

STATISTICAL REVIEW AND EVALUATION
CARCINOGENICITY

NDA #: 21-083

Name of Drug: Rapamune (sirolimus) oral solution

Applicant: Wyeth Ayerst

Documents Reviewed: Volumes 51-59 and electronic data submission

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Key Words: Peto, trend test, pairwise comparisons, adjusted p-values, adjusted α -levels

Summary of Review

- In this review, a tumor is declared "rare" if the incidence in the control group is $\leq 1\%$ and "common" if the incidence in the control group is $> 1\%$.
- For positive linear trend analyses, "rare" tumors are tested using a significance level of 0.025; "common" tumors are tested using a significance level of 0.005.
- For pairwise comparisons, "rare" tumors are tested using a significance level of 0.05, while "common" tumors are tested using a significance level of 0.01.
- Problems related to the maximum tolerated dose (MTD) being exceeded were seen in the mouse study. The male portion of this study was terminated early after 29 weeks, the female portion of this study was terminated early after 86 weeks, and the female high dose group was modified from receiving the highest dose to actually receiving the lowest dose. As a result, no conclusions are drawn in this review about possible carcinogenic effects in male mice (they were not followed long enough for any conclusions to be drawn). The pharmacologist will have to determine whether female mice were followed for an adequate length of time. In addition, the trend tests for female mice could only compare the control, low, and medium dose female mice. The pharmacologist will have to determine whether a wide enough range of doses were studied for female mice.
- In the female mice, a positive dose mortality trend was detected in survival (i.e., mortality was found to increase with dose). No dose mortality trend was detected in the rat study. The trend tests used in this review which look at tumor incidence adjust for differences in intercurrent mortality.
- The percent loss in group mean body weights compared to controls was greater than 10% in the medium and high dose male rats (15% and 22%, respectively), and also in the low, medium, and "high" dose female mice (14%, 21%, and 16%, respectively). The pharmacologist will have to determine if these dose groups can be considered appropriate for the rat study, i.e., close to MTD.

- The only significant trend test found in the rat study was for the incidence of testicular interstitial cell adenomas ($p=0.004$). Pairwise comparisons for this tumor were not significant in the low and medium dose male groups ($p=0.974$ and $p=0.063$, respectively), but were marginally significant in the high dose male group ($p=0.013$; the significance level used here is 0.01 as this tumor was seen in 5% of the control group and is thus classified as "common").
- The only significant trend test found in the female mice (recall that these only compare control, low, and medium dose groups) was for the incidence of lymphoma ($p=0.002$; lymphoma occurred at a rate of 5% in the control group and was thus considered "common"). Pairwise comparisons for lymphoma were found to be significant in all female mice dose groups ($p=0.003$ for the low dose group, $p=0.003$ for the medium dose group, and $p<0.001$ for the "high" dose group). No other pairwise comparisons for the "high" dose female group were found to be significant.

I. Background

Two animal carcinogenicity studies (Study 103 in rats and Study 104 in mice) were included in this NDA submission. Rapamune, an immunosuppressant, was administered orally by gavage once daily in both studies to evaluate its carcinogenic potential.

In study 103, male and female CD VAF rats were dosed for 104 weeks at dosages of 0, 0, 0.05, 0.1, and 0.2 mg/kg/day. There were 65 rats/sex in each of the two control groups and the low, medium, and high dose groups. Control groups were combined for analysis. Approximately 55 tissues from each animal were examined grossly and microscopically.

In study 104, male and female CD-1 VAF mice were dosed at 0, 0, 12.5, 25, and 50 (lowered to 6 mg/kg/day in the females at week 31) mg/kg/day for 29 (males) or 86 (females) weeks. There were 60 mice/sex in the first control group, 75 mice/sex in the second control group, and 75 mice/sex in each of the low, medium, and high dose groups. Control groups were combined for analysis. Approximately 55 tissues were examined grossly and microscopically from all females. Only certain tissues were examined from the various male groups microscopically (all were examined in the first control group and the high dose group, and about 8 were examined from the low and medium dose groups). Normally this would restrict our conclusions from the trend test for males to only those tissues that were examined microscopically for all male animals. However, this point is moot since the study was unable to follow male mice long enough to assess carcinogenic potential in the male mice (see below).

The sponsor notes that while the original intent of Study 104 was to assess the carcinogenic potential of Rapamune, the health status of the mice was compromised by skin lesions, especially in the male mice. It was determined that all dosed groups in the males had exceeded the maximum tolerated dose (MTD), as had the high dose group in the females. As a result, the male portion of the study was terminated after 29 weeks and the female portion of the study was modified by lowering the high dose group (50 mg/kg/day) to approximately half of what the low dose group was receiving (i.e., 6 mg/kg/day) at week 31. The female portion of the study was also terminated early at 86 weeks due to similar problems with the low and medium dose groups. Thus, the study failed to assess carcinogenic potential in male mice but still provides some information about carcinogenic potential in female mice, although not as much as originally planned due to the problems with the high dose group and early termination. It is unclear whether the problems with skin lesions were related to the animals (the sponsor notes that such lesions have been seen in their and other laboratories with CD-1 mice but at a much

lower incidence and severity) or to Rapamune which is an immunosuppressant (incidence of the lesions appeared to be dose-related).

II. Methods

For each species and sex, the sponsor and reviewer analyzed palpable, nonpalpable-lethal, and nonpalpable-nonlethal tumors separately, then combined the results using Peto et al.¹ procedures. For a particular tumor type of interest, the incidence data can be summarized in a 2xD table, where D is the number of dose groups. The first row contains the number of animals with the tumor of interest, and the second row contains the number of animals without the tumor. However, this summary table can be misleading. If the toxicity of the drug causes animals to die early by some non-cancer related cause, fewer animals will be at risk for tumors in the higher dose groups. Thus, even if the drug also increases the tumor rate, the overall incidence of that tumor in the high dose groups may be smaller than in the control groups. To adjust for the effect that potential differential mortality between the dose groups has on tumor occurrence, the Peto prevalence method breaks up study time into several discrete intervals. The intervals used in the rat study were weeks 1-52, weeks 53-78, weeks 79-91, weeks 92-104, and terminal sacrifice. The intervals used for the female mice were weeks 1-52, weeks 53-78, weeks 79-86, and terminal sacrifice. No analysis was performed by either the reviewer or the sponsor for male mice. The data can thus be represented by several 2xD tables, one for each time interval. Note that Peto et al. point out that "the effects of differences in longevity on numbers of tumor-bearing animals can be very substantial, and so, whether or not they appear to be they should routinely be corrected for when presenting experimental results."

The dose groups can also be assigned weights in the statistical analysis to test various hypotheses. For example, using weights of (0, 1, ..., D) gives the trend test which is sensitive to a linear dose effect. Using equal weights (1, 1, ..., 1) gives a test of association between dose and tumor rate without specifying the form of the relationship. Weight can also be set equal to the actual doses given. Finally, choosing weights close to the actual biological effect of the doses will result in the most sensitive test, but in practice this effect is not known. Linear weights or dose weights are often used. The sponsor used both linear and dose weights in their analysis. As results were similar between the two, this reviewer used dose weights.

For the tumor type of interest, each tumor is classified as "fatal", "non-fatal", or "mortality independent tumors". P-values are calculated for the three classes separately, and then combined to yield a single p-value for the tumor type. Both exact and asymptotic p-values are calculated for most tumor types (statisticians in CDER routinely use the exact method to test for positive linear trend when the number of total tumors across treatment groups is 10 or smaller).

One-sided p-values may be more appropriate than two-sided p-values, since they are more conservative and we are only interested in whether increased doses *increase* tumor incidence. One-sided p-values are reported in this review.

As so many sex/species/organ/tumor type combinations are tested, a simple application of a 0.05 decision rule does not appropriately control the overall false positive rate. It has been

¹ Peto R, Pike MC, Day NE, Gray RG, Lee PN, Parish S, Peto J, Richards S, and Wahrendorf J (1980). "Guidelines for Simple, Sensitive Significance Tests for Carcinogenic Effects in Long-term Animal Experiments", in Long-term and Short-term Screening Assays for Carcinogens: An Critical Appraisal, World Health Organization.

suggested by Drs. Lin and Rahman² that if the tumor is "rare" the cutoff should be 0.025 and if the tumor is "common" the cutoff should be 0.005. Tumors are defined as rare or common using historical control data or the control group in the study being analyzed (in this review, the control group is used). The usual practice at FDA is to classify a tumor as common if it occurs in the control group at an incidence of greater than 1%. Using simulation tests on CD-1 rats and CD(BR) mice, Lin and Rahman found that the overall false positive rate resulting from the use of the α -levels 0.025 and 0.005 in the tests for linear trend in a two-species-two-sex study is about 10%. These false-positive rates are judged by the Center for Drug Evaluation and Research as the most appropriate in a regulatory setting.

For pairwise comparisons, the levels of significance that are used are 0.05 for rare tumors and 0.01 for common tumors.

III. Analysis

Rat Study 103

Both the reviewer's and the sponsor's analyses used the Peto et al. procedures described above. Reviewer analyses for male rats (exact and asymptotic trend tests) can be found in Appendix 1. Reviewer analyses for female rats (exact and asymptotic trend tests) are given in Appendix 2.

As described above, for the trend test Drs. Lin and Rahman suggest that if a tumor is "rare" it be tested using a significance level of 0.025. "Common" tumors are to be tested using a significance level of 0.005. Using this rule, the only significant trend test found in the rat study was for the incidence of testicular interstitial cell adenomas ($p=0.004$). Pairwise comparisons for this tumor were not significant in the low and medium dose male groups ($p=0.974$ and $p=0.063$, respectively), but were marginally significant in the high dose male group ($p=0.013$; the significance level used here, as suggested by Drs. Lin and Rahman, is 0.01 as this tumor was seen in 5% of the control group and is thus classified as "common"). Note that none of the testicular interstitial cell adenomas were classified by the sponsor as fatal (2 of the high dose males who developed these tumors had cause of death coded as "undetermined"; the remaining animals who developed these tumors had cause of death coded as "tumor did not cause death").

