

Spontaneous Neoplastic Lesions in the Crl:CD1 (ICR) Mouse in Control Groups from 18 Month to 2 Year Studies

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INTRODUCTION

The data presented in these tables was gathered from 1800 animals (900 males and 900 females) from 14 toxicology studies of at least 78 weeks duration. 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 Crl:CD1 (ICR) mice, maintained as control animals, in studies of 78-104 weeks duration. Diagnoses in this compilation 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 variant of the lesion.

COMMON STUDY PARAMETERS

The 14 studies included in this publication were initiated between 2002 and 2006 in five different laboratories. All studies used male and female Crl:CD1 (ICR) mice from Charles River Laboratories production sites.

The mice in these studies were from control groups of dietary, dermal or gavage studies and were approximately 4-7 weeks of age at study initiation. Some groups were untreated while others received the study vehicle, all served as control groups.

The mice included in this publication were generally housed in pairs or groups in hanging wire mesh cages, fed a standard laboratory diet such as Purina 5002 Certified Rodent Chow and had free access to water. Animals in the dermal study were singly housed. 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 over a period of several years, there was some variation in environmental conditions. 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. Information on the health monitoring, other than that associated with pathological examination conducted in accordance with scheduled or moribund sacrifices, was not available.

DATA SETS PRESENTED

Survival data are presented by study as the actual number surviving to terminal sacrifice and as a percent survival at terminal sacrifice (Tables 1 and 2). The survival data are also presented in graphic form (Graphs 1 and 2). Survival data were not available for all studies at the time of publication. Only those studies for which data were available are represented on the graphs.

The overall incidences of all neoplastic lesions observed in any organ are reported and summarized by sex in Tables 3 and 4. These data also include neoplastic lesions from mice that died or were found moribund and killed prior to terminal sacrifice. It does

not include information from mice that were killed at any interim sacrifice or mice that were part of any satellite groups such as metabolism subgroups. 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, lung and whole body/multiple organ.

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 publication, the number of studies is 14 for males and 14 for females. It is important for the reader to realize that occasionally a specific tissue/organ was not examined in a particular study.

Total Number of Organs (Total # Organs)

This number represents the sum of the total number of tissues or organs examined in all of the control groups from all studies combined. Widespread tumors which showed involvement of multiple organs were listed on the basis of the 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 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 a specific organ in all studies examined.

Percent of Total

These values represent the particular 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 value 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.

ADDITIONAL INFORMATION

If additional information is desired regarding the conduct of these studies or the incidence of a particular neoplasm, please contact Mary Giknis through Charles River Technical Support Services (800.338.9680), or via e-mail at MLAGIKNIS@verizon.net. We will gladly provide assistance if we are able.

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. 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 outlined in International Classification of Rodent Tumors: The Mouse, as recommended by the Society of Toxicologic Pathologists (6).

Adrenal:

Subcapsular Adenoma = Subcapsular Tumor

Cortex, Adenoma = Cortical Adenoma

Cortex, Carcinoma = Cortical Carcinoma

Gall Bladder:

Adenoma = Papilloma/Papillary Adenoma

Lung:

Bronchiolo-alveolar Adenoma = Pulmonary Adenoma

Bronchiolo-alveolar Carcinoma = Pulmonary Carcinoma

Whole Body/Multiple Organ:

Lymphoma, Malignant = Follicular Center Cell Lymphoma, Lymphocytic Lymphoma, Lymphoblastic Lymphoma, Granular Lymphoblastic Leukemia, Malignant Lymphoma

ABBREVIATIONS

NA = Not available at the time of publication.

ACKNOWLEDGEMENTS

Our special thanks to Joe Frank, Pat Mirley and all of the contributing laboratories without whose help this publication would not have been possible.

REQUEST FOR DATA

The purpose of these publications is to assist you, our clients, in evaluating your data. Our aim is to provide you with the data that you need to do your job well. We welcome any suggestions that you may have to improve this document as well as suggested topics for future documents. However, please realize that the publication is only as good as the data. To this end we invite you to participate in and support this worthwhile project by sending us your control data. If you or someone at your laboratory is willing to participate, please contact Mary Giknis through Charles River Laboratories, 251 Ballardvale Street, Wilmington, MA 01887 or at MLAGIKNIS@verizon.net.

