosarcoma		2	0.13	2	0.77	1.43
Neurofibrosarcoma		1	0.07	1	0.77	0.77
Osteosarcoma		1	0.07	1	1.67	1.67
Pilomatrixoma, Benign		5	0.33	5	0.87	1.85
Rhabdomyosarcoma		2	0.13	2	0.77	1.43
Schwannoma, Malignant		5	0.33	5	1.43	2.00
Sebaceous Gland Adenoma		12	0.78	6	0.87	4.62
Squamous Cell Papilloma		26	1.70	13	0.87	6.00
Trichoepithelioma, Benign		6	0.39	4	1.43	4.29
Trichofolliculoma, Benign		1	0.07	1	1.85	1.85
MAMMARY GLAND	23	1531				
Adenoma		4	0.26	4	0.87	2.00
Adenocarcinoma		7	0.46	5	0.87	3.33
Fibroma		3	0.20	2	1.54	1.67
Fibroadenoma		15	0.98	8	1.67	5.77

Table 3: Neoplasms/Males (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
Fibrosarcoma		1	0.07	1	2.00	2.00
Lipoma		1	0.07	1	2.00	2.00
ADRENAL	23	1531				
Cortex, Adenoma		36	2.35	17	0.91	8.00
Cortex, Carcinoma		10	0.65	10	0.77	2.00
Pheochromocytoma, Benign		181	11.82	22	1.43	22.86
Pheochromocytoma, Malignant		25	1.63	14	1.43	5.00
PANCREAS	23	1531				
Acinar Cell, Adenoma		22	1.44	9	1.43	11.43
Acinar Cell, Carcinoma		7	0.46	6	0.87	3.33
Islet Cell, Adenoma		106	6.92	15	1.67	25.71
Islet Cell, Carcinoma		47	3.07	13	0.77	14.00
Mixed Adenoma		1	0.07	1	0.87	0.87
PITUITARY	23	1531				
Adenoma		714	46.64	23	0.77	70.00
Carcinoma		42	2.74	9	0.77	36.00
Craniopharyngioma		1	0.07	1	1.67	1.67
Ganglioneuroma		1	0.07	1	0.77	0.77
Granular Cell Tumor, Malignant		1	0.07	1	1.43	1.43
THYROID	23	1531				
C-Cell, Adenoma		120	7.84	21	1.43	14.29
C-Cell, Carcinoma		21	1.37	11	1.43	14.81
Follicular Cell, Adenoma		41	2.68	15	1.67	12.00
Follicular Cell, Carcinoma		15	0.98	10	0.87	3.85
PARATHYROID	23	1531				
Adenoma		32	2.09	13	0.77	8.33
BRAIN	23	1531				
Astrocytoma, Malignant		13	0.85	8	0.87	3.33
Ependymoma		1	0.07	1	1.43	1.43
Glioma, Malignant		3	0.20	3	0.91	1.92
Granular Cell Tumor, Benign		6	0.39	6	0.91	2.00
Granular Cell Tumor, Malignant		4	0.26	3	1.43	2.86
Hemangiosarcoma		1	0.07	1	1.92	1.92

Table 3: Neoplasms/Males (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
Meningeal Sarcoma		1	0.07	1	0.87	0.87
Oligodendroglioma		2	0.13	2	1.43	2.00
SPINAL CORD	23	1531				
Astrocytoma, Malignant		1	0.07	1	0.77	0.77
PERIPHERAL NERVE	23	1531				
SKELETAL MUSCLE	23	1531				
Fibroma		1	0.07	1	2.00	2.00
Hemangiosarcoma		1	0.07	1	1.67	1.67
Rhabdomyosarcoma		3	0.20	3	1.43	2.00
Sarcoma		1	0.07	1	2.00	2.00
BONE	23	1531				
Chondrosarcoma		3	0.20	3	0.87	2.00
Hemangiosarcoma		1	0.07	1	2.00	2.00
Osteoma, Benign		2	0.13	2	1.43	2.00
Osteosarcoma		1	0.07	1	1.67	1.67
HEART	23	1531				
Endocardial Schwannoma, Malignant		2	0.14	2	0.77	1.67
Mediastinal Tissue Mesothelioma, Malignant		4	0.26	4	0.91	1.85
BLOOD VESSEL	23	1531				
BONE MARROW	23	1531				
Lymphoma, Malignant		1	0.07	1	1.67	1.67
SPLEEN	23	1531				
Fibrosarcoma		1	0.07	1	0.77	0.77
Liposarcoma		2	0.13	2	1.43	1.67
THYMUS	23	1531				
Thymoma, Malignant		3	0.20	3	0.77	2.00