No dose mortality trend in survival was detected in the rat study. However, as suggested by Peto et al., the trend tests used in this review which look at tumor incidence still adjust for differences in intercurrent mortality. Using the rule of thumb suggested in the draft Guidance for Industry³, exposure to the drug can be considered adequate as more than 20-30 animals were still alive at 80-90 weeks for both male and female high dose groups.

² Lin KK and Rahman MA (1998), "Overall False Positive Rates in Tests for Linear Trend in Tumor Incidence in Animal Carcinogenicity Studies of New Drugs", *Journal of Biopharmaceutical Statistics* 8(1), pgs. 1-15.

³ Draft Guidance for Industry, "On Statistical Aspects of Design, Analysis, and Interpretation of Animal Carcinogenicity Studies", Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, Maryland.

The percent loss in group mean body weights compared to controls was greater than 10% in the medium and high dose male rats (15% and 22%, respectively). The pharmacologist will have to determine if these dose groups received doses close to MTD.

Mouse Study 104

The sponsor's analyses used the Peto et al. procedures described above. As the reviewer validated the sponsor's analyses in the rat study (i.e., reviewer results were found to be the same as sponsor results), and the sponsor performed the correct analyses for the mouse study, this reviewer did not repeat the analyses. Hence, conclusions in this review for the mouse study are based on sponsor results.

Recall that problems related to the maximum tolerated dose (MTD) being exceeded were seen in the mouse study. The male portion of this study was terminated early after 29 weeks, the female portion of this study was terminated early after 86 weeks, and the female high dose group was modified from receiving the highest dose to actually receiving the lowest dose. As a result, no conclusions are drawn in this review about possible carcinogenic effects in male mice (they were not followed long enough for any conclusions to be drawn). The pharmacologist will have to determine whether female mice were followed for an adequate length of time. In addition, the trend tests for female mice could only compare the control, low, and medium dose female mice. The pharmacologist will have to determine whether a wide enough range of doses were studied for female mice.

Again using the rules for significance levels suggested by Drs. Lin and Rahman, the only significant trend test found in the female mice was for the incidence of lymphoma ($p=0.002$; lymphoma occurred at a rate of 5% in the control group and was thus considered "common"). Pairwise comparisons for lymphoma were found to be significant in all female mice dose groups ($p=0.003$ for the low dose group, $p=0.003$ for the medium dose group, and $p<0.001$ for the "high" dose group). Overall, approximately 83% of these tumors were classified by the sponsor as fatal (6/7=86% of the control group, 7/10=70% of the low dose group, 8/9=89% of the medium dose group, and 12/14=86% of the "high" dose group who developed this tumor had cause of death coded as "tumor caused death"; the remaining animals with this tumor had cause of death coded as "tumor did not cause death"; no significant differences were found in cause of death between dose groups: Fisher's exact two-sided $p=0.80$). No other pairwise comparisons for the "high" dose female group were found to be significant.

In the female mice, a positive dose mortality trend was detected in survival (i.e., mortality was found to increase with dose; two-sided $p=0.003$ for the linear trend test comparing control, low, and medium dose groups). Survival was also decreased in the "high" dose females compared to controls (two-sided $p<0.001$ for the pairwise comparison between "high" dose and control). The trend tests used in this review which look at tumor incidence adjust for differences in intercurrent mortality. Using the rule of thumb suggested in the draft Guidance for Industry (see above reference), exposure to the drug can be considered adequate as more than 20-30 animals were still alive at 80-90 weeks for the female medium and "high" dose groups (note that the medium dose group is probably the most appropriate to use here).

The percent loss in group mean body weights compared to controls was greater than 10% in the low, medium, and "high" dose female mice (14%, 21%, and 16%, respectively). The pharmacologist will have to determine if these dose groups can be considered close to MTD.

IV. Discussion

As is common practice in the Center for Drug Evaluation and Research, in this review a tumor is declared "rare" if the incidence in the control group is $\leq 1\%$ and "common" if the incidence in the control group is $> 1\%$. As suggested by Drs. Lin and Rahman, for positive linear trend analyses, "rare" tumors are tested using a significance level of 0.025, while "common" tumors are tested using a significance level of 0.005. For pairwise comparisons, "rare" tumors are tested using a significance level of 0.05, and "common" tumors are tested using a significance level of 0.01.

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HFD-590

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This review contains 30 pages (including appendices).

APPEARS THIS WAY
ON ORIGINAL

Appendix 1: Analysis of Carcinogenic Potential in Male Rat
Test of Dose-Response (Tumor) Positive Linear Trend
Study No.

Run Date & Time: June 4, 1999 (14:10)

Source: C:\NDAS\RAPCARC\RAT103\st95103.lis

Note: Dose Levels Included: CTRL1 CTRL2 LOW MED HIGH (0 0 0.05 0.1 0.2)
Missing value in Tumor-Caused Death is treated as tumor not causing death
Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
CECUM	(10)	) FA 87	1	2 0 0 0 0	1.000 0.921 1.000
X-MALIGNANT LYMPHOMA	(165)	) FA 87	2	32 45 41 48 47	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	2 0 0 0 0	
CECUM	(10)	) FA 105	1	0 0 0 0 1	0.247 0.064 1.000
X-HISTIOCYTIC SARCOMA	(553)	) FA 105	2	16 28 18 29 29	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 0 0 1	
CERVICAL CORD	(11)	) IN 92-103	1	0 1 0 0 0	0.377 0.265 1.000
M-ASTROCYTOMA	(475)	) IN 92-103	2	13 11 12 13 8	
		FA 88	1	0 0 0 0 1	
		FA 88	2	36 47 44 53 49	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 1 0 0 1	
CERVICAL CORD	(11)	) FA 88	1	0 0 0 0 1	0.217 0.050 1.000
M-MIXED GLIOMA	(479)	) FA 88	2	36 47 44 53 49	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 0 0 1	
CERVICAL LYMPH	(12)	) FA 62	1	0 0 0 0 1	0.602 0.541 1.000
X-MALIGNANT LYMPHOMA	(163)	) FA 62	2	65 59 62 59 59	
		FA 84	1	1 0 0 0 0	
		FA 84	2	47 50 48 53 51	
		FA 87	1	1 0 0 0 0	
		FA 87	2	43 48 46 53 50	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	2 0 0 0 1	
COLON	(15)	) FA 87	1	1 0 0 0 0	1.000 0.844 1.000
X-MALIGNANT LYMPHOMA	(164)	) FA 87	2	30 42 39 47 45	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 0 0	
COLON	(15)	) FA 81	1	1 0 0 0 0	1.000 0.834 1.000
M-ADENOCARCINOMA	(263)	) FA 81	2	38 47 41 48 48	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 0 0	
DUODENUM	(16)	) IN 92-103	1	1 0 0 0 0	1.000 0.827 1.000
X-MALIGNANT LYMPHOMA	(272)	) IN 92-103	2	7 9 10 10 7	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1 0 0 0 0	
DUODENUM	(16)	) FA 105	1	0 0 0 0 1	0.241 0.061 1.000
X-HISTIOCYTIC SARCOMA	(386)	) FA 105	2	16 28 18 29 28	
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0 0 0 0 1	

EPIDIDYMIDES	(17	) FA 87	1	1	0	0	0	0	1.000	0.834	1.000
X-MALIGNANT LYMPHOMA	(274	) FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0			
ADRENAL CORTEX	(2	) FA 70	1	0	0	0	0	1	0.399	0.285	1.000
X-MALIGNANT LYMPHOMA	(226	) FA 70	2	63	57	60	58	56			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	48	53	51			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	1			
ADRENAL CORTEX	(2	) IN 53-78	1	0	0	1	0	0	0.662	0.637	0.997
B-CORTICAL ADENOMA	(264	) IN 53-78	2	9	7	11	6	8			
		IN 79-91	1	2	0	0	0	1			
		IN 79-91	2	19	8	12	2	10			
		IN 92-103	1	0	1	0	0	0			
		IN 92-103	2	13	11	12	13	8			
		IN 104-106	1	1	1	0	0	1			
		IN 104-106	2	20	33	29	39	32			
Spontaneous tumor pct: 4% in ctrl. - Total			-	3	2	1	0	2			
ADRENAL CORTEX	(2	) IN 92-103	1	1	0	0	0	0	0.352	0.242	1.000
X-HISTIOCYTIC SARCOMA	(325	) IN 92-103	2	12	12	12	13	8			
		FA 77	1	0	0	0	0	1			
		FA 77	2	58	55	56	54	54			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	1			
ADRENAL CORTEX	(2	) IN 104-106	1	0	1	0	0	0	1.000	0.847	1.000
M-CORTICAL CARCINOMA	(570	) IN 104-106	2	21	33	29	39	33			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0			
HARDERIAN GLAND	(21	) IN 104-106	1	0	0	1	1	0	0.534	0.512	1.000
M-SQUAMOUS CELL CARCINOMA	(577	) IN 104-106	2	21	34	28	38	33			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	1	0			
HEART	(22	) FA 62	1	0	0	0	0	1	0.754	0.713	1.000
X-MALIGNANT LYMPHOMA	(155	) FA 62	2	65	59	62	59	59			
		FA 83	1	1	0	0	0	0			
		FA 83	2	49	52	49	53	52			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	48	53	51			
		FA 87	1	1	0	0	0	0			
		FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: 2% in ctrl. - Total			-	3	0	0	0	1			
HEART	(22	) IN 92-103	1	0	2	0	0	0	0.591	0.559	0.995
M-ENDOCARDIAL SCHWANNOMA	(447	) IN 92-103	2	13	10	12	13	8			
		IN 104-106	1	1	1	1	1	2			
		IN 104-106	2	20	33	28	38	31			
Spontaneous tumor pct: 3% in ctrl. - Total			-	1	3	1	1	2			
ILEUM	(23	) FA 87	1	1	0	0	0	0	1.000	0.850	1.000
X-MALIGNANT LYMPHOMA	(166	) FA 87	2	28	40	38	47	46			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0			
ILEUM	(23	) FA 105	1	0	0	0	0	1	0.241	0.061	1.000
X-HISTIOCYTIC SARCOMA	(556	) FA 105	2	16	28	18	29	28			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1			

