Spontaneous Neoplasms and Survival in Wistar Han Rats: Compilation of Control Group Data

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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 (1, 2). 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 (2).

The histopathology and survival data presented in this publication were gathered from ten control groups of animals from 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 or Europe by contract laboratories 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.

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 Wistar Han rats maintained as control animals until approximately 108 - 112 weeks of age. 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 studies included in this publication were initiated prior to 1999 at four different industrial or contract testing facilities in the United States or Europe. All studies used Wistar Han rats. This outbred stock of rat was rederived by GlaxoWellcome from the Han Wistar stock supplied by BRL. VAF/Plus® animals were transferred to Charles River UK in 1996 and then transferred to Charles River Laboratories in the U.S. in 1997 and rederived into an isolator maintained Foundation Colony. The rats in the reported studies were from control groups of dietary, gavage, or inhalation dosing studies and were approximately 4-8 weeks of age at study initiation.

Rats included in this publication were housed, 2-5 rats/cage, 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 or SDS Rat and Mouse No.1 with or without nitrite supplementation.

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 & 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; kidney; pituitary; thyroid; adrenal; pancreas; ovary; uterus; cervix; vagina; mammary gland; testes; skin/subcutis; thymus; lymph nodes; and hemolymphoreticular system.

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 10 for males and 10 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.

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

<u>Liver:</u> BILE DUCT ADENOMA = cholangioma

Uterus:

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

Skin: BASAL CELL CARCINOMA = malignant basal cell tumor

Adrenal:

CORTEX, CARCINOMA= cortex, adenocarcinoma PHEOCHROMOCYTOMA, BENIGN= medulla neoplasm, benign PHEOCHROMOCYTOMA, MALIGNANT= medulla neoplasm, malignant

Pituitary:

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

Thyroid:

FOLLICULAR CELL CARCINOMA = follicular cell adenocarcinoma

Body: WHOLE BODY/MULTIPLE ORGAN = primary site undetermined

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- 2. Maronpot, R.R., Montgomery, C.A. Jr., Boorman, G.A., and McConnell, E.E. (1986). National toxicology program nomenclature for hepatoproliferative lesions of rats. Toxicol. Pathol. 14:263-273.

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

Study Identification	1	2	3	4	5	6	7	8	9	10
Study Initiation Date	n/a	1997	1999							
Total Number on Study	55	55	55	55	55	55	55	55	55	60
Number Surviving to Termination	43	47	41	45	44	42	48	46	36	45
% Survival	78.2	85.5	74.5	81.8	80.0	76.4	87.3	83.6	65.5	75.0
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104

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

Study Identification	1	2	3	4	5	6	7	8	9	10
Study Initiation Date	n/a	1997	1999							
Total Number on Study	55	55	55	55	55	55	55	55	65	60
Number Surviving to Termination	39	41	37	37	41	33	43	46	34	36
% Survival	70.9	74.5	67.3	67.3	74.5	60.0	78.2	83.6	52.3	60
Study Duration in Weeks	104	104	104	104	104	104	104	104	104	104

GRAPH 1: Male Survival - 104 Weeks 100.0 90.0 80.0 70.0 Percent Survival 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -3 7 8 9 4 5 6 10 Study Identification