REFERENCES

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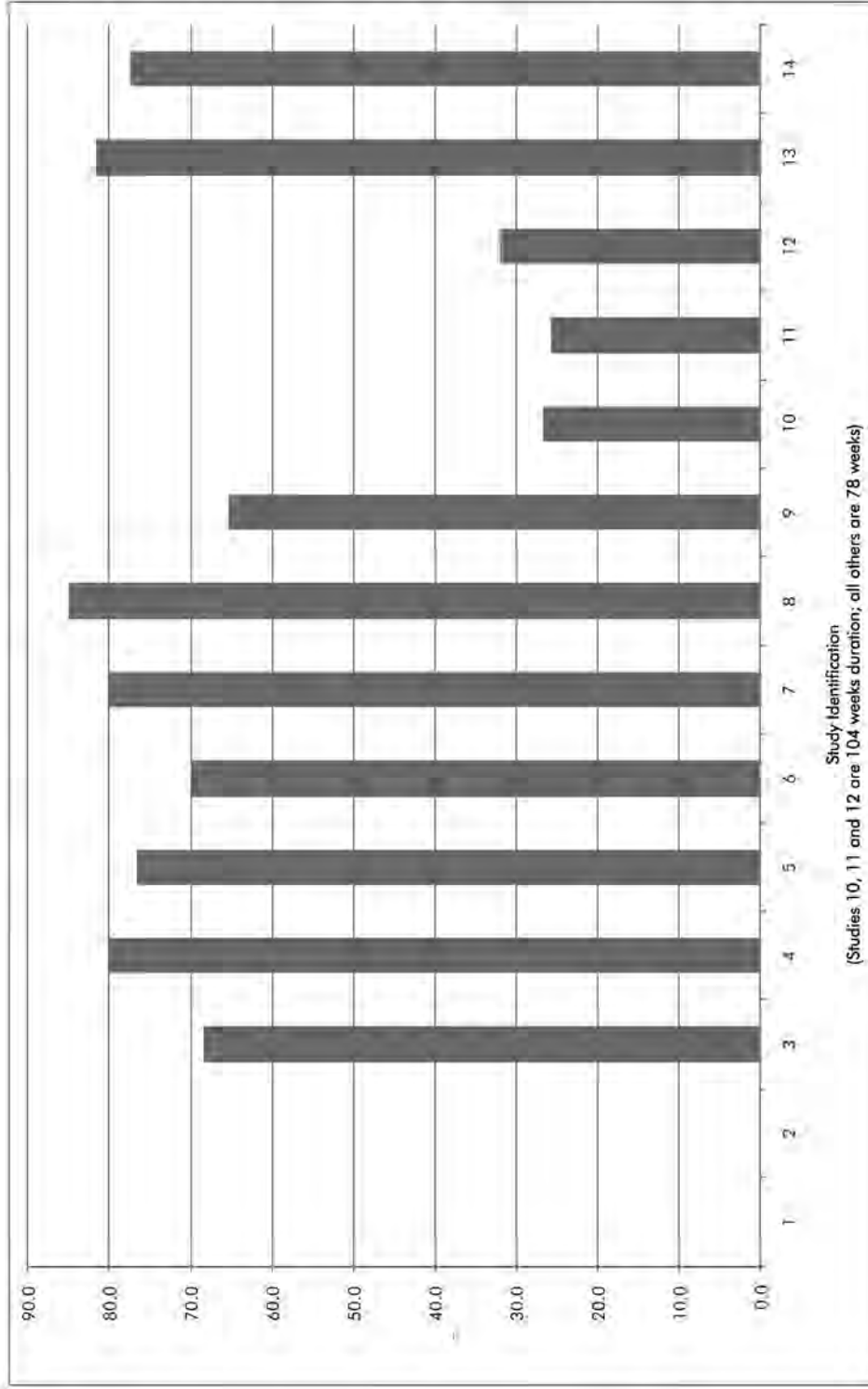
Table 1: Summary of Individual Study Information and Survival/Males