JEJUNUM	(24	) FA 105	1	0	0	0	0	1	
X-HISTIOCYTIC SARCOMA	(555	) FA 105	2	16	28	18	29	28	0.241 0.061 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
KIDNEYS	(25	) FA 62	1	0	0	0	0	1	0.602 0.541 1.000
X-MALIGNANT LYMPHOMA	(161	) FA 62	2	65	59	62	59	59	
		FA 84	1	1	0	0	0	0	
		FA 84	2	47	50	48	53	51	
		FA 87	1	1	0	0	0	0	
		FA 87	2	43	48	46	53	50	
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	0	0	0	1	
KIDNEYS	(25	) IN 92-103	1	0	1	0	0	0	1.000 0.812 1.000
M-LIPOSARCOMA	(35	) IN 92-103	2	13	11	12	13	8	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
KIDNEYS	(25	) FA 105	1	0	0	0	0	1	0.247 0.064 1.000
X-HISTIOCYTIC SARCOMA	(382	) FA 105	2	16	28	18	29	29	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
KIDNEYS	(25	) IN 104-106	1	0	0	0	0	1	0.211 0.048 1.000
B-TUBULAR CELL ADENOMA	(401	) IN 104-106	2	21	34	29	39	32	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
LIVER	(26	) FA 21	1	0	0	0	0	1	0.593 0.559 0.998
X-MALIGNANT LYMPHOMA	(113	) FA 21	2	65	64	65	65	64	
		FA 62	1	0	0	0	0	1	
		FA 62	2	65	59	62	59	59	
		FA 83	1	1	0	0	0	0	
		FA 83	2	49	52	49	53	52	
		FA 84	1	1	0	0	0	0	
		FA 84	2	47	50	48	53	51	
		FA 87	1	2	0	0	0	0	
		FA 87	2	42	48	46	53	50	
Spontaneous tumor pct: 3% in ctrl. - Total			-	4	0	0	0	2	
LIVER	(26	) IN 53-78	1	1	0	0	0	0	0.553 0.528 0.982
B-HEPATOCELLULAR ADENOMA	(159	) IN 53-78	2	8	7	12	6	8	
		IN 79-91	1	2	0	1	0	0	
		IN 79-91	2	18	8	11	2	11	
		IN 104-106	1	1	0	0	3	2	
		IN 104-106	2	20	34	29	36	31	
		FA 84	1	1	0	0	0	0	
		FA 84	2	47	50	48	53	51	
Spontaneous tumor pct: 4% in ctrl. - Total			-	5	0	1	3	2	
LIVER	(26	) IN 92-103	1	1	0	0	0	0	0.115 0.073 0.973
X-HISTIOCYTIC SARCOMA	(322	) IN 92-103	2	12	12	12	13	8	
		FA 77	1	0	0	0	0	1	
		FA 77	2	58	55	56	54	54	
		FA 89	1	0	0	0	1	0	
		FA 89	2	36	47	44	52	48	
		FA 105	1	0	0	0	0	1	
		FA 105	2	16	28	18	29	29	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	1	2	

LUMBAR CORD	(27	) FA 84	1	1	0	0	0	0	0	1.000 0.830 1.000
X-MALIGNANT LYMPHOMA	(225	) FA 84	2	47	49	48	53	51		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0	
LUMBAR CORD	(27	) IN 104-106	1	0	0	0	0	0	1	0.212 0.049 1.000
M-ASTROCYTOMA	(477	) IN 104-106	2	21	33	29	39	32		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1	
LUNG	(29	) FA 62	1	0	0	0	0	0	1	0.596 0.534 1.000
X-MALIGNANT LYMPHOMA	(154	) FA 62	2	65	59	62	59	59		
		FA 83	1	1	0	0	0	0	0	
		FA 83	2	49	52	49	53	52		
		FA 84	1	1	0	0	0	0	0	
		FA 84	2	47	50	48	53	51		
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	0	0	0	1	
LUNG	(29	) IN 92-103	1	1	0	0	0	0	0	0.115 0.073 0.973
X-HISTIOCYTIC SARCOMA	(321	) IN 92-103	2	12	12	12	13	8		
		FA 77	1	0	0	0	0	0	1	
		FA 77	2	58	55	56	54	54		
		FA 89	1	0	0	0	1	0		
		FA 89	2	36	47	44	52	48		
		FA 105	1	0	0	0	0	0	1	
		FA 105	2	16	28	18	29	29		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	1	2	
LUNG	(29	) IN 79-91	1	0	0	0	0	0	1	0.044 0.021 0.971
B-BRONCHIOALVEOLAR ADENOM	(379	) IN 79-91	2	21	8	12	2	10		
		IN 92-103	1	0	0	1	0	0		
		IN 92-103	2	13	12	11	13	8		
		IN 104-106	1	0	0	0	0	1		
		IN 104-106	2	21	34	29	39	32		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	2	
LUNG	(29	) IN 104-106	1	0	0	0	1	0		0.461 0.376 1.000
M-BRONCHIOALVEOLAR CARCIN	(406	) IN 104-106	2	21	34	29	38	33		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	1	0	
ADRENAL MEDULLA	(3	) IN 79-91	1	1	0	0	0	0	1	0.945 0.935 0.997
B-PHEOCHROMOCYTOMA	(338	) IN 79-91	2	20	8	12	2	10		
		IN 92-103	1	0	5	0	1	0		
		IN 92-103	2	13	7	12	12	8		
		IN 104-106	1	5	7	6	6	4		
		IN 104-106	2	16	27	23	33	29		
Spontaneous tumor pct: 14% in ctrl. - Total				-	6	12	6	7	5	
MAMMARY GLAND	(30	) IN 79-91	1	1	0	0	0	0	0	1.000 0.869 1.000
B-FIBROMA	(169	) IN 79-91	2	20	8	12	2	11		
		IN 92-103	1	1	0	0	0	0	0	
		IN 92-103	2	12	12	12	13	8		
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	0	0	0	0	
MAMMARY GLAND	(30	) IN 104-106	1	0	0	0	0	0	1	0.211 0.048 1.000
M-FIBROSARCOMA	(393	) IN 104-106	2	21	34	29	39	32		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1	

MAMMARY GLAND	(30	) IN 79-91	1	1	0	0	0	0	0	0.913 0.882 1.000	
B-FIBROADENOMA	(77	) IN 79-91	2	20	8	12	2	11			
		IN 92-103	1	0	1	0	0	0			
		IN 92-103	2	13	11	12	13	8			
		IN 104-106	1	1	0	1	1	0			
		IN 104-106	2	20	34	28	38	33			
Spontaneous tumor pct: 2% in ctrl. - Total				-	2	1	1	1	0		
MAMMARY GLAND	(30	) IN 79-91	1	0	0	0	0	0	1	0.535 0.476 0.999	
M-ADENOCARCINOMA	(96	) IN 79-91	2	21	8	12	2	10			
		IN 92-103	1	0	1	0	0	0			
		IN 92-103	2	13	11	12	13	8			
		IN 104-106	1	0	1	0	0	0			
		IN 104-106	2	21	33	29	39	33			
Spontaneous tumor pct: 2% in ctrl. - Total				-	0	2	0	0	1		
MESENTERIC LYMPH	(32	) FA 62	1	0	0	0	0	0	1	0.403 0.288 1.000	
X-MALIGNANT LYMPHOMA	(156	) FA 62	2	65	58	61	59	59			
		FA 84	1	1	0	0	0	0			
		FA 84	2	47	50	47	53	51			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	1		
MESENTERIC LYMPH	(32	) FA 77	1	0	0	0	0	0	1	0.198 0.040 1.000	
X-HISTIOCYTIC SARCOMA	(323	) FA 77	2	58	55	55	54	54			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	0	0	1		
MESENTERIC LYMPH	(32	) IN 92-103	1	0	1	0	0	0	0	1.000 0.812 1.000	
X-HEMANGIOMA	(616	) IN 92-103	2	13	11	12	13	8			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0		
MULTISYSTEMIC	(34	) FA 21	1	0	0	0	0	0	1	0.335 0.299 0.977	
M-MALIGNANT LYMPHOMA	(118	) FA 21	2	65	64	65	65	64			
		FA 62	1	0	0	0	0	0	1		
		FA 62	2	65	59	62	59	59			
		FA 70	1	0	0	0	0	0	1		
		FA 70	2	63	57	60	58	56			
		FA 83	1	1	0	0	0	0	0		
		FA 83	2	49	52	49	53	52			
		FA 84	1	1	0	0	0	0	0		
		FA 84	2	47	50	48	53	51			
		FA 87	1	2	0	0	0	0	0		
		FA 87	2	42	48	46	53	50			
Spontaneous tumor pct: 3% in ctrl. - Total				-	4	0	0	0	3		
MULTISYSTEMIC	(34	) IN 92-103	1	1	0	0	0	0	0		0.035 0.018 0.823
M-HISTIOCYTIC SARCOMA	(134	) IN 92-103	2	12	12	12	13	8			
		FA 55	1	0	0	0	0	0	1		
		FA 55	2	55	61	65	60	60			
		FA 77	1	0	0	0	0	0	1		
		FA 77	2	58	55	56	54	54			
		FA 89	1	0	0	0	1	0			
		FA 89	2	36	47	44	52	48			
		FA 105	1	0	0	0	0	0	1		
		FA 105	2	16	28	18	29	29			
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	1	3		