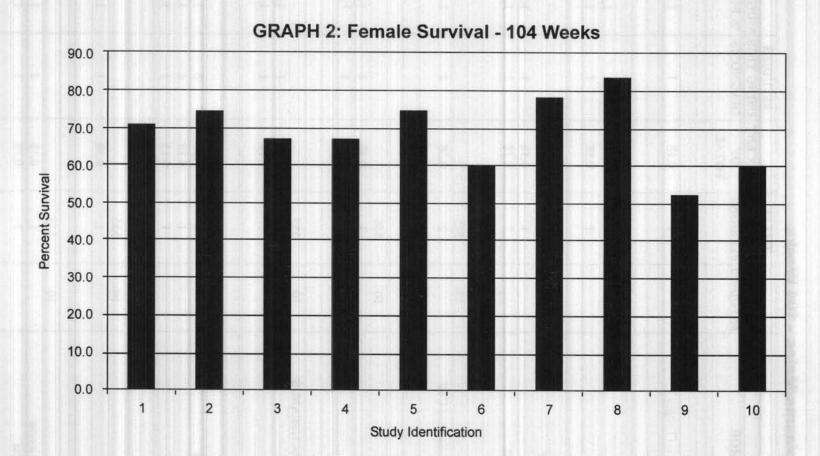


TABLE 3: Neoplasms/Males -104 Weeks

		TOTAL		#STUDIES		
		#ORGANS	PERCENT		MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES		OF	DIAGNOSIS	% FOUND	% FOUND
			TOTAL		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,,
ORAL CAVITY	10	555				
Squamous Cell Carcinoma (Tongue)	10	1	0.18	1	1.67	1.67
Squamous cen caremona (Tongue)		1	0.10	1	1.07	1.07
SALIVARY GLAND	10	555				
Adenoma		1	0.18	1	1.82	1.82
Adenocarcinoma		1	0.18	1	1.82	1.82
ABDOMINAL CAVITY	10	555				
Lipoma	10	1	0.18	1	1.82	1.82
Mesothelioma, Malignant		1	0.18	1	1.82	1.82
Mesothenoma, Wanghant		1	0.16	1	1.02	1.02
STOMACH	10	555				
Nonglandular Mucosa/Squamous Cell Papilloma		2	0.36	2	1.82	1.82
SMALL INTESTINE	10	555				
Carcinoma	10	1	0.18	1	1.82	1.82
Sarcoma		1	0.18	1	1.82	1.82
LARGE INTESTINE/CECUM/ANUS	10	555				
Leiomyoma		1	0.18	1	1.82	1.82
Leiomyosarcoma		1	0.18	1	1.67	1.67
LIVER	10	555				
Hepatocellular Adenoma	10	555 6	1.08	6	1.67	1.82
Sarcoma		1	0.18	1	1.82	1.82
Bile Duct Sarcoma		1	0.18	1	1.82	1.82
NASAL CAVITY	10	555				
Adenoma		1	0.18	1	1.82	1.82
LUNG	10	555				
Bronchioloalveolar Carcinoma	10	1	0.18	1	1.67	1.67
Squamous Cell Carcinoma		1	0.18	1	1.67	1.67

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

		TOTAL		#STUDIES			
		#ORGANS	PERCENT	USING THIS	MINIMIIM	MAXIMUM	
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF	DIAGNOSIS	% FOUND	% FOUND	
Location and Tomor	"STODIES	"LLDIONS	TOTAL	Dirigitosis	70 1 00110	70 2 3 5 1 1 2	
KIDNEY	10	555					
Hemangiosarcoma		1	0.18	1	1.82	1.82	
Lipoma		1	0.18	1	1.82	1.82	
Liposarcoma		1	0.18	1	1.82	1.82	
Tubular Cell Adenoma		2	0.36	2	1.82	1.82	
Tubular Cell Carcinoma		2	0.36	2	1.67	1.82	
TESTIS	10	555					
Interstitial Cell Adenoma		12	2.16	6	1.67	10.91	
Mesothelioma, Malignant		2	0.36	1	3.64	3.64	
Seminoma		1	0.18	1	1.82	1.82	
SEMINAL VESICLE	10	555					
Adenocarcinoma	10		0.18	1	1.82	1.82	
Adenocarcinoma		1	0.18	I	1.02	1.02	
PROSTATE	10	555					
Adenoma		2	0.36	2	1.67	1.82	
Adenocarcinoma		2	0.36	2	1.82	1.82	
EPIDIDYMIS	10	555					
	10	4	0.72	3	1.82	3.64	
Mesothelioma, Malignant		4	0.72	3	1.62	3.04	
SKIN/SUBCUTIS	10	555					
Basal Cell Tumor, Benign		7	1.26	4	1.82	5.45	
Basal Cell Carcinoma		2	0.36	1	3.64	3.64	
Chrondrosarcoma		1	0.18	1	1.82	1.82	
Fibroma		27	4.86	10	1.67	10.91	
Fibrosarcoma		2	0.36	1	3.64	3.64	
Hemangioma		1	0.18	1	1.82	1.82	
Hemangiosarcoma		1	0.18	1	1.82	1.82	
Keratoacanthoma		28	5.05	8	1.67	14.55	
Lipoma		7	1.26	5	1.82	3.64	
Myxoma		2	0.36	2	1.82	1.82	
Pilomatrixoma		2	0.36	1	3.64	3.64	
Sebaceous Cell Adenoma		2	0.36	1	3.64	3.64	
Sebaceous Cell Carcinoma		1	0.18	1	1.67	1.67	
Schwannoma, Malignant		4	0.72	4	1.67	1.82	
Squamous Cell Papilloma		6	1.08	5	1.67	3.64	
- James Con Lupinomu			1.00		1.07	2.01	