Table 3: Neoplasms/Males (cont'd.)

		TOTAL		# STUDIES		
		# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	# STUDIES	# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
LYMPH NODES	23	1531				
Hemangioma		2	0.13	2	1.67	2.00
Hemangiosarcoma		4	0.26	2	1.85	4.29
WHOLE BODY/MULTIPLE ORGAN	23	1531				
Hemangioma		3	0.20	2	0.77	3.33
Hemangiosarcoma		1	0.07	1	1.67	1.67
Histiocytic Sarcoma		31	2.02	15	0.77	6.00
Leukemia, Granulocytic		8	0.52	7	1.43	2.86
Leukemia, Mononuclear Cell		1	0.07	1	2.00	2.00
Lymphoma, Malignant		25	1.63	12	0.91	6.00
EYE	23	1531				
Amelanotic Melanoma, Benign		1	0.07	1	1.92	1.92
Harderian Gland, Adenoma		1	0.07	1	2.00	2.00
Harderian Gland, Adenocarcinoma		1	0.07	1	1.92	1.92
Lacrimal Gland, Hemangioma		1	0.07	1	1.67	1.67
Leiomyosarcoma		1	0.07	1	1.67	1.67
EAR	23	1531				
Melanoma, Malignant		1	0.07	1	1.67	1.67
Neural Crest Tumor		1	0.07	1	2.00	2.00
Pinna, Papilloma		1	0.07	1	1.43	1.43
Zymbal's Gland, Adenoma		2	0.13	2	1.67	2.00
Zymbal's Gland, Carcinoma		12	0.78	9	0.77	4.00

Table 4: Neoplasms/Females-104 Weeks

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
ORAL CAVITY	24	1729				
Squamous Cell Papilloma		1	0.06	1	0.87	0.87
Squamous Cell Carcinoma		4	0.23	3	1.00	2.00
Tongue, Granular Cell Tumor, Benign		1	0.06	1	2.00	2.00
Tooth, Ameloblastoma, Malignant		1	0.06	1	2.00	2.00
SALIVARY GLAND	24	1729				
Adenocarcinoma		1	0.06	1	2.00	2.00
ESOPHAGUS	24	1729				
STOMACH	24	1729				
Nonglandular Mucosa/Squamous Cell Papilloma		2	0.12	2	1.67	1.67
Teratocarcinoma		1	0.06	1	2.00	2.00
SMALL INTESTINE	24	1729				
Leiomyoma		1	0.06	1	2.00	2.00
Leiomyosarcoma		4	0.23	3	0.87	2.00
LARGE INTESTINE/CECUM/ANUS	24	1729				
Leiomyosarcoma		1	0.06	1	1.67	1.67
Lipoma		2	0.12	2	1.43	1.85
LIVER	24	1729				
Bile Duct Adenoma		7	0.40	5	1.43	6.12
Hemangiosarcoma		1	0.06	1	0.50	0.50
Hepatocellular Adenoma		35	2.02	13	0.77	13.33
Hepatocellular Carcinoma		7	0.40	7	0.77	1.67
Histiocytic Sarcoma		2	0.12	1	1.00	1.00
Lymphosarcoma		1	0.06	1	0.50	0.50
GALL BLADDER	24	1729				