MULTISYSTEMIC	(34	) IN 92-103	1	0	1	0	0	0		1.000 0.812 1.000
B-HEMANGIOMA	(617	) IN 92-103	2	13	11	12	13	8		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0		
PANCREAS	(36	) IN 79-91	1	2	2	0	0	0		0.929 0.913 0.999
B-ISLET CELL ADENOMA	(145	) IN 79-91	2	19	5	12	2	11		
		IN 104-106	1	3	1	3	4	1		
		IN 104-106	2	18	33	26	35	32		
Spontaneous tumor pct: 6% in ctrl. - Total			-	5	3	3	4	1		
PANCREAS	(36	) FA 87	1	1	0	0	0	0		1.000 0.835 1.000
X-MALIGNANT LYMPHOMA	(167	) FA 87	2	42	47	46	53	49		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0		
PANCREAS	(36	) IN 53-78	1	0	0	0	1	0		0.317 0.302 1.000
B-ACINAR CELL ADENOMA	(287	) IN 53-78	2	9	7	12	5	7		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0		
PANCREAS	(36	) FA 77	1	0	0	0	0	1		0.048 0.010 0.989
X-HISTIOCYTIC SARCOMA	(324	) FA 77	2	57	54	56	54	53		
		FA 105	1	0	0	0	0	1		
		FA 105	2	16	28	18	29	29		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	2		
PANCREAS	(36	) IN 53-78	1	0	0	1	0	0		0.715 0.691 1.000
M-ISLET CELL CARCINOMA	(347	) IN 53-78	2	9	7	11	6	7		
		IN 104-106	1	0	0	0	1	0		
		IN 104-106	2	21	34	29	38	33		
		FA 93	1	1	0	0	0	0		
		FA 93	2	32	46	41	52	42		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	1	1	0		
PARATHYROID	(37	) IN 92-103	1	0	0	0	0	1		0.487 0.452 0.992
B-ADENOMA	(496	) IN 92-103	2	13	10	11	12	7		
		IN 104-106	1	0	1	3	2	0		
		IN 104-106	2	21	32	23	36	33		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	3	2	1		
PARATHYROID	(37	) FA 105	1	0	0	0	0	1		0.258 0.069 1.000
X-HISTIOCYTIC SARCOMA	(557	) FA 105	2	16	27	15	28	29		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1		
PITUITARY	(38	) FA 80	1	1	0	0	0	0		1.000 0.824 1.000
M-CARCINOMA	(100	) FA 80	2	52	54	51	53	53		
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0		

PITUITARY
B-ADENOMA

(38
(19

) IN 53-78	1	1	0	1	0	1
) IN 53-78	2	3	6	7	2	6
IN 79-91	1	6	0	1	1	3
IN 79-91	2	9	5	7	1	8
IN 92-103	1	0	2	4	1	1
IN 92-103	2	8	3	5	9	6
IN 104-106	1	11	12	10	5	4
IN 104-106	2	10	22	19	34	29
FA 60	1	0	0	1	0	0
FA 60	2	64	60	63	59	60
FA 65	1	1	0	0	1	0
FA 65	2	62	59	62	57	59
FA 66	1	0	0	0	0	1
FA 66	2	62	59	61	57	58
FA 70	1	0	0	1	0	0
FA 70	2	62	57	59	57	57
FA 71	1	2	1	0	0	0
FA 71	2	59	56	59	57	56
FA 75	1	0	0	0	1	0
FA 75	2	58	56	58	55	55
FA 76	1	1	0	0	2	0
FA 76	2	57	56	57	53	55
FA 77	1	1	0	0	0	0
FA 77	2	56	55	56	53	55
FA 78	1	0	0	2	0	0
FA 78	2	56	55	54	53	54
FA 79	1	0	0	1	0	0
FA 79	2	55	54	52	53	54
FA 80	1	0	0	1	0	0
FA 80	2	53	54	50	53	53
FA 81	1	1	1	1	0	0
FA 81	2	51	53	49	53	53
FA 82	1	0	1	0	0	0
FA 82	2	50	52	49	52	53
FA 83	1	1	0	0	0	0
FA 83	2	48	52	49	52	52
FA 85	1	0	1	0	0	0
FA 85	2	45	49	47	52	51
FA 86	1	2	0	0	0	0
FA 86	2	43	49	47	52	51
FA 87	1	2	0	0	0	0
FA 87	2	41	48	46	52	50
FA 91	1	0	0	1	0	0
FA 91	2	35	46	41	51	47
FA 93	1	1	1	0	0	0
FA 93	2	33	45	41	51	43
FA 94	1	1	0	0	0	0
FA 94	2	30	45	41	51	43
FA 95	1	0	0	1	0	0
FA 95	2	28	45	38	50	41
FA 96	1	0	1	0	0	0
FA 96	2	28	44	37	49	39
FA 97	1	0	1	0	0	0
FA 97	2	27	42	37	49	38
FA 98	1	0	0	0	0	1
FA 98	2	26	42	37	48	37
FA 99	1	0	1	0	0	0

1.000 1.000 1.000

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		FA 99	2	26	40	34	46	36	
		FA 100	1	0	1	0	1	0	
		FA 100	2	25	38	34	44	36	
		FA 101	1	1	0	0	0	0	
		FA 101	2	23	37	33	43	35	
		FA 102	1	1	1	0	0	0	
		FA 102	2	22	36	32	42	35	
		FA 103	1	0	1	2	1	0	
		FA 103	2	22	35	30	41	35	
Spontaneous tumor pct: 45%	in ctrl.	- Total	-	33	25	27	13	11	
PITUITARY	(38)	) FA 83	1	0	1	0	0	0	
M-GANGLIONEUROMA	(52)	) FA 83	2	49	51	49	52	52	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	1	0	0	0	
PROSTATE	(39)	) FA 62	1	0	0	0	0	1	
X-MALIGNANT LYMPHOMA	(168)	) FA 62	2	65	59	62	59	59	
		FA 87	1	2	0	0	0	0	
		FA 87	2	42	48	46	53	50	
Spontaneous tumor pct: 2%	in ctrl.	- Total	-	2	0	0	0	1	
PROSTATE	(39)	) FA 67	1	0	0	1	0	0	
M-CARCINOMA	(238)	) FA 67	2	63	59	60	58	58	
		FA 78	1	1	0	0	0	0	
		FA 78	2	56	55	56	54	54	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	1	0	1	0	0	
PROSTATE	(39)	) FA 77	1	0	0	0	0	1	
X-HISTIOCYTIC SARCOMA	(326)	) FA 77	2	58	55	56	54	54	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	0	0	0	1	
SALIVARY GLAND	(40)	) FA 62	1	0	0	0	0	1	
X-MALIGNANT LYMPHOMA	(211)	) FA 62	2	65	58	62	59	59	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	0	0	0	1	
SEMINAL VESICLE	(42)	) FA 77	1	0	0	0	0	1	
X-HISTIOCYTIC SARCOMA	(327)	) FA 77	2	47	49	52	49	54	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	0	0	0	1	
SKIN	(44)	) IN 53-78	1	0	0	0	0	1	
X-HISTIOCYTIC SARCOMA	(132)	) IN 53-78	2	9	7	12	6	7	
		IN 79-91	1	0	0	0	1	0	
		IN 79-91	2	21	8	12	1	11	
		IN 92-103	1	1	0	0	0	0	
		IN 92-103	2	12	12	12	13	8	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	1	0	0	1	1	
SKIN	(44)	) IN 79-91	1	0	0	0	1	0	
M-MYXOSARCOMA	(140)	) IN 79-91	2	21	8	12	1	11	
		IN 92-103	1	0	0	0	1	0	
		IN 92-103	2	13	12	12	12	8	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	0	0	2	0	
SKIN	(44)	) IN 79-91	1	0	1	0	0	0	
M-NEUROFIBROSARCOMA	(204)	) IN 79-91	2	21	7	12	2	11	
Spontaneous tumor pct: <= 1%	in ctrl.	- Total	-	0	1	0	0	0	

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1.000 0.827 1.000

0.607 0.545 1.000

0.834 0.796 1.000

0.197 0.039 1.000

0.197 0.039 1.000

0.218 0.048 1.000

0.226 0.176 0.998

0.321 0.207 1.000

1.000 0.763 1.000

SKIN	(44	)	IN 53-78	1	1	0	0	0	0		
B-FIBROMA	(268	)	IN 53-78	2	8	7	12	6	8	1.000	0.999 1.000
			IN 79-91	1	2	0	1	0	0		
			IN 79-91	2	19	8	11	2	11		
			IN 92-103	1	1	1	0	0	0		
			IN 92-103	2	12	11	12	13	8		
			IN 104-106	1	3	6	4	1	0		
			IN 104-106	2	18	28	25	38	33		
Spontaneous tumor pct: 11% in ctrl. - Total				-	7	7	5	1	0		
SKIN	(44	)	IN 79-91	1	1	0	0	0	0	1.000	0.763 1.000
X-MALIGNANT LYMPHOMA	(277	)	IN 79-91	2	20	8	12	2	11		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0		
SKIN	(44	)	IN 79-91	1	0	0	1	0	0	0.174	0.139 0.997
B-KERATOACANTHOMA	(310	)	IN 79-91	2	21	8	11	2	11		
			IN 104-106	1	0	0	0	1	1		
			IN 104-106	2	21	34	29	38	32		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	1	1		
SKIN	(44	)	IN 79-91	1	1	0	0	0	0	0.944	0.926 0.999
B-LIPOMA	(380	)	IN 79-91	2	20	8	12	2	11		
			IN 92-103	1	2	0	1	1	0		
			IN 92-103	2	11	12	11	12	8		
			IN 104-106	1	2	3	1	2	1		
			IN 104-106	2	19	31	28	37	32		
Spontaneous tumor pct: 6% in ctrl. - Total				-	5	3	2	3	1		
SKIN	(44	)	IN 0-52	1	0	1	0	0	0	0.914	0.882 1.000
M-FIBROSARCOMA	(41	)	IN 0-52	2	0	3	0	5	3		
			IN 79-91	1	2	0	0	0	0		
			IN 79-91	2	19	8	12	2	11		
			IN 92-103	1	0	0	0	1	0		
			IN 92-103	2	13	12	12	12	8		
			IN 104-106	1	0	1	0	1	0		
			IN 104-106	2	21	33	29	38	33		
Spontaneous tumor pct: 3% in ctrl. - Total				-	2	2	0	2	0		
SKIN	(44	)	IN 79-91	1	0	0	1	0	0	0.463	0.528 1.000
B-TRICHOEPITHELIOMA	(484	)	IN 79-91	2	21	8	11	2	11		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	0	0		
SKIN	(44	)	IN 92-103	1	0	0	0	1	0	0.695	0.642 1.000
M-RHABDOMYOSARCOMA	(501	)	IN 92-103	2	13	12	12	12	8		
			IN 104-106	1	0	1	0	0	0		
			IN 104-106	2	21	33	29	39	33		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	1	0		
SKIN	(44	)	IN 53-78	1	0	1	0	0	0	1.000	0.819 1.000
M-BASAL CELL CARCINOMA	(520	)	IN 53-78	2	9	6	12	6	8		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0		
SKIN	(44	)	IN 92-103	1	0	1	0	0	1	0.307	0.266 0.993
B-BASAL CELL TUMOR	(524	)	IN 92-103	2	13	11	12	13	7		
			IN 104-106	1	0	0	1	2	0		
			IN 104-106	2	21	34	28	37	33		
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	1	2	1		