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

		TOTAL						
			PERCENT	USING THIS	MINIMUM	MAXIMUM		
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND		
MAMMARY GLAND	10	555						
Fibroadenoma	-	4	0.72	2	3.33	3.64		
ADRENAL	10	555						
Cortex Adenoma		6	1.08	3	1.82	7.27		
Cortex Carcinoma		4	0.72	4	1.82	1.82		
Pheochromocytoma, Benign		18	3.24	9	1.67	12.73		
Pheochromocytoma, Malignant		2	0.36	2	1.82	1.82		
PANCREAS	10	555						
Adenoma		3	0.54	1	5.45	5.45		
Islet Cell, Adenoma		41	7.39	10	1.82	20.00		
Islet Cell, Adenocarcinoma		2	0.36	2	1.67	1.82		
Acinar Islet Cell, Adenoma		3	0.54	3	1.82	1.82		
PITUITARY	10	555						
Adenoma		177	31.89	10	21.82	50.91		
Carcinoma		3	0.54	2	1.82	3.64		
THYROID	10	555						
C-Cell Adenoma		56	10.09	10	3.64	18.33		
C-Cell Carcinoma		7	1.26	4	1.82	5.45		
Follicular Cell Adenoma		32	5.77	10	1.67	12.73		
Follicular Cell Carcinoma		9	1.62	7	1.67	3.64		
PARATHYROID	10	555						
Adenoma		3	0.54	2	1.82	3.64		
BRAIN	10	555						
Granular Cell Meningioma, Benign	10	6	1.08	4	1.82	3.64		
Granular Cell Meningioma, Malignant		3	0.54	2	1.82	3.64		
Astrocytoma, Malignant		2	0.36	2	1.82	1.82		
Oligodendrocytic Glioma		2	0.36	1	3.64	3.64		
MUSCLE	10	555						
Chondroma		1	0.18	1	1.82	1.82		
Hemangiosarcoma		4	0.72	4	1.82	1.82		

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

		TOTAL		#STUDIES			
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM	
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND	
BONE	10	555					
Osteosarcoma		2	0.36	2	1.67	1.82	
HEART	10	555					
Endocardial Schwannoma, Malignant		3	0.54	2	1.82	3.64	
SPLEEN	10	555					
Hemangioma		1	0.18	1	1.82	1.82	
THYMUS	10	555					
Adenoma		1	0.18	1	1.82	1.82	
Carcinoma		1	0.18	1	1.82	1.82	
Thymoma, Benign		13	2.34	8	1.67	5.45	
Thymoma, Mixed		1	0.18	1	1.82	1.82	
LYMPH NODES (ALL)	10	555					
Hemangioma		44	7.93	9	1.67	12.73	
Hemangiosarcoma		16	2.88	6	1.82	10.00	
WHOLE BODY/MULTIPLE ORGAN	10	555					
Mesothelioma, Malignant		1	0.18	1	1.82	1.82	
Lymphoma		2	0.36	1	3.33	3.33	
Histiocytic Sarcoma		1	0.18	1	1.67	1.67	
EYE	10	555					
Schwannoma		1	0.18	1	1.82	1.82	
ADIPOSE TISSUE	10	555					
Anaplastic Carcinoma		1	0.18	1	1.82	1.82	
FOOT/LEG	10	555					
Hemangiosarcoma		1	0.18	1	1.82	1.82	
HARDERIAN GLAND	10	555					
Carcinoma		1	0.18	1	1.82	1.82	