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Study Initiation Date	2002	2003	2003	2003	2004	2004	2004	2004	2005	2005	2005	2005	2006	2006
Total Number on Study	110	50	60	60	60	60	50	60	75	60	70	50	60	75
Number Surviving to Termination	NA	NA	41	48	46	42	40	51	49	16	18	16	49	58
% Survival	NA	NA	68.33	80.00	76.67	70.00	80.00	85.00	65.33	26.67	25.71	32.00	81.67	77.33
Study Duration in Weeks	104	104	78	78	78	78	78	78	96	104	104	104	78	78

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

Study Identification	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Study Initiation Date	2002	2003	2003	2003	2004	2004	2004	2004	2005	2005	2005	2005	2006	2006
Total Number on Study	110	50	60	60	60	60	50	60	75	60	70	50	60	75
Number Surviving to Termination	NA	NA	43	50	47	45	41	44	44	20	21	17	49	61
% Survival	NA	NA	71.67	83.33	78.33	75.00	82.00	73.33	58.67	33.33	30.00	34.00	81.67	81.33
Study Duration in Weeks	104	104	78	78	78	78	78	78	96	104	104	104	78	78

Graph 1: Male Survival



Graph 2: Female Survival

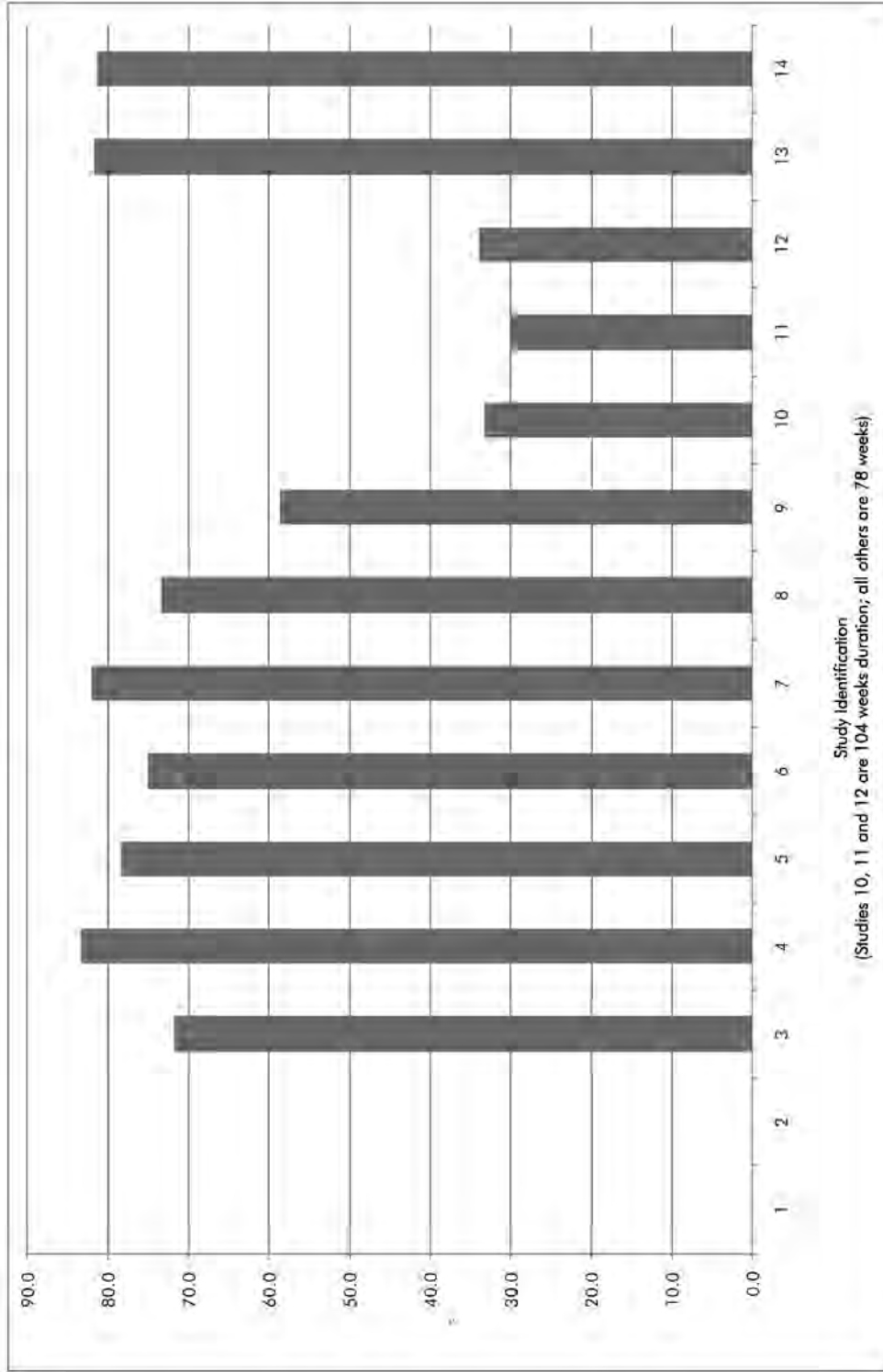


Table 3: Neoplasms/Males

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
ORAL CAVITY	14	900				
SALIVARY GLAND	14	900				
ESOPHAGUS	14	900				
MESENTERY	14	900				
STOMACH	14	900				
SMALL INTESTINE	14	900				
LARGE INTESTINE/CECUM/ANUS	14	900				
Adenocarcinoma		1	0.11	1	2.00	2.00
Leiomyosarcoma		2	0.22	2	1.43	1.67
LIVER	14	900				
Hepatocellular Adenoma		75	8.33	14	1.43	20.00
Hepatocellular Carcinoma		32	3.56	11	1.67	15.00
Hemangioma		4	0.44	4	1.33	2.00