SKIN	(44	)	IN 79-91	1	0	0	0	0	1	0.507	0.461	0.999
B-SEBACEOUS GLAND ADENOMA	(525	)	IN 79-91	2	21	8	12	2	10			
			IN 104-106	1	1	0	2	0	0			
			IN 104-106	2	20	34	27	39	33			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	2	0	1			
SKIN	(44	)	IN 104-106	1	3	3	3	1	0	0.995	0.987	1.000
B-SQUAMOUS CELL PAPILLOMA	(531	)	IN 104-106	2	18	31	26	38	33			
Spontaneous tumor pct: 5% in ctrl.	-	Total	-	-	3	3	3	1	0			
SPLEEN	(46	)	FA 21	1	0	0	0	0	1	0.036	0.016	0.885
X-MALIGNANT LYMPHOMA	(114	)	FA 21	2	65	63	64	64	64			
			FA 62	1	0	0	0	0	1			
			FA 62	2	65	58	61	58	59			
			FA 70	1	0	0	0	0	1			
			FA 70	2	63	56	59	57	56			
			FA 84	1	1	0	0	0	0			
			FA 84	2	47	49	48	52	51			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	0	0	3			
SPLEEN	(46	)	IN 92-103	1	0	1	0	0	0	1.000	0.808	1.000
M-FIBROSARCOMA	(548	)	IN 92-103	2	13	11	12	12	8			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	1	0	0	0			
SQUAMOUS STOMACH	(47	)	FA 87	1	1	0	0	0	0	1.000	0.834	1.000
X-MALIGNANT LYMPHOMA	(271	)	FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	0	0	0			
STOMACH	(48	)	IN 92-103	1	1	0	0	0	0	1.000	0.819	1.000
X-MALIGNANT LYMPHOMA	(389	)	IN 92-103	2	10	12	12	13	8			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	0	0	0			
TESTES	(49	)	FA 55	1	0	0	0	0	1	0.195	0.038	1.000
X-HISTIOCYTIC SARCOMA	(133	)	FA 55	2	65	61	65	60	60			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	0	0	0	0	1			
TESTES	(49	)	IN 79-91	1	2	0	0	0	1	0.004	0.002	0.086
B-INTERSTITIAL CELL ADENO	(158	)	IN 79-91	2	19	8	12	2	10			
			IN 92-103	1	0	0	0	1	1			
			IN 92-103	2	13	12	12	12	7			
			IN 104-106	1	1	4	0	7	8			
			IN 104-106	2	20	30	29	32	25			
Spontaneous tumor pct: 5% in ctrl.	-	Total	-	-	3	4	0	8	10	(Exact	P<0.005)	
TESTES	(49	)	FA 87	1	1	0	0	0	0	1.000	0.834	1.000
X-MALIGNANT LYMPHOMA	(273	)	FA 87	2	43	48	46	53	50			
Spontaneous tumor pct: <= 1% in ctrl.	-	Total	-	-	1	0	0	0	0			

THYMUS	(51	) FA 62	1	0	0	0	0	1	
X-MALIGNANT LYMPHOMA	(152	) FA 62	2	63	55	59	56	55	0.861 0.827 1.000
		FA 83	1	1	0	0	0	0	
		FA 83	2	47	49	46	50	50	
		FA 84	1	1	0	0	0	0	
		FA 84	2	45	47	45	50	49	
		FA 87	1	2	0	0	0	0	
		FA 87	2	40	45	43	50	48	
Spontaneous tumor pct: 3% in ctrl. - Total			-	4	0	0	0	1	
THYMUS	(51	) FA 72	1	0	0	0	1	0	
M-THYMOMA	(193	) FA 72	2	57	53	56	54	53	0.671 0.639 1.000
		FA 76	1	0	1	0	0	0	
		FA 76	2	57	52	54	53	52	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	1	0	
THYMUS	(51	) FA 89	1	0	0	0	1	0	
X-HISTIOCYTIC SARCOMA	(384	) FA 89	2	34	44	41	49	46	0.446 0.372 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0	
THYROIDIS	(52	) IN 79-91	1	1	1	0	0	0	
B-FOLLICULAR CELL ADENOMA	(157	) IN 79-91	2	20	6	11	2	11	0.898 0.863 1.000
		IN 104-106	1	0	1	0	1	0	
		IN 104-106	2	21	33	29	38	33	
Spontaneous tumor pct: 2% in ctrl. - Total			-	1	2	0	1	0	
THYROIDIS	(52	) IN 53-78	1	1	0	0	0	0	
B-C-CELL ADENOMA	(248	) IN 53-78	2	8	7	10	6	5	0.819 0.802 0.989
		IN 79-91	1	1	0	0	0	0	
		IN 79-91	2	20	7	11	2	11	
		IN 92-103	1	2	2	1	2	0	
		IN 92-103	2	9	8	10	11	8	
		IN 104-106	1	4	3	1	4	4	
		IN 104-106	2	17	31	28	35	29	
Spontaneous tumor pct: 10% in ctrl. - Total			-	8	5	2	6	4	
THYROIDIS	(52	) IN 92-103	1	1	0	0	0	1	
M-FOLLICULAR CELL CARCINO	(289	) IN 92-103	2	10	10	11	12	7	0.393 0.351 0.992
		IN 104-106	1	0	1	0	0	1	
		IN 104-106	2	21	33	29	39	32	
		FA 87	1	1	0	0	0	0	
		FA 87	2	41	45	45	53	50	
		FA 95	1	0	0	0	1	0	
		FA 95	2	27	44	38	50	41	
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	1	0	1	2	
URINARY BLADDER	(56	) FA 87	1	1	0	0	0	0	
X-MALIGNANT LYMPHOMA	(275	) FA 87	2	42	46	45	52	50	1.000 0.836 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0	
URINARY BLADDER	(56	) FA 89	1	0	0	0	1	0	
X-HISTIOCYTIC SARCOMA	(427	) FA 89	2	35	45	43	51	48	0.448 0.374 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0	

BONE MARROW	(7	) FA 21	1	0	0	0	0	1	
X-MALIGNANT LYMPHOMA	(116	) FA 21	2	65	64	65	65	64	0.205 0.167 0.961
		FA 62	1	0	0	0	0	1	
		FA 62	2	65	59	62	59	59	
		FA 70	1	0	0	0	0	1	
		FA 70	2	63	57	60	58	56	
		FA 83	1	1	0	0	0	0	
		FA 83	2	49	52	49	53	52	
		FA 84	1	1	0	0	0	0	
		FA 84	2	47	50	48	53	51	
		FA 87	1	1	0	0	0	0	
		FA 87	2	43	48	46	53	50	
Spontaneous tumor pct: 2% in ctrl. - Total			-	3	0	0	0	3	
BONE MARROW	(7	) FA 77	1	0	0	0	0	1	
X-HISTIOCYTIC SARCOMA	(328	) FA 77	2	58	55	56	54	54	0.197 0.039 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
BRAIN	(9	) FA 62	1	0	0	0	0	1	
X-MALIGNANT LYMPHOMA	(153	) FA 62	2	65	59	62	59	59	0.600 0.539 1.000
		FA 83	1	1	0	0	0	0	
		FA 83	2	49	52	49	53	52	
		FA 87	1	1	0	0	0	0	
		FA 87	2	43	48	46	53	50	
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	0	0	0	1	
BRAIN	(9	) IN 104-106	1	0	2	0	2	1	
M-ASTROCYTOMA	(48	) IN 104-106	2	21	32	29	37	32	0.487 0.455 0.983
		FA 43	1	0	1	0	0	0	
		FA 43	2	65	62	65	63	63	
		FA 81	1	0	0	0	1	0	
		FA 81	2	53	54	50	53	53	
		FA 88	1	0	0	0	0	1	
		FA 88	2	36	47	44	53	49	
		FA 103	1	0	1	0	0	0	
		FA 103	2	22	35	32	42	35	
Spontaneous tumor pct: 3% in ctrl. - Total			-	0	4	0	3	2	
BRAIN	(9	) IN 104-106	1	0	0	0	0	1	
B-LIPOMA	(573	) IN 104-106	2	21	34	29	39	32	0.211 0.048 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
BRAIN	(9	) FA 86	1	0	0	0	0	1	
M-UNDIFFERENTIATED GLIOMA	(624	) FA 86	2	46	49	47	53	50	0.207 0.045 1.000
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	

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Appendix 2: Analysis of Carcinogenic Potential in Female Rat
 Test of Dose-Response (Tumor) Positive Linear Trend
 Study No.