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

		TOTAL		#STUDIES		
		#ORGANS	PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
HEMOLYMPHORETICULAR SYSTEM	10	555				
Granulocytic Leukemia, Malignant		2	0.36	2	1.82	1.82
Hemangiosarcoma		3	0.54	1	5.45	5.45
Histiocytic Sarcoma		3	0.54	2	1.82	3.64
Lymphocytic Lymphoma, Malignant		8	1.44	5	1.82	5.45
Lymphosarcoma		3	0.54	1	5.45	5.45
Mononuclear Cell Leukemia		1	0.18	1	1.82	1.82
Pleomorphic Lymphoma, Malignant		2	0.36	2	1.82	1.82
TAIL	10	555				
Squamous Cell Papilloma		1	0.18	1	1.82	1.82
THORACIC CAVITY	10	555				
Schwannoma, Malignant		1	0.18	1	1.82	1.82
ZYMBAL'S GLAND	10	555				
Carcinoma	10	1	0.18	1	1.82	1.82

TABLE 4: Neoplasms/Females -104 Weeks

		TOTAL		#STUDIES		
			PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF TOTAL	DIAGNOSIS	% FOUND	% FOUND
ORAL CAVITY	10	565				
Squamous Cell Carcinoma	10	3	0.53	2	1.82	3.64
Tongue - Papilloma		1	0.18	1	1.82	1.82
Tongue - Granular Cell Tumor		2	0.35	2	1.82	1.82
SALIVARY GLAND	10	565				
Adenocarcinoma		1	0.18	1	1.82	1.82
ABDOMINAL CAVITY	10	565				1.00
Mesothelioma, Malignant		1	0.18	1	1.82	1.82
MESENTERY	10	565				
Lipoma		1	0.18	1	1.54	1.54
STOMACH	10	565				
Nonglandular Mucosa/Squamous Cell Papilloma		1	0.18	1	1.67	1.67
SMALL INTESTINE	10	565				
Fibroma		1	0.18	1	1.82	1.82
Leiomyoma		1	0.18	1	1.82	1.82
Leiomyosarcoma		0	0.00	0	0.00	0.00
Adenocarcinoma		2	0.35	1	3.08	3.08
LIVER	10	565				
Hepatocellular Adenoma		2	0.35	2	1.67	1.82
Hepatocellular Adenocarcinoma		1	0.18	1	1.82	1.82
Bile Duct Adenoma		1	0.18	1	1.54	1.54
OVARY	10	565				
Mixed Sex Cord Stromal Tumor, Benign		2	0.35	2	1.82	1.82
Granulosa/Thecal Cell Tumor		2	0.35	2	1.82	1.82
Tubulo-Stromal Adenoma		6	1.06	4	1.82	3.64
Papillary Adenoma		1	0.18	1	1.82	1.82
Thecoma		1	0.18	1	1.54	1.54

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

		TOTAL		#STUDIES			
			PERCENT	USING THIS	MINIMUM	MAXIMUM	
LOCATION AND TUMOR	#STUDIES		OF TOTAL	DIAGNOSIS	% FOUND	% FOUND	
UTERUS	10	F.C.F.	101112				
	10	565	0.52	2	1.82	1.82	
Adenoma Adenocarcinoma		3 13	0.53 2.30	7	1.67	5.45	
Deciduoma		13	0.18	1	1.82	1.82	
		24	6.02	8	1.82	16.92	
Endometrial Polyp		34			1.54	1.82	
Hemangioma		3	0.35	2			
Hemangiosarcoma		-	0.53	2	1.67	3.64	
Endometrial Stromal Polyp		35	6.19 1.06	4	14.55 1.54	20.00	
Endometrial Stromal Sarcoma Squamous Cell Carcinoma		6	0.18	6	1.82	1.82	
CEDVIV	10	565					
CERVIX Polyp, Benign	10	2	0.35	2	1.54	1.82	
**				3	1.54	1.82	
Granular Cell Tumor, Benign		3	0.53	3		1.82	
Schwannoma, Benign		1	0.18	1	1.82		
Stromal Cell Sarcoma		1	0.18	1	1.54	1.54	
Adenocarcinoma		1	0.18	1	1.67	1.67	
VAGINA	10	565					
Leiomyosarcoma		1	0.18	1	1.54	1.54	
Stromal Polyp		1	0.18	1	1.82	1.82	
Granular Cell Tumor		6	1.06	1	10.00	10.00	
Squamous Cell Carcinoma		1	0.18	1	1.67	1.67	
CLITORAL GLAND	10	565					
Carcinoma		1	0.18	1	1.82	1.82	
Schwannoma, Benign		1	0.18	1	1.82	1.82	
SKIN/SUBCUTIS	10	565					
Basal Cell Tumor, Benign	10	4	0.71	4	1.54	1.82	
Fibroma		9	1.59	6	1.54	5.45	
Fibrosarcoma		1	0.18	1	1.54	1.54	
Keratoacanthoma		2	0.18	1	3.64	3.64	
Lipoma		1	0.33	1	1.82	1.82	
Myxoma		1	0.18	1	1.82	1.82	
Sebaceous Cell Adenoma		2	0.18	2	1.82	1.82	
Squamous Cell Carcinoma		2	0.35	2	1.67	1.82	
Papilloma		1	0.33	1	1.54	1.54	
Тартопа		1	0.10	1	1.54	1.54	