Hemangiosarcoma		2	0.22	2	1.33	1.67
Cholangioma		1	0.11	1	1.67	1.67
GALL BLADDER	14	900				
Adenoma		1	0.11	1	1.67	1.67
NASAL CAVITY	14	900				
DIAPHRAGM	14	900				
LUNG	14	900				
Bronchiolo-alveolar Adenoma		123	13.67	12	8.00	38.00
Bronchiolo-alveolar Carcinoma		52	5.78	12	1.43	20.00
KIDNEY	14	900				
Adenoma		2	0.22	2	1.33	2.00
Carcinoma		1	0.11	1	1.33	1.33

Table 3: Neoplasms/Males (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
URINARY BLADDER	14	900				
PENIS	14	900				
Mixed Malignant Tumor		1	0.11	1	2.00	2.00
PREPUTIAL GLAND	14	899				
Adenoma		1	0.11	1	2.04	2.04
Squamous Cell Carcinoma		1	0.11	1	2.04	2.04
TESTIS	14	900				
Interstitial Cell Adenoma		3	0.33	2	1.43	4.00
SEMINAL VESICLE	14	897				
Granular Cell Tumor		1	0.11	1	2.13	2.13
Adenoma		1	0.11	1	2.13	2.13
PROSTATE	14	900				
Adenoma		1	0.11	1	1.67	1.67
Adenocarcinoma		2	0.22	2	1.33	2.00
EPIDIDYMIS	14	900				
Hemangiopericytoma		1	0.11	1	1.67	1.67
MAMMARY GLAND	14	900				
Carcinoma		2	0.22	2	1.33	1.67
SKIN	14	900				
Fibroma		1	0.11	1	2.00	2.00
Sebaceous Cell Adenoma		4	0.44	3	1.67	4.00
Basal Cell Adenoma		5	0.56	5	1.33	1.67
Basal Cell Carcinoma		3	0.33	3	1.67	1.67
Squamous Cell Papilloma		22	2.44	7	1.67	10.00
Squamous Cell Carcinoma		2	0.22	2	1.43	2.00
Trichoepithelioma		4	0.44	3	1.33	3.33
ADRENAL	14	897				
Subcapsular Tumor		5	0.56	1	10.64	10.64
Cortex, Adenoma		19	2.12	8	1.43	5.00
Cortex, Carcinoma		1	0.11	1	1.33	1.33
Pheochromocytoma, Benign		1	0.11	1	1.33	1.33
Pheochromocytoma, Malignant		1	0.11	1	1.67	1.67