Run Date & Time: June 4, 1999 (15:56)

Source: C:\NDAS\RAPCARC\RAT103\st95103.lis

Note: Dose Levels Included: CTRL1 CTRL2 LOW MED HIGH (0 0 0.05 0.1 0.2)
 Missing value in Tumor-Caused Death is treated as tumor not causing death
 Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLES-----	EXACT ASYMP ASYMP PROB PROB PROB /CONT CORR =P(STAT .GE. OBSERVED)
CERVICAL LYMPH	(12	) FA 96	1	0 1 0 0 0	1.000 0.832 1.000
X-HISTIOCYTIC SARCOMA	(335	) FA 96	2	28 29 35 32 30	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 1 0 0 0	
CERVIX	(13	) IN 53-78	1	0 0 0 1 0	0.125 0.094 0.927
B-FIBROMA	(291	) IN 53-78	2	15 13 11 11 10	
		IN 79-91	1	0 0 0 1 0	
		IN 79-91	2	16 15 10 12 16	
		IN 92-103	1	0 0 0 2 0	
		IN 92-103	2	19 14 28 13 15	
		IN 104-106	1	0 0 1 0 1	
		IN 104-106	2	15 20 14 21 19	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 0 1 4 1	
CERVIX	(13	) FA 80	1	0 0 0 0 1	0.390 0.281 1.000
X-HISTIOCYTIC SARCOMA	(340	) FA 80	2	50 48 53 48 48	
		FA 92	1	0 1 0 0 0	
		FA 92	2	34 33 43 36 35	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 1 0 0 1	
CERVIX	(13	) IN 92-103	1	1 0 1 0 0	0.693 0.671 1.000
M-STROMAL SARCOMA	(468	) IN 92-103	2	18 14 27 15 15	
		IN 104-106	1	0 0 0 1 0	
		IN 104-106	2	15 20 15 20 20	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	1 0 1 1 0	
CERVIX	(13	) IN 92-103	1	0 0 1 0 0	0.637 0.584 1.000
M-GRANULAR CELL TUMOR	(628	) IN 92-103	2	19 14 27 15 15	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 0 1 0 0	
COLON	(15	) FA 89	1	0 0 0 0 1	0.176 0.031 1.000
M-SCHWANNOMA	(473	) FA 89	2	42 35 45 37 33	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 0 0 0 1	
DUODENUM	(16	) FA 78	1	0 1 0 0 0	1.000 0.824 1.000
M-LEIOMYOSARCOMA	(293	) FA 78	2	51 48 52 48 51	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 1 0 0 0	
DUODENUM	(16	) FA 96	1	0 1 0 0 0	1.000 0.827 1.000
X-HISTIOCYTIC SARCOMA	(386	) FA 96	2	29 29 36 31 28	
Spontaneous tumor pct: <= 1% in ctrl. - Total	-	-	-	0 1 0 0 0	

ADRENAL CORTEX	(2	)	IN 79-91	1	0	1	0	1	0	0.814	0.787	0.999
B-CORTICAL ADENOMA	(264	)	IN 79-91	2	16	14	10	12	16			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	19	13	28	15	15			
			IN 104-106	1	1	0	1	2	0			
			IN 104-106	2	14	20	14	19	20			
Spontaneous tumor pct: 2%			in ctrl. - Total	-	1	2	1	3	0			
ADRENAL CORTEX	(2	)	IN 104-106	1	0	0	0	1	0	0.450	0.373	1.000
M-CORTICAL CARCINOMA	(570	)	IN 104-106	2	15	20	15	20	20			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	0	0	0	1	0			
HEART	(22	)	FA 92	1	0	1	0	0	0	1.000	0.830	1.000
X-HISTIOCYTIC SARCOMA	(443	)	FA 92	2	34	33	43	36	35			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	0	1	0	0	0			
HEART	(22	)	IN 79-91	1	2	0	0	0	0	0.791	0.759	0.999
M-ENDOCARDIAL SCHWANNOMA	(447	)	IN 79-91	2	14	15	10	13	16			
			IN 92-103	1	0	1	0	0	0			
			IN 92-103	2	19	13	28	15	15			
			IN 104-106	1	1	0	0	1	0			
			IN 104-106	2	14	20	15	20	19			
			FA 105	1	0	0	0	0	1			
			FA 105	2	15	20	15	21	19			
Spontaneous tumor pct: 3%			in ctrl. - Total	-	3	1	0	1	1			
JEJUNUM	(24	)	IN 92-103	1	0	1	0	0	0	1.000	0.819	1.000
M-LEIOMYOSARCOMA	(521	)	IN 92-103	2	18	11	27	13	11			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	0	1	0	0	0			
KIDNEYS	(25	)	FA 68	1	1	0	0	0	0	1.000	0.822	1.000
M-LIPOsarcoma	(35	)	FA 68	2	59	57	57	56	57			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	1	0	0	0	0			
KIDNEYS	(25	)	FA 96	1	0	1	0	0	0	1.000	0.912	1.000
X-HISTIOCYTIC SARCOMA	(382	)	FA 96	2	29	30	36	32	30			
			FA 104	1	0	1	0	0	0			
			FA 104	2	20	24	27	24	24			
Spontaneous tumor pct: 2%			in ctrl. - Total	-	0	2	0	0	0			
KIDNEYS	(25	)	IN 79-91	1	1	0	0	0	0	1.000	0.816	1.000
B-TUBULAR CELL ADENOMA	(401	)	IN 79-91	2	15	15	10	13	16			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	1	0	0	0	0			
KIDNEYS	(25	)	FA 89	1	0	0	1	0	0	0.605	0.597	1.000
M-RENAL MESENCHYMAL TUMOR	(485	)	FA 89	2	43	39	46	40	39			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	0	0	1	0	0			
KIDNEYS	(25	)	IN 104-106	1	0	0	0	0	1	0.219	0.051	1.000
B-LIPOMA	(581	)	IN 104-106	2	15	20	15	21	19			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	0	0	0	0	1			
LIVER	(26	)	IN 104-106	1	1	0	0	1	0	0.726	0.680	1.000
B-HEPATOCELLULAR ADENOMA	(159	)	IN 104-106	2	14	20	15	20	20			
Spontaneous tumor pct: <= 1%			in ctrl. - Total	-	1	0	0	1	0			

LIVER	(26	) FA 75	1	1	0	0	0	0	1.000	0.826	1.000
M-HEPATOCELLULAR CARCINOM	(218	) FA 75	2	53	53	54	54	54			
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	1	0	0	0	0			

LIVER	(26	) IN 104-106	1	1	0	0	0	0	0.621	0.592	0.997
X-HISTIOCYTIC SARCOMA	(322	) IN 104-106	2	14	20	15	21	20			

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	FA 70	1	0	0	1	0	0
	FA 70	2	57	57	56	56	57
	FA 79	1	0	0	0	0	1
	FA 79	2	50	49	53	49	50
	FA 80	1	0	0	0	0	1
	FA 80	2	50	48	53	48	48
	FA 92	1	0	1	0	0	0
	FA 92	2	34	33	43	36	35
	FA 96	1	0	1	0	0	0
	FA 96	2	29	30	36	32	30
	FA 104	1	0	1	0	0	0
	FA 104	2	20	24	27	24	24
Spontaneous tumor pct: 3% in ctrl. - Total		-	1	3	1	0	2

LUNG	(29	) FA 79	1	0	0	0	0	1	0.263	0.211	0.994
X-HISTIOCYTIC SARCOMA	(321	) FA 79	2	50	49	53	49	50			

	FA 80	1	0	0	0	0	1
	FA 80	2	50	48	53	48	48
	FA 92	1	0	1	0	0	0
	FA 92	2	34	33	43	36	35
	FA 104	1	0	1	0	0	0
	FA 104	2	20	24	27	24	24
Spontaneous tumor pct: 2% in ctrl. - Total		-	0	2	0	0	2

LUNG	(29	) IN 79-91	1	1	0	0	0	0	1.000	0.816	1.000
B-BRONCHIOALVEOLAR ADENOM	(379	) IN 79-91	2	15	15	10	13	16			
Spontaneous tumor pct: <= 1% in ctrl. - Total		-	1	0	0	0	0				

LUNG	(29	) IN 79-91	1	1	0	0	0	0	1.000	0.816	1.000
M-BRONCHIOALVEOLAR CARCIN	(406	) IN 79-91	2	15	15	10	13	16			
Spontaneous tumor pct: <= 1% in ctrl. - Total		-	1	0	0	0	0				

LUNG	(29	) IN 92-103	1	0	1	0	0	0	1.000	0.825	1.000
M-MESOTHELIOMA	(620	) IN 92-103	2	19	13	28	15	15			
Spontaneous tumor pct: <= 1% in ctrl. - Total		-	0	1	0	0	0				

ADRENAL MEDULLA	(3	) IN 79-91	1	0	0	0	0	1	0.633	0.596	0.999
B-PHEOCHROMOCYTOMA	(338	) IN 79-91	2	16	15	10	13	15			

	IN 92-103	1	0	1	0	0	0
	IN 92-103	2	19	13	28	15	15
	IN 104-106	1	1	0	1	0	0
	IN 104-106	2	14	20	14	21	20
Spontaneous tumor pct: 2% in ctrl. - Total		-	1	1	1	0	1

MAMMARY GLAND	(30	)	IN 53-78	1	1	0	0	0	0	0.992 0.983 1.000
B-FIBROMA	(169	)	IN 53-78	2	14	13	11	12	10	
			IN 79-91	1	1	1	1	0	0	
			IN 79-91	2	15	14	9	13	16	
			IN 92-103	1	0	1	2	0	0	
			IN 92-103	2	19	13	26	15	15	
			IN 104-106	1	0	3	1	1	0	
			IN 104-106	2	15	17	14	20	20	
Spontaneous tumor pct: 5% in ctrl. - Total				-	2	5	4	1	0	
MAMMARY GLAND	(30	)	IN 53-78	1	1	0	0	0	0	0.754 0.708 0.999
B-LIPOMA	(187	)	IN 53-78	2	14	13	11	12	10	
			IN 79-91	1	0	0	0	0	1	
			IN 79-91	2	16	15	10	13	15	
			IN 104-106	1	0	2	0	0	0	
			IN 104-106	2	15	18	15	21	20	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1	2	0	0	1	
MAMMARY GLAND	(30	)	IN 79-91	1	1	0	0	0	0	1.000 0.908 1.000
M-FIBROSARCOMA	(393	)	IN 79-91	2	15	15	10	13	16	
			IN 104-106	1	0	1	0	0	0	
			IN 104-106	2	15	19	15	21	20	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1	1	0	0	0	
MAMMARY GLAND	(30	)	IN 79-91	1	1	0	0	0	0	1.000 0.816 1.000
B-ADENOLIPOMA	(404	)	IN 79-91	2	15	15	10	13	16	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0	
MAMMARY GLAND	(30	)	IN 79-91	1	0	1	0	0	0	0.839 0.793 1.000
M-NEUROFIBROSARCOMA	(491	)	IN 79-91	2	16	14	10	13	16	
			IN 92-103	1	0	0	1	0	0	
			IN 92-103	2	19	14	27	15	15	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	1	0	0	
MAMMARY GLAND	(30	)	IN 0-52	1	0	0	1	2	0	0.999 0.999 1.000
B-FIBROADENOMA	(77	)	IN 0-52	2	0	3	0	2	4	
			IN 53-78	1	6	4	3	3	3	
			IN 53-78	2	9	9	8	9	7	
			IN 79-91	1	12	8	4	4	3	
			IN 79-91	2	4	7	6	9	13	
			IN 92-103	1	14	10	20	7	8	
			IN 92-103	2	5	4	8	8	7	
			IN 104-106	1	9	11	6	15	7	
			IN 104-106	2	6	9	9	6	13	
Spontaneous tumor pct: 57% in ctrl. - Total				-	41	33	34	31	21	
MAMMARY GLAND	(30	)	IN 0-52	1	0	0	0	2	1	0.981 0.978 0.998
M-ADENOCARCINOMA	(96	)	IN 0-52	2	0	3	1	2	3	
			IN 53-78	1	4	6	4	3	1	
			IN 53-78	2	11	7	7	9	9	
			IN 79-91	1	8	3	1	2	2	
			IN 79-91	2	8	12	9	11	14	
			IN 92-103	1	4	3	7	3	2	
			IN 92-103	2	15	11	21	12	13	
			IN 104-106	1	5	4	3	4	4	
			IN 104-106	2	10	16	12	17	16	
Spontaneous tumor pct: 28% in ctrl. - Total				-	21	16	15	14	10	