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

		TOTAL		#STUDIES		
			PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES		OF TOTAL	DIAGNOSIS		% FOUND
MAMMARY GLAND	10	565				
Adenoma	10	8	1.42	5	1.82	3.64
Adenocarcinoma		31	5.49	9	1.82	13.33
Fibroadenoma		125	22.12	10	10.91	33.85
ADRENAL	10	565				
Cortex Adenoma		4	0.71	3	1.82	3.64
Cortex Adenocarcinoma		1	0.18	1	1.67	1.67
Pheochromocytoma, Benign		5	0.88	4	1.54	3.64
Pheochromocytoma, Malignant		6	1.06	6	1.54	1.82
PANCREAS	10	565				
Islet Cell Adenoma		10	1.77	6	1.82	5.45
Islet Cell Adenocarcinoma		1	0.18	1	1.67	1.67
Acinar-Islet Cell Adenoma		1	0.18	1	1.82	1.82
Ductular Adenocarcinoma		1	0.18	1	1.67	1.67
PITUITARY	10	565				
Adenoma		265	46.90	10	1.67	61.82
Adenocarcinoma		23	4.07	9	1.82	10.91
THYROID	10	565				
C-Cell Adenoma		58	10.27	9	3.64	21.82
C-Cell Carcinoma		2	0.35	2	1.82	1.82
Follicular Cell Adenoma		20	3.54	9	1.54	9.09
Follicular Cell Carcinoma		3	0.53	2	1.82	3.64
PARATHYROID	10	565				
Adenoma		1	0.18	1	1.82	1.82
BRAIN	10	565				
Granular Cell Meningioma, Benign		4	0.71	4	1.67	1.82
SPINAL CORD	10	565				
Granular Cell Tumor		2	0.35	2	1.82	1.82
MUSCLE	10	565				
Granular Cell Tumor, Benign	10	1	0.18	1	1.82	1.82
Hemangiosarcoma		1	0.18	1	1.82	1.82

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

		TOTAL		#STUDIES		
			PERCENT	USING THIS	MINIMUM	MAXIMUM
LOCATION AND TUMOR	#STUDIES	#LESIONS	OF	DIAGNOSIS	% FOUND	% FOUND
			TOTAL			
HEART	10	565				
Liposarcoma, Mediastinum		1	0.18	1	1.67	1.67
SPLEEN	10	565				
Hemangioma	10	1	0.18	1	1.82	1.82
Histiocytic Sarcoma		1	0.18	1	1.82	1.82
THYMUS	10	565				
Thymoma, Benign		26	4.60	9	1.82	10.00
Thymoma, Malignant		2	0.35	2	1.82	1.82
LYMPH NODES	10	565				
Hemangioma		16	2.83	5	1.82	10.91
Hemangiosarcoma		4	0.71	4	1.82	1.82
WHOLE BODY/MULTIPLE ORGAN	10	565				
Mesothelioma		1	0.18	1	1.82	1.82
EAR	10	565				
Granular Cell Tumor, Benign		1	0.18	1	1.82	1.82
BONE MARROW	10	565				
Hemangioma		1	0.18	1	1.82	1.82
HEMOLYMPHORETICULAR SYSTEM	10	565				
Malignant Lymphocytic Lymphoma		3	0.53	3	1.54	1.82
Histiocytic Sarcoma		4	0.71	1	6.15	6.15
ZYMBAL GLAND	10	565				
Carcinoma		1	0.18	1	1.54	1.54