Table 4: Neoplasms/Females (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
MESENTERY	24	1729				
Fibrosarcoma		2	0.12	2	0.91	1.43
NASAL CAVITY	24	1729				
LUNG	24	1729				
Adenoma, Alveolar/Bronchiolar		3	0.17	3	0.77	1.43
Adenocarcinoma, Alveolar/Bronchiolar		2	0.12	2	0.77	1.43
Leiomyoma		1	0.06	1	1.43	1.43
Mesothelioma		1	0.06	1	0.77	0.77
KIDNEY	24	1729				
Adenocarcinoma/Tubular Adenocarcinoma		2	0.12	2	0.77	1.85
Lipoma		3	0.17	3	0.50	1.67
Liposarcoma		5	0.29	5	0.77	1.85
Transitional Cell Carcinoma		2	0.12	2	0.50	2.00
URINARY BLADDER	24	1729				
Leiomyosarcoma		1	0.06	1	1.43	1.43
Transitional Cell Carcinoma		1	0.06	1	1.67	1.67
Urothelial Papilloma		2	0.12	2	1.43	1.67
Urothelial Carcinoma		1	0.06	1	2.00	2.00
OVARY	24	1729				
Cystadenocarcinoma		1	0.06	1	2.00	2.00
Granulosa Cell Tumor, Benign		1	0.06	1	1.67	1.67
Granulosa Cell Tumor, Malignant		2	0.12	2	1.67	2.00
Papilloma		1	0.06	1	1.67	1.67
Sertoli Cell Tumor, Benign		2	0.12	2	1.85	1.96
Thecal Cell Tumor, Benign		3	0.17	3	1.43	2.00
Thecal Cell Tumor, Malignant		3	0.17	3	0.87	1.85
CERVIX	24	1729				
Fibroma		1	0.06	1	0.50	0.50
Granular Cell Tumor, Benign		2	0.12	2	1.43	1.43
Polyps		2	0.12	1	1.00	1.00
Stromal Sarcoma		4	0.23	4	0.77	1.43

Table 4: Neoplasms/Females (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
VAGINA	24	1729				
Granular Cell Tumor, Benign		3	0.17	2	1.43	3.33
Granular Cell Tumor, Malignant		1	0.06	1	1.43	1.43
Leiomyoma		1	0.06	1	2.00	2.00
Leiomyosarcoma		1	0.06	1	1.85	1.85
Schwannoma, Malignant		2	0.12	1	3.33	3.33
Stromal Sarcoma		2	0.12	2	0.87	2.04
Squamous Cell Papilloma		3	0.17	3	0.87	1.67
Squamous Cell Carcinoma		1	0.06	1	1.43	1.43
CLITORAL GLAND	24	1729				
Adenoma		2	0.12	1	3.33	3.33
UTERUS	24	1729				
Adenoma		1	0.06	1	1.85	1.85
Adenocarcinoma		1	0.06	1	1.67	1.67
Endometrial Stromal Polyp		41	2.37	16	0.91	11.67
Endometrial Carcinoma		3	0.17	3	0.77	2.00
Fibrosarcoma/Stromal Sarcoma		15	0.87	7	1.43	18.00
Granular Cell Tumor, Benign		1	0.06	1	2.00	2.00
Hemangioma		30	1.74	6	1.43	15.00
Leiomyoma		6	0.35	6	0.87	2.00
Leiomysarcoma		1	0.06	1	1.43	1.43
Schwannoma, Malignant		1	0.06	1	1.67	1.67
Squamous Cell Carcinoma		1	0.06	1	0.77	0.77
MAMMARY GLAND	24	1729				
Adenoma		145	8.39	20	1.67	32.00
Adenocarcinoma		410	23.71	22	8.57	58.33
Carcinosarcoma		6	0.35	3	1.67	5.00
Fibroma		8	0.46	2	1.43	5.38
Fibroadenoma		711	41.12	24	13.33	61.22
Fibrosarcoma		3	0.17	2	1.54	1.67
Lipoma/Adenolipoma		5	0.29	2	2.00	3.08
Neurofibrosarcoma		2	0.12	2	0.77	1.85
SKIN	24	1729				
Basal Cell Tumor, Benign		2	0.12	2	1.43	1.67
Chondrosarcoma		1	0.06	1	2.00	2.00
Fibroma		10	0.58	7	0.91	3.33