MAMMARY GLAND
B-ADENOMA

(30	) IN 0-52	1	0	0	0	0	1
(98	) IN 0-52	2	0	3	1	4	3
	IN 53-78	1	0	2	2	2	0
	IN 53-78	2	15	11	9	10	10
	IN 79-91	1	4	6	4	2	1
	IN 79-91	2	12	9	6	11	15
	IN 92-103	1	2	2	3	1	3
	IN 92-103	2	17	12	25	14	12
	IN 104-106	1	2	4	2	1	6
	IN 104-106	2	13	16	13	20	14
Spontaneous tumor pct: 17% in ctrl. - Total			-	8	14	11	6 11

0.658 0.643 0.918

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MESENTERIC LYMPH
X-HISTIOCYTIC SARCOMA

(32	) FA 92	1	0	1	0	0	0
(323	) FA 92	2	34	33	43	36	34
	FA 96	1	0	1	0	0	0
	FA 96	2	29	30	36	32	29
Spontaneous tumor pct: 2% in ctrl. - Total			-	0	2	0	0 0

1.000 0.910 1.000

MULTISYSTEMIC
M-MALIGNANT LYMPHOMA
Spontaneous tumor pct: <= 1% in ctrl. - Total

(34	) IN 104-106	1	0	0	0	0	1
(118	) IN 104-106	2	15	20	15	21	19
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0 1

0.219 0.051 1.000

MULTISYSTEMIC
M-HISTIOCYTIC SARCOMA

(34	) IN 104-106	1	1	0	0	0	0
(134	) IN 104-106	2	14	20	15	21	20
	FA 70	1	0	0	1	0	0
	FA 70	2	57	57	56	56	57
	FA 79	1	0	0	0	0	1
	FA 79	2	50	49	53	49	50
	FA 80	1	0	0	0	0	1
	FA 80	2	50	48	53	48	48
	FA 92	1	0	1	0	0	0
	FA 92	2	34	33	43	36	35
	FA 96	1	0	1	0	0	0
	FA 96	2	29	30	36	32	30
	FA 104	1	0	1	0	0	0
	FA 104	2	20	24	27	24	24
Spontaneous tumor pct: 3% in ctrl. - Total			-	1	3	1	0 2

0.621 0.592 0.997

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ON ORIGINAL

OVARIES
B-THECOMA

(35	) IN 79-91	1	0	0	0	1	0
(392	) IN 79-91	2	16	15	10	12	16
	IN 92-103	1	0	0	1	0	0
	IN 92-103	2	19	14	27	15	15
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	0 0

0.467 0.448 1.000

PANCREAS
B-ISLET CELL ADENOMA

(36	) IN 92-103	1	1	0	2	0	0
(145	) IN 92-103	2	18	14	26	15	15
	IN 104-106	1	1	1	0	0	0
	IN 104-106	2	14	19	15	21	20
Spontaneous tumor pct: 2% in ctrl. - Total			-	2	1	2	0 0

0.970 0.937 1.000

PANCREAS
B-ACINAR CELL ADENOMA

(36	) IN 79-91	1	0	0	0	1	0
(287	) IN 79-91	2	16	15	10	12	16
	IN 92-103	1	0	0	1	0	0
	IN 92-103	2	19	14	27	15	15
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	0 0

0.467 0.448 1.000

PANCREAS	(36	) FA 92	1	0	1	0	0	0	
X-HISTIOCYTIC SARCOMA	(324	) FA 92	2	34	33	43	36	35	1.000 0.911 1.000
		FA 96	1	0	1	0	0	0	
		FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0	2	0	0	0	

PANCREAS	(36	) IN 79-91	1	1	0	0	0	0	
M-ISLET CELL CARCINOMA	(347	) IN 79-91	2	15	15	10	13	16	1.000 0.816 1.000
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	1	0	0	0	0	

PARATHYROID	(37	) IN 92-103	1	1	0	1	0	0	
B-ADENOMA	(496	) IN 92-103	2	17	14	26	12	12	0.955 0.927 1.000
		IN 104-106	1	1	2	0	1	0	
		IN 104-106	2	14	18	13	18	18	
Spontaneous tumor pct: 3%		in ctrl. - Total	-	2	2	1	1	0	

PITUITARY	(38	) IN 92-103	1	0	1	0	0	0	
M-CARCINOMA	(100	) IN 92-103	2	19	13	26	14	15	0.206 0.179 0.868
		IN 104-106	1	0	0	0	1	2	
		IN 104-106	2	15	20	15	20	18	
		FA 60	1	0	0	0	1	0	
		FA 60	2	63	60	60	58	59	
		FA 80	1	0	1	0	0	0	
		FA 80	2	50	47	53	48	48	
		FA 81	1	0	1	0	0	0	
		FA 81	2	50	46	53	46	45	
		FA 89	1	0	0	0	0	1	
		FA 89	2	43	39	47	40	38	
		FA 98	1	0	0	1	0	0	
		FA 98	2	28	27	33	31	28	
		FA 100	1	0	0	1	0	0	
		FA 100	2	26	27	29	28	26	
		FA 104	1	0	0	0	1	0	
		FA 104	2	20	25	27	23	24	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	0	3	2	3	3	

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PITUITARY	(38	) IN 0-52	1	0	0	0	1	0	
B-ADENOMA	(19	) IN 0-52	2	0	1	1	2	2	0.539 0.532 0.724
		IN 53-78	1	3	2	2	4	1	
		IN 53-78	2	3	2	1	2	3	
		IN 79-91	1	6	2	0	0	4	
		IN 79-91	2	1	3	1	1	3	
		IN 92-103	1	7	4	13	1	5	
		IN 92-103	2	4	6	6	5	3	
		IN 104-106	1	10	13	10	13	15	
		IN 104-106	2	5	7	5	8	5	
		FA 38	1	0	1	0	0	0	
		FA 38	2	64	63	65	63	64	
		FA 43	1	0	0	0	0	1	
		FA 43	2	64	63	65	63	63	
		FA 47	1	0	1	0	0	0	
		FA 47	2	64	62	65	63	62	
		FA 49	1	0	0	0	0	1	
		FA 49	2	64	62	65	63	61	
		FA 51	1	0	0	0	1	0	
		FA 51	2	64	62	65	61	61	
		FA 53	1	0	0	1	0	0	

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FA 53	2	64 62 63 61 60
FA 55	1	0 1 1 0 0
FA 55	2	63 61 62 61 60
FA 57	1	0 0 1 0 1
FA 57	2	63 61 61 60 59
FA 58	1	0 1 0 0 0
FA 58	2	63 60 61 60 59
FA 59	1	0 0 1 1 0
FA 59	2	63 60 60 59 59
FA 60	1	1 1 0 0 0
FA 60	2	62 59 60 59 59
FA 61	1	1 0 0 0 0
FA 61	2	61 59 59 58 59
FA 63	1	0 1 1 0 0
FA 63	2	61 57 57 58 57
FA 65	1	0 0 0 1 0
FA 65	2	61 57 57 57 57
FA 67	1	0 0 0 1 0
FA 67	2	59 57 57 56 57
FA 69	1	1 0 0 0 0
FA 69	2	58 57 57 56 56
FA 70	1	1 0 0 0 1
FA 70	2	56 57 57 56 55
FA 71	1	0 1 0 0 0
FA 71	2	55 56 56 56 55
FA 72	1	0 1 0 1 2
FA 72	2	55 54 56 55 53
FA 73	1	1 0 1 0 0
FA 73	2	54 54 55 55 53
FA 74	1	0 0 1 0 0
FA 74	2	54 54 54 55 53
FA 75	1	0 2 0 0 0
FA 75	2	54 51 54 54 53
FA 76	1	2 0 0 0 0
FA 76	2	51 51 54 53 53
FA 77	1	0 1 1 1 0
FA 77	2	51 50 53 50 53
FA 78	1	1 0 0 1 2
FA 78	2	50 50 53 49 51
FA 79	1	0 0 0 1 1
FA 79	2	50 49 53 48 49
FA 80	1	0 0 0 2 2
FA 80	2	50 48 53 46 46
FA 81	1	0 0 0 0 1
FA 81	2	50 47 53 46 44
FA 82	1	0 3 1 2 1
FA 82	2	49 43 52 44 42
FA 83	1	1 0 1 1 0
FA 83	2	48 43 51 43 42
FA 84	1	0 3 0 0 0
FA 84	2	46 40 51 42 42
FA 85	1	0 0 1 0 1
FA 85	2	46 40 50 42 41
FA 86	1	0 0 2 2 0
FA 86	2	46 40 48 40 41
FA 88	1	1 1 1 0 0
FA 88	2	44 39 47 40 39