Table 3: Neoplasms/Males (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
PANCREAS	14	897				
Islet Cell, Adenoma		1	0.11	1	2.13	2.13
PITUITARY	14	900				
Adenoma		1	0.11	1	1.67	1.67
THYROID	14	900				
Follicular Cell, Adenoma		4	0.44	4	1.33	2.00
PARATHYROID	14	900				
BRAIN	14	900				
Meningioma		1	0.11	1	1.33	1.33
SPINAL CORD	14	900				
PERIPHERAL NERVE	14	900				
SKELETAL MUSCLE	14	900				
BONE	14	900				
Osteoma		1	0.11	1	1.67	1.67
Osteosarcoma		1	0.11	1	2.00	2.00
HEART	14	900				
BLOOD VESSEL	14	900				
Hemangioma		1	0.11	1	2.00	2.00
Hemangiosarcoma		5	0.56	1	4.55	4.55
BONE MARROW	14	900				
SPLEEN	14	900				
Hemangioma		2	0.22	2	1.33	1.67
Hemangiosarcoma		1	0.11	1	1.33	1.33
THYMUS	14	900				

Table 3: Neoplasms/Males (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
LYMPH NODES	14	900				
Hemangiosarcoma		1	0.11	1	2.00	2.00
WHOLE BODY/MULTIPLE ORGAN	14	899				
Lymphoma, Malignant		21	2.34	8	1.33	10.20
EYE	14	900				
EAR	14	900				
HARDERIAN GLAND	14	900				
Adenoma		13	1.44	5	2.67	6.67

Table 4: Neoplasms/Females

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	THIS	% FOUND	% FOUND
ORAL CAVITY	14	900				
SALIVARY GLAND	14	900				
ESOPHAGUS	14	900				
MESENTERY	14	900				
STOMACH	14	900				
SMALL INTESTINE	14	900				
Adenocarcinoma		1	0.11	1	1.43	1.43
LARGE INTESTINE/CECUM/ANUS	14	900				
Leiomyosarcoma		1	0.11	1	1.67	1.67
LIVER	14	897				
Hepatocellular Adenoma		3	0.33	3	1.43	2.13
Hepatocellular Carcinoma		2	0.22	2	1.43	1.67
Hemangiosarcoma		3	0.33	3	1.33	1.67
GALL BLADDER	14	900				
Adenoma		1	0.11	1	1.67	1.67
NASAL CAVITY	14	900				
DIAPHRAGM	14	900				
Fibrosarcoma		1	0.11	1	2.00	2.00
LUNG	14	899				
Adenoma		52	5.78	10	1.67	16.00
Carcinoma		30	3.34	11	1.43	20.00
KIDNEY	14	900				
Transitional Cell Carcinoma		1	0.11	1	1.67	1.67

Table 4: Neoplasms/Females (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	THIS	% FOUND	% FOUND
URINARY BLADDER	14	900				
OVARY	14	899				
Granulosa Cell Tumor		1	0.11	1	2.04	2.04
Luteoma		11	1.22	6	1.67	5.00
Cystadenoma		17	1.89	9	1.33	13.33
Mesothelioma		1	0.11	1	1.43	1.43
Hemangioma		2	0.22	2	1.67	2.04
UTERUS	14	899				
Stromal Polyp		1	0.11	1	2.04	2.04
Leiomyoma		13	1.45	10	1.33	3.33
Leiomyosarcoma		8	0.89	5	1.67	5.00
Hemangioma		1	0.11	1	2.04	2.04
Hemangiosarcoma		1	0.11	1	1.67	1.67
CERVIX	14	900				
Endometrial Stromal Sarcoma		2	0.22	2	1.67	2.00
Leiomyoma		4	0.44	4	1.33	1.67
Leiomyosarcoma		2	0.22	2	1.43	1.67
VAGINA	14	900				
CLITORAL GLAND	14	900				
Adenocarcinoma		1	0.11	1	1.43	1.43
SKIN	14	900				
Basal Cell Adenoma		2	0.22	2	1.43	2.00
Keratoacanthoma		4	0.44	4	1.33	2.00
Sebaceous Adenoma		1	0.11	1	1.33	1.33
Squamous Cell Papilloma		3	0.33	2	2.00	3.33
Fibroma		68	7.56	12	2.00	25.00
Fibrosarcoma		5	0.56	5	1.33	2.00
Hemangioma		1	0.11	1	1.67	1.67
Hemangiosarcoma		2	0.22	2	1.67	1.67
Neurofibroma		1	0.11	1	1.67	1.67
Liposarcoma		1	0.11	1	2.00	2.00
MAMMARY GLAND	14	900				
Fibroadenoma		2	0.22	2	1.33	2.00
Carcinoma		12	1.33	6	1.33	12.00
Hemangiosarcoma		8	0.89	4	3.33	3.33
ADRENAL	14	899				