Table 4: Neoplasms/Females (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
Fibrosarcoma		4	0.23	4	1.43	2.00
Hemangioma		17	0.98	5	1.67	6.67
Hemangiosarcoma		8	0.46	6	1.00	2.04
Keratoacanthoma		6	0.35	5	1.43	2.86
Lipoma		16	0.93	10	0.91	7.14
Myxoma		2	0.12	2	0.87	1.67
Myxosarcoma		10	0.58	4	0.91	5.22
Pilomatrixoma, Benign		1	0.06	1	0.50	0.50
Rhabdomyosarcoma		1	0.06	1	2.00	2.00
Schwannoma, Benign		1	0.06	1	2.00	2.00
Schwannoma, Malignant		2	0.12	2	1.67	2.00
Sebaceous Gland Adenocarcinoma		1	0.06	1	1.43	1.43
Squamous Cell Papilloma		2	0.12	2	1.43	1.67
Squamous Cell Carcinoma		2	0.12	2	1.67	2.00
ADRENAL	24	1729				
Cortex, Adenoma		64	3.70	19	1.43	34.00
Cortex, Carcinoma		12	0.69	8	0.91	4.29
Pheochromocytoma, Benign		37	2.14	15	1.43	10.00
Pheochromocytoma, Malignant		13	0.75	7	1.43	8.33
PANCREAS	24	1729				
Acinar Cell, Adenoma		3	0.17	2	1.96	3.33
Acinar Cell, Carcinoma		1	0.06	1	1.96	1.96
Islet Cell, Adenoma		59	3.41	18	1.43	14.29
Islet Cell, Carcinoma		19	1.10	11	0.77	4.29
Leiomyosarcoma		1	0.06	1	0.77	0.77
PITUITARY	24	1729				
Adenoma		1206	69.75	24	26.00	92.00
Carcinoma		117	6.77	18	1.43	58.00
Ganglioneuroma		1	0.06	1	0.77	0.77
THYROID	24	1729				
C-Cell, Adenoma		124	7.17	23	2.86	16.67
C-Cell, Carcinoma		8	0.46	6	0.77	4.00
Follicular Cell, Adenoma		20	1.16	13	1.43	6.12
Follicular Cell, Carcinoma		10	0.58	7	0.87	3.33
Ganglioneuroma		1	0.06	1	1.43	1.43

Table 4: Neoplasms/Females (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
PARATHYROID	24	1729				
Adenoma		23	1.33	12	1.00	4.35
BRAIN	24	1729				
Astrocytoma, Benign		1	0.06	1	2.04	2.04
Astrocytoma, Malignant		9	0.52	4	1.67	2.31
Ganglioneuroma, Benign		1	0.06	1	1.67	1.67
Glioma, Malignant		1	0.06	1	1.43	1.43
Granular Cell Tumor, Benign		5	0.29	4	1.00	2.00
Granular Cell Tumor, Malignant		2	0.12	2	1.43	1.67
Meningeal Sarcoma		1	0.06	1	2.00	2.00
Oliodendrogioma, Malignant		2	0.12	2	0.50	2.00
SPINAL CORD	24	1729				
PERIPHERAL NERVE	24	1729				
SKELETAL MUSCLE	24	1729				
Rhabdomyosarcoma		1	0.06	1	1.67	1.67
BONE	24	1729				
HEART	24	1729				
Endocardial Schwannoma, Malignant		4	0.23	1	3.08	3.08
BLOOD VESSEL	24	1729				
BONE MARROW	24	1729				
Histiocytic Sarcoma		1	0.06	1	0.50	0.50
SPLEEN	24	1729				
Hemangiosarcoma		1	0.06	1	1.43	1.43
Lymphosarcoma		1	0.06	1	0.50	0.50

Table 4: Neoplasms/Females (cont'd.)