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APPEARS THIS WAY
ON ORIGINAL

FA 89	1	3	1	1	1	1
FA 89	2	40	38	46	39	38
FA 90	1	3	1	1	1	1
FA 90	2	36	36	44	38	35
FA 91	1	1	1	1	2	0
FA 91	2	34	34	43	36	35
FA 92	1	1	0	2	1	0
FA 92	2	33	34	41	35	35
FA 93	1	1	1	0	0	1
FA 93	2	32	31	41	35	34
FA 94	1	1	0	2	1	2
FA 94	2	31	31	39	34	32
FA 95	1	2	0	2	1	0
FA 95	2	29	31	37	32	31
FA 96	1	0	1	1	0	1
FA 96	2	29	30	35	32	29
FA 97	1	0	1	1	0	1
FA 97	2	28	27	34	32	28
FA 98	1	0	0	1	2	1
FA 98	2	28	27	33	29	27
FA 99	1	0	0	0	1	0
FA 99	2	27	27	32	28	26
FA 100	1	2	0	0	1	1
FA 100	2	24	27	30	27	25
FA 102	1	1	1	0	2	0
FA 102	2	21	26	28	25	24
Spontaneous tumor pct: 75% in ctrl. - Total	-	51	46	51	47	48

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PITUITARY	(38	) FA 36	1	0	1	0	0	0	1.000	0.824	1.000
M-GANGLIONEUROMA	(52	) FA 36	2	64	64	65	63	64			
Spontaneous tumor pct: <= 1% in ctrl. - Total	-		-	0	1	0	0	0			
SALIVARY GLAND	(40	) IN 104-106	1	0	0	0	0	1	0.219	0.051	1.000
X-MALIGNANT LYMPHOMA	(211	) IN 104-106	2	15	20	15	21	19			
Spontaneous tumor pct: <= 1% in ctrl. - Total	-		-	0	0	0	0	1			
SALIVARY GLAND	(40	) FA 96	1	0	1	0	0	0	1.000	0.829	1.000
X-HISTIOCYTIC SARCOMA	(387	) FA 96	2	29	30	36	32	30			
Spontaneous tumor pct: <= 1% in ctrl. - Total	-		-	0	1	0	0	0			
SCIATIC NERVE	(41	) FA 80	1	0	0	0	0	1	0.396	0.286	1.000
X-HISTIOCYTIC SARCOMA	(336	) FA 80	2	50	48	53	48	48			
		FA 104	1	0	1	0	0	0			
		FA 104	2	20	24	27	24	24			
Spontaneous tumor pct: <= 1% in ctrl. - Total	-		-	0	1	0	0	1			
SKELETAL MUSCLE	(43	) IN 79-91	1	0	0	0	0	1	0.556	0.503	1.000
X-HISTIOCYTIC SARCOMA	(337	) IN 79-91	2	16	15	10	13	15			
		IN 92-103	1	0	2	0	0	0			
		IN 92-103	2	19	12	28	15	15			
Spontaneous tumor pct: 2% in ctrl. - Total	-		-	0	2	0	0	1			

SKIN	(44	) IN 53-78	1	0	0	1	0	0	
X-HISTIOCYTIC SARCOMA	(132	) IN 53-78	2	15	13	10	12	10	0.390 0.341 0.999
		IN 79-91	1	0	0	0	0	1	
		IN 79-91	2	16	15	10	13	15	
		IN 92-103	1	0	1	0	0	0	
		IN 92-103	2	19	13	28	15	15	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	1	0	1	
SKIN	(44	) IN 0-52	1	0	0	0	0	1	0.333 0.108 1.000
M-MYXOSARCOMA	(140	) IN 0-52	2	0	3	1	4	3	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
SKIN	(44	) IN 92-103	1	0	0	0	1	0	0.329 0.306 1.000
B-KERATOACANTHOMA	(310	) IN 92-103	2	19	14	28	14	15	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0	
SKIN	(44	) IN 104-106	1	0	0	1	0	0	0.615 0.629 1.000
B-LIPOMA	(380	) IN 104-106	2	15	20	14	21	20	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	1	0	0	
SKIN	(44	) IN 53-78	1	0	0	0	0	1	0.163 0.027 1.000
M-FIBROSARCOMA	(41	) IN 53-78	2	15	13	11	12	9	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
SPLEEN	(46	) FA 96	1	0	1	0	0	0	1.000 0.829 1.000
X-HISTIOCYTIC SARCOMA	(383	) FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
SPLEEN	(46	) IN 104-106	1	0	0	0	0	1	0.219 0.051 1.000
M-UNDIFFERENTIATED SARCOM	(607	) IN 104-106	2	15	20	15	21	19	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	0	1	
STOMACH	(48	) FA 96	1	0	1	0	0	0	1.000 0.829 1.000
X-HISTIOCYTIC SARCOMA	(385	) FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
STOMACH	(48	) FA 94	1	0	0	0	1	0	0.398 0.348 1.000
M-UNDIFFERENTIATED SARCOM	(429	) FA 94	2	32	31	41	34	34	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0	
THYMUS	(51	) FA 32	1	0	0	0	1	0	0.394 0.340 1.000
M-MESOTHELIOMA	(105	) FA 32	2	63	62	62	60	61	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	0	0	1	0	
THYMUS	(51	) IN 104-106	1	0	1	0	0	0	1.000 0.840 1.000
M-THYMOMA	(193	) IN 104-106	2	14	18	15	20	20	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
THYMUS	(51	) FA 96	1	0	1	0	0	0	1.000 0.828 1.000
X-HISTIOCYTIC SARCOMA	(384	) FA 96	2	28	29	35	31	28	
Spontaneous tumor pct: <= 1% in ctrl. - Total			-	0	1	0	0	0	
THYROID	(52	) IN 104-106	1	0	2	0	2	0	0.792 0.749 1.000
B-FOLLICULAR CELL ADENOMA	(157	) IN 104-106	2	15	18	15	19	20	
Spontaneous tumor pct: 2% in ctrl. - Total			-	0	2	0	2	0	

THYROIDIS	(52	)	IN 79-91	1	1	0	0	1	0	0.949 0.936 0.999
B-C-CELL ADENOMA	(248	)	IN 79-91	2	15	15	10	12	16	
			IN 92-103	1	2	2	0	2	0	
			IN 92-103	2	17	12	28	13	15	
			IN 104-106	1	1	3	5	2	1	
			IN 104-106	2	14	17	10	19	19	
Spontaneous tumor pct: 7% in ctrl. - Total				-	4	5	5	5	1	
THYROIDIS	(52	)	IN 79-91	1	0	0	1	1	0	0.493 0.474 1.000
M-FOLLICULAR CELL CARCINO	(289	)	IN 79-91	2	16	15	9	12	16	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	0	1	1	0	
THYROIDIS	(52	)	IN 92-103	1	1	0	0	0	0	0.386 0.280 1.000
M-C-CELL CARCINOMA	(405	)	IN 92-103	2	18	14	28	15	15	
			IN 104-106	1	0	0	0	0	1	
			IN 104-106	2	15	20	15	21	19	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	1	
THYROIDIS	(52	)	IN 79-91	1	0	1	0	0	0	1.000 0.816 1.000
M-UNDIFFERENTIATED CARCIN	(493	)	IN 79-91	2	16	14	10	13	16	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0	
VAGINA	(58	)	IN 92-103	1	0	1	0	0	0	0.216 0.172 0.982
M-STROMAL SARCOMA	(179	)	IN 92-103	2	19	13	28	15	15	
			IN 104-106	1	0	0	0	0	1	
			IN 104-106	2	15	20	15	21	19	
			FA 69	1	1	0	0	0	0	
			FA 69	2	58	57	57	56	57	
			FA 83	1	0	0	0	1	0	
			FA 83	2	49	43	52	43	43	
			FA 86	1	0	0	0	0	1	
			FA 86	2	46	40	50	42	40	
Spontaneous tumor pct: 2% in ctrl. - Total				-	1	1	0	1	2	
VAGINA	(58	)	IN 53-78	1	0	1	1	0	0	0.821 0.780 1.000
B-FIBROMA	(234	)	IN 53-78	2	15	12	10	12	10	
			IN 104-106	1	0	0	1	0	0	
			IN 104-106	2	15	20	14	21	20	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	2	0	0	
VAGINA	(58	)	FA 80	1	0	0	0	0	1	0.390 0.281 1.000
X-HISTIOCYTIC SARCOMA	(339	)	FA 80	2	50	48	53	48	48	
			FA 92	1	0	1	0	0	0	
			FA 92	2	34	33	43	36	35	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	1	
VAGINA	(58	)	IN 92-103	1	1	0	0	0	0	1.000 0.825 1.000
M-SQUAMOUS CELL CARCINOMA	(400	)	IN 92-103	2	18	14	28	15	15	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	1	0	0	0	0	
BONE MARROW	(7	)	FA 96	1	0	1	0	0	0	1.000 0.829 1.000
X-HISTIOCYTIC SARCOMA	(328	)	FA 96	2	29	30	36	32	30	
Spontaneous tumor pct: <= 1% in ctrl. - Total				-	0	1	0	0	0	

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BRAIN	(9	) IN 79-91	1	1	0	0	0	0	
M-ASTROCYTOMA	(48	) IN 79-91	2	15	15	10	13	15	1.000 0.948 1.000
		IN 104-106	1	0	1	0	0	0	
		IN 104-106	2	15	19	15	21	20	
		FA 96	1	1	0	0	0	0	
		FA 96	2	28	31	36	32	30	
Spontaneous tumor pct: 2%		in ctrl. - Total	-	2	1	0	0	0	

BRAIN	(9	) FA 74	1	0	0	0	1	0	
M-EPENDYMOMA	(518	) FA 74	2	54	54	55	54	53	0.398 0.341 1.000
Spontaneous tumor pct: <= 1%		in ctrl. - Total	-	0	0	0	1	0	

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