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

Study Identification		2	3	4	5	6	7	8	9	10
LIVER	55	55	55	55	55	55	55	55	55	60
Hepatocellular Adenoma			1	1	1	1			1	1
Sarcoma						1				
Bile Duct Sarcoma									1	
KIDNEY	55	55	55	55	55	55	55	55	55	60
	33	33		33	33	33		33	33	00
Hemangiosarcoma		I					1			
Lipoma		1					1			
Liposarcoma		I				1			1	
Tubular Cell Adenoma						I		1	1	1
Tubular Cell Carcinoma								I		1
TESTIS	55	55	55	55	55	55	55	55	55	60
Interstitial Cell Adenoma		2		1	1			1	6	1
Mesothelioma, Malignant									2	
Seminoma						1				
SKIN/SUBCUTIS	55	55,	55	55	55	55	55	55	55	60
Basal Cell Tumor, Benign			1	2	1	3				
Basal Cell Carcinoma				2						
Chrondrosarcoma		1								
Fibroma	3	3	2	2	6	2	2	3	3	1
Fibrosarcoma								2		
Hemangioma								1		
Hemangiosarcoma							1			
Keratoacanthoma	2		5	8	3	4	3		2	1
Lipoma		1				1	1	2	2	
Myxoma							1		1	
Pilomatrixoma									2	

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
Sebaceous Cell Adenoma	2									
Sebaceous Cell Carcinoma	2									1
			1					1	1	1
Schwannoma, Malignant		1	I			1	1	1	2	l
Squamous Cell Papilloma		1				1	1		2	1
ADRENAL	55	55	55	55	55	55	55	55	55	60
Cortex Adenoma					1		1		4	
Cortex Carcinoma				1	1		1		1	
Pheochromocytoma, Benign	2	1		3	1	1	1	1	7	1
Pheochromocytoma, Malignant					1				1	
PANCREAS	55	55	55	55	55	55	55	55	55	60
Adenoma									3	
Islet Cell, Adenoma	1	5	4	6	11	6	1	2	3	2
Islet Cell, Adenocarcinoma	1									1
Acinar Islet Cell, Adenoma	1							1	1	
PITUITARY	55	55	55	55	55	55	55	55	55	60
Adenoma	22	15	12	14	18	12	15	19	28	22
Carcinoma					1	2				
THYROID	55	55	55	55	55	55	55	55	55	60
C-Cell Adenoma	2	2	4	4	9	8	2	4	10	11
C-Cell Carcinoma	3	_	·	2	1		-	1	10	
Follicular Cell Adenoma	1	1	6	6	7	3	1	3	3	1
Follicular Cell Carcinoma	1	2	1	3	1		1	2		1

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

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1	2	3	4	5	6	7	8	9	10
55	55	55	55	55	55	55	55	55	60
					1				
	1								
1	1	1		2	2		3	2	1
				1					
55	55	55	55	55	55	55	55	55	60
7	4	5	7	7	6	4	3		1
3		1	3	1	2				6
55	55	55	55	55	55	55	55	55	60
		1			1				
								3	
			1					2	
		3	1	2	1	1		_	
								3	
								1	
	1				1				
	55 7 3	55 55 55 7 4 3 3	1 2 3 55 55 55 1 1 1 1 1 1 55 55 55 7 4 5 3 1 55 55 55 1 1 1 55 55 55 1 1 1	1 2 3 4 55 55 55 55 1 1 1 1 55 55 55 55 7 4 5 7 3 1 3 55 55 55 55 55 55 55 55	1 2 3 4 5 55 55 55 55 55 1 1 1 2 1 1 1 2 1 1 1 2 2 1 1 3 1 3 1 3 1 3 1 55 55 55 55 55 55 55 55 55 55 1 1 1 1	1 2 3 4 5 6 55 55 55 55 55 1 1 1 2 2 2 2 1 3 1 3 1 2 55 55 55 55 55 55 55 55 55 55 1 3 1 2 55 55 55 55 55 1 1 1 1	1 2 3 4 5 6 7 55 55 55 55 55 55 1 1 1 2 2 1 1 1 2 2 2 2 1 3 1 3 1 2 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 1 1 1 1	55 55 55 55 55 55 55 1 1 1 2 2 3 1 1 1 2 2 3 55 55 55 55 55 55 7 4 5 7 7 6 4 3 3 1 3 1 2 55 55 55 55 55 55 55 55 55 55 55 55	1 2 3 4 5 6 7 8 9 55 55 55 55 55 55 55 1 1 1 2 2 3 2 1 1 1 2 2 3 2 55 55 55 55 55 55 55 7 4 5 7 7 6 4 3 3 1 3 1 2 3 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 55 3 1 2 1 1 3 1 2 1 1