		TOTAL		# STUDIES		
LOCATION AND TUMOR	# STUDIES	# ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
		# LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
THYMUS	24	1729				
Lymphoma, Malignant		1	0.06	1	2.00	2.00
Thymoma, Benign		5	0.29	4	0.50	2.86
Thymoma, Malignant		5	0.29	4	0.77	1.67
LYMPH NODES	24	1729				
Hemangiosarcoma		2	0.12	2	1.67	1.85
Lymphoma, Malignant		1	0.06	1	1.43	1.43
WHOLE BODY/MULTIPLE ORGAN	24	1729				
Hemangiosarcoma		1	0.06	1	1.43	1.43
Histiocytic Sarcoma		18	1.04	11	1.67	3.08
Leukemia, Granulocytic		4	0.23	2	1.43	2.73
Leukemia, Mononuclear Cell		1	0.06	1	0.91	0.91
Lymphoma, Malignant		26	1.51	13	1.43	10.00
EYE	24	1729				
Amelanotic Melanoma, Benign		1	0.06	1	1.67	1.67
Fibroma		2	0.12	2	1.43	1.43
Squamous Cell Carcinoma		1	0.06	1	1.43	1.43
EAR	24	1729				
Pinna, Papilloma		1	0.06	1	1.43	1.43
Zymbal's Gland, Carcinoma		5	0.29	5	1.43	2.00

Table 5: Incidence of Neoplasms by Study for Selected Organs/Males

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
LIVER	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	
Anaplastic Carcinoma		1																						
Hepatocellular Adenoma	5				1	1				3	1	2	2	2	1	1	4	3	3	4	1	1	2	
Hepatocellular Carcinoma	1	1	1	3	1	1	1	1	4	4	3	1	3	2				3		2				
PITUITARY	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	
Adenoma	1	58	28	37	34	30	22	32	38	34	36	34	49	40	25	23	14	21	29	27	36	37	29	
Carcinoma	1		1									2			1	2	18	13	3		1			
Craniopharyngioma																							1	
Ganglioneuroma	1																							
Granular Cell Tumor, Malignant											1													
THYROID	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	
C-Cell, Adenoma	13	12	3	11		3	6		5	1	9	10	9	1	1	3	5	3	3	6	5	6	5	
C-Cell, Carcinoma				2	8	1	1			1	1		1					1	1			2	2	
Follicular Cell, Adenoma	3	2	2	4	1	6	2	6	1					4			1	2		3	1	3		
Follicular Cell, Carcinoma	3	1	1	1	2	1	2					2			1	1								
ADRENAL	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	
Cortex, Adenoma	5		1	1	2	1	2	4	1		3	2		1		2	3	1	4		2		1	
Cortex, Carcinoma	1			1		1	1	1			1	1		1					1					
Medulla Neoplasm, Benign	18	18	7	11	6	6	9	7	8	8	13	16	10	8	5	9	4	7	8	1	4	4	1	
Medulla Neoplasm, Malignant			1	5		1	2		1	2	1	1	2	2			2	1	3		1		1	

Table 5: Incidence of Neoplasms by Study for Selected Organs/Males (cont'd)