Table 4: Neoplasms/Females (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	THIS	% FOUND	% FOUND
Subcapsular Tumor		4	0.44	4	1.67	2.04
Cortex, Adenoma		1	0.11	1	1.67	1.67
Cortex, Carcinoma		1	0.11	1	2.00	2.00
Pheochromocytoma, Benign		3	0.33	3	1.43	2.00
Pheochromocytoma, Malignant		1	0.11	1	1.43	1.43
PANCREAS	14	899				
Islet Cell, Adenoma		2	0.22	2	1.43	2.04
PITUITARY	14	899				
Adenoma		4	0.44	4	1.33	2.04
THYROID	14	900				
PARATHYROID	14	900				
BRAIN	14	900				
SPINAL CORD	14	900				
PERIPHERAL NERVE	14	900				
SKELETAL MUSCLE	14	900				
BONE	14	900				
Osteoma		2	0.22	2	1.67	1.67
Osteosarcoma		4	0.44	4	1.43	1.67
HEART	14	900				
BLOOD VESSEL	14	900				
BONE MARROW	14	900				
SPLEEN	14	900				
THYMUS	14	900				

Table 4: Neoplasms/Females (cont.)

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	THIS	% FOUND	% FOUND
				DIAGNOSIS		
LYMPH NODES	14	897				
Hemangioma		1	0.11	1	1.67	1.67
WHOLE BODY/MULTIPLE ORGAN	14	900				
Histiocytic Sarcoma		26	2.89	9	1.67	11.67
Lymphoma, Malignant		112	12.44	13	3.33	44.00
Monocytic Leukemia		2	0.22	2	1.67	1.67
Myeloid Leukemia		8	0.89	3	1.33	6.67
EYE	14	900				
EAR	14	900				
HARDERIAN GLAND	14	900				
Adenoma		8	0.89	6	1.33	4.29
Adenocarcinoma		1	0.11	1	1.67	1.67

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
LIVER													
Hepatocellular Adenoma	110	50	60	60	60	60	50	60	75	60	70	50	60
Hepatocellular Carcinoma	5	10	5	4	12	6	3	5	10	1	1	4	5
Hemangioma	5	2	6	1	9	1	1	3	2	1			1
Hemangiosarcoma		1	1					1	1				
Cholangioma				1									1
LUNG													
Bronchiolo-alveolar Adenoma	110	50	60	60	60	60	50	60	75	60	70	50	60
Bronchiolo-alveolar Carcinoma		19	12	5	11	17	11	7	6		12	5	11
		5	9	6	2	5	1	1	6		1	10	4
WHOLE BODY/MULTIPLE ORGAN													
Lymphoma, Malignant	110	49	60	60	60	60	50	60	75	60	70	50	60
		5	1	3	2	2		4	1	3			

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
LIVER														
Hepatocellular Adenoma	110	47	60	60	60	60	50	60	75	60	70	50	60	75
Hepatocellular Carcinoma		1						1		1	1			
Hemangiosarcoma			1		1				1					
LUNG														
Adenoma	110	49	60	60	60	60	50	60	75	60	70	50	60	75
Carcinoma		4		5	7	3	8	1	9		7	4		4
		4	1		1	1	1	2		3	1	10	4	2
WHOLE BODY/MULTIPLE ORGAN														
Histiocytic Sarcoma	110	50	60	60	60	60	50	60	75	60	70	50	60	75
Lymphoma, Malignant				2	1	3		7		3	2	3	3	2
Monocytic Leukemia		22	3	4	20	6	9	8	9	2	7	2	14	6
Myeloid Leukemia			1					1						
				4		3			1					

NOTES

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NOTES

[illegible]