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

IADEL V. IIIVIA				, – ,	,		J. J			
Study Identification	1	2	3	4	5	6	7	8	9	10
LIVER	55	55	55	55	55	55	55	55	65	60
Hepatocellular Adenoma						1				1
Hepatocellular Adenocarcinoma								1		
Bile Duct Adenoma									1	
OVARY	55	55	55	55	55	55	55	55	65	60
Mixed Sex Cord Stromal Tumor, Benign			1				1			
Granulosa/Thecal Cell Tumor					1	1				
Tubulo-Stromal Adenoma	2		2	1		1				
Papillary Adenoma							1			
Thecoma									1	
UTERUS	55	55	55	55	55	55	55	55	65	60
Adenoma			1	1			1			
Adenocarcinoma	2	2	3			3	1	1		1
Deciduoma					1					
Endometrial Polyp	5	4	2	1		3	5	3	11	
Hemangioma			1						1	
Hemangiosarcoma		2								1
Endometrial Stromal Polyp			8	8	8	11				
Endometrial Stromal Sarcoma			1	1	1	1			1	1
Squamous Cell Carcinoma					1					
CERVIX	55	55	55	55	55	55	55	55	65	60
Polyp, Benign							1		1	
Granular Cell Tumor, Benign		1						1	1	
Schwannoma, Benign							1			
Stromal Cell Sarcoma									1	
Adenocarcinoma										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
VAGINA	55	55	55	55	55	55	55	55	65	60
Leiomyosarcoma									1	
Stromal Polyp				1						
Granular Cell Tumor										6
Squamous Cell Carcinoma										1
SKIN/SUBCUTIS	55	55	55	55	55	55	55	55	65	60
Basal Cell Tumor, Benign			1	33	1	33	33	1	1	00
Fibroma	1	1	1	2	1	3		1	1	
Fibrosarcoma		•			1	3			1	
Keratoacanthoma				2						
Lipoma						1				
Myxoma	1									
Sebaceous Cell Adenoma	1			1						
Squamous Cell Carcinoma				1						1
Papilloma									1	
MAMMARY GLAND	55	55	55	55	55	55	55	55	65	60
Adenoma	1	2	2		1					2
Adenocarcinoma	4	3	6	2	2	1	1		4	8
Fibroadenoma	9	12	13	17	14	10	11	6	22	11
ADRENAL	55	55	55	55	55	55	55	55	(5	60
Cortex Adenoma	1	33	33	33	33	33	33	2	65	60
Cortex Adenocarcinoma	1					1		2		1
Pheochromocytoma, Benign						1		2	1	1
Pheochromocytoma, Malignant		1	1			I	1	1	1	1
Theoenioniocytoma, wanghant		1	1				I	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
PANCREAS	55	55	55	55	55	55	55	55	65	60
Islet Cell Adenoma	1		3			2	1	1		2
Islet Cell Adenocarcinoma										1
Acinar-Islet Cell Adenoma		1								
Ductular Adenocarcinoma										1
PITUITARY	55	55	55	55	55	55	55	55	65	60
Adenoma	26	26	27	31	34	30	26	26	38	1
Adenocarcinoma	6	1	2	2	2	4	2	1		3
THYROID	55	55	55	55	55	55	55	55	65	60
C-Cell Adenoma		2	5	4	12	7	2	3	10	13
C-Cell Carcinoma	1		1							
Follicular Cell Adenoma	2		5	3	3	3	1	1	1	1
Follicular Cell Carcinoma		1	2							
THYMUS	55	55	55	55	55	55	55	55	65	60
Thymoma, Benign	3	2	3	4	2	2	3	1		6
Thymoma, Malignant			1			1				
HEMOLYMPHORETICULAR SYSTEM	55	55	55	55	55	55	55	55	65	60
Malignant Lymphocytic Lymphoma		1						1	1	
Histiocytic Sarcoma										