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
PANCREAS	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	60	70	60	60	60
Acinar Cell, Adenoma									3		2	8	1		1	3		1	2					1
Acinar Cell, Carcinoma			1													1	1				1	1	2	
Islet Cell, Adenoma	8	20	1	6	3				2	2	16	18	7	2	8	5	4	4						
Islet Cell, Carcinoma	1		1	1	3				1	1	9	9	7	2	4	7		1						
Mixed Adenoma			1																					
MAMMARY GLAND	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	60
Adenoma			1														1						1	1
Adenocarcinoma	2	1		1							1													2
Fibroma	2																				1			
Fibroadenoma	3	2			1		3		1	2		2								1				
Fibrosarcoma						1																		
Lipoma						1																		
WHOLE BODY/MULTIPLE ORGAN	130	115	60	110	54	50	52	50	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	60
Hemangioma	1															2								
Hemangiosarcoma																							1	
Histiocytic Sarcoma	1	4		4	2				3	2	3	2	1	1	2	1	1	3					1	
Leukemia, Granulocytic								1		1	1		2		1	1		1						
Leukemia, Mononuclear Cell																		1						
Lymphoma, Malignant	4		1	1	3	3			3		4		2	1	1	1					1			

Table 6: Incidence of Neoplasms by Study for Selected Organs/Females

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
LIVER	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Bile Duct Adenoma			1					3	1		1											1		
Hemangiosarcoma																								1
Hepatocellular Adenoma	1			3	1				8	2	1		2	2	3	3			1		1			7
Hepatocellular Carcinoma	1	1							1	1	1	1							1					
Histiocytic Sarcoma																								2
Lymphosarcoma																								1
PITUITARY	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Adenoma	97	83	40	46	41	46	39	43	43	49	52	53	60	47	30	34	13	16	41	39	47	49	38	160
Carcinoma	3		2	3	1				3	1	1	7	4	3	11	8	26	29	8		2		1	4
Ganglioneuroma	1																							
THYROID	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
C-Cell, Adenoma	9	8	7	8	9	4	3		5	4	7	8	2	2	3	2	5	2	2	4	5	6	5	14
C-Cell, Carcinoma	1	1		1		2				1														2
Follicular Cell, Adenoma	2	2	1	2	1		1	3		1		1		1	1							1		3
Follicular Cell, Carcinoma		1	2	1	1											1						1		3
Ganglioneuroma										1														
ADRENAL	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Cortex, Adenoma	3	2	1		1			16	1	2	2	1		1	1	1	17	3	2	1	3	1		5
Cortex, Carcinoma		2		1	1			2			1	3			1			1						
Pheochromocytoma, Benign	2	4	1		2	2	2	2		1	3	4		6		1	2					2		3
Pheochromocytoma, Malignant					2	2	1		5			1									1	1		

Table 6: Incidence of Neoplasms by Study for Selected Organs/Females (cont'd)

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
PANCREAS	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Acinar Cell, Adenoma								1											2					
Acinar Cell, Carcinoma								1																
Islet Cell, Adenoma	3	6	1		3		2	4	1	1	6	10	4		1	3		1	1	1		2		9
Islet Cell, Carcinoma	1		1				1			1	2	3	1	2		2			1					4
Leiomyosarcoma	1																							
MAMMARY GLAND	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Adenoma	22	10	1			1	1			2	2	2	4	1	16	16	8	8	9	6	4	2	1	29
Adenocarcinoma	37	11	12	19	17	13	15	14	35	6	32	33	21	22			11	15	18	6	14	8	10	41
Carcinosarcoma			1				2		3															
Fibroma	7													1										
Fibroadenoma	74	58	17	40	27	23	22	30	8	36	33	37	32	18	21	18	23	23	22	14	26	12	17	80
Fibrosarcoma	2								1															
Lipoma/Adenolipoma	4						1																	
Neurofibrosarcoma	1				1																			
WHOLE BODY/MULTIPLE ORGAN	130	115	60	110	54	50	51	49	60	70	70	70	70	60	50	50	50	50	60	70	60	60	60	200
Hemangiosarcoma																								1
Histiocytic Sarcoma	4		1	3	1				1		2	2			1	1		1	1					
Leukemia, Granulocytic					3																			1
Leukemia, Mononuclear Cell					1																			
Lymphoma, Malignant			2			5		1	3	2	2	4	1	2	1		1		1					1

