

## APPENDIX B (Female-Rats)

NDA 20-864 MAXALT

### Analysis of Carcinogenic Potential in Female Rats Test of Dose-Response (Tumor) Positive Linear Trend

Program Author: Ted Guo, PH.D. CDER/FDA

**Note:**

- Dose Levels Included: CTRL LOW MED HIGH (0 2 25 125)
- Missing value in Tumor-Caused Death is treated as tumor not causing death
- Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

**TABLE I.B (Female-Rats):**

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2x2 CONTINGENCY -----TABLE-----	EXACT PROB	ASYMP TOTIC	ASYMP (CONTI NUITY CORR)
LARGE INTESTINE ADENOMA	(12000 ) (70 )	IN 105-105	1 2	1 66 31	1.0000	0.7189	0.7226
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1 0			
LIVER HEPATOCELLULAR ADENOMA	(14000 ) (1660 )	IN 92-104 IN 92-104	1 2	1 14 7	0.8642	0.8404	0.8416
Spontaneous tumor rate 3% in ctrl. - Total			-	2 1 65 30 3 1			
LIVER HEPATOCELLULAR CARCINOMA	(14000 ) (1670 )	IN 92-104 IN 92-104	1 2	0 15 6	0.5973	0.7660	0.7680
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0 1			
PANCREAS ACINUS ADENOMA	(18014 ) (70 )	IN 92-104 IN 92-104	1 2	0 15 7	0.2955	0.0636	0.0647
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0 0			
PANCREAS ISLET ADENOMA	(18073 ) (70 )	IN 105-105 IN 105-105	1 2	2 65 29	0.6374	0.7286	0.7306
Spontaneous tumor rate 2% in ctrl. - Total			-	2 2			
PERITONEUM HEMANGIOPERICYTOMA	(21000 ) (1575 )	IN 105-105 IN 105-105	1 2	1 66 31	1.0000	0.7189	0.7226
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1 0			
ADRENAL PHEOCHROMOCYTOMA	(22000 ) (3060 )	IN 105-105 IN 105-105	1 2	1 66 31	1.0000	0.7189	0.7226
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1 0			
ADRENAL CORTEX ADENOCARCINOMA	(22080 ) (60 )	IN 92-104 IN 92-104	1 2	0 15 7	0.6590	0.7632	0.7660
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0 0			

Statistical Reviewer: Kooros Mahjoob

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ADRENAL CORTEX	(22080	)	IN 92-104	1	1	0	
ADENOMA	(70	)	IN 92-104	2	14	7	1.0000 0.8289 0.8307
			IN 105-105	1	1	0	
			IN 105-105	2	66	31	
Spontaneous tumor rate 2%		in ctrl.	- Total	-	2	0	
PARATHYROID	(27000	)	IN 79-91	1	0	0	
ADENOMA	(70	)	IN 79-91	2	8	8	0.6800 0.7471 0.7505
Spontaneous tumor rate LE 1%		in ctrl.	- Total	-	0	0	
PITUITARY	(29000	)	IN 53-78	1	0	0	
ADENOMA	(70	)	IN 53-78	2	4	0	0.8110 0.8110 0.8113
			IN 79-91	1	2	2	
			IN 79-91	2	1	3	
			IN 92-104	1	3	0	
			IN 92-104	2	1	0	
			IN 105-105	1	52	20	
			IN 105-105	2	15	10	
			FA 57	1	0	1	
			FA 57	2	97	47	
			FA 61	1	1	0	
			FA 61	2	96	47	
			FA 67	1	0	0	
			FA 67	2	94	47	
			FA 70	1	0	1	
			FA 70	2	94	46	
			FA 72	1	1	0	
			FA 72	2	92	46	
			FA 77	1	1	0	
			FA 77	2	91	46	
			FA 79	1	0	1	
			FA 79	2	90	45	
			FA 80	1	1	1	
			FA 80	2	89	44	
			FA 81	1	0	0	
			FA 81	2	89	44	
			FA 83	1	1	0	
			FA 83	2	88	44	
			FA 86	1	0	0	
			FA 86	2	86	42	
			FA 87	1	0	1	
			FA 87	2	86	40	
			FA 88	1	1	0	
			FA 88	2	85	40	
			FA 89	1	1	0	
			FA 89	2	84	39	
			FA 90	1	0	0	
			FA 90	2	84	39	
			FA 91	1	1	0	
			FA 91	2	82	38	
			FA 92	1	0	0	
			FA 92	2	82	38	
			FA 93	1	2	0	
			FA 93	2	79	38	
			FA 94	1	0	2	
			FA 94	2	79	36	
			FA 95	1	1	0	
			FA 95	2	78	36	
			FA 96	1	1	0	
			FA 96	2	77	36	
			FA 97	1	2	0	
			FA 97	2	75	36	
			FA 98	1	1	2	
			FA 98	2	74	34	
			FA 99	1	1	0	
			FA 99	2	73	34	
			FA 100	1	1	1	
			FA 100	2	72	33	
			FA 102	1	0	0	
			FA 102	2	72	33	

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		FA 103	1	1	2			
		FA 103	2	68	31			
		FA 104	1	1	0			
		FA 104	2	67	31			
		FA 105	1	0	1			
		FA 105	2	67	30			
Spontaneous tumor rate 76%	in ctrl.	- Total	-	76	35			
THYROID PARAFOLLICULAR CE (31099)	) IN 92-104	1	0	0		0.6200	0.6330	0.6347
CARCINOMA (410)	) IN 92-104	2	15	7				
	IN 105-105	1	1	0				
	IN 105-105	2	66	31				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0			
THYROID PARAFOLLICULAR CE (31099)	) IN 53-78	1	1	0		0.7496	0.7578	0.7586
ADENOMA (70)	) IN 53-78	2	6	2				
	IN 79-91	1	1	0				
	IN 79-91	2	7	8				
	IN 92-104	1	1	0				
	IN 92-104	2	14	7				
	IN 105-105	1	5	4				
	IN 105-105	2	62	27				
Spontaneous tumor rate 8%	in ctrl.	- Total	-	8	4			
THYROID FOLLICULAR CELL (31413)	) IN 105-105	1	0	1		0.0937	0.0611	0.0620
CARCINOMA (410)	) IN 105-105	2	67	30				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	0	1			
THYROID FOLLICULAR CELL (31413)	) IN 79-91	1	1	0		1.0000	0.7605	0.7638
ADENOMA (70)	) IN 79-91	2	7	8				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0			
KIDNEY TUBULE (33112)	) IN 105-105	1	1	0		1.0000	0.7189	0.7226
ADENOMA (70)	) IN 105-105	2	66	31				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0			
OVARY (40000)	) IN 53-78	1	0	0		0.4031	0.3417	0.3439
GRANULOSA CELL TUMOR (1560)	) IN 53-78	2	7	2				
	IN 105-105	1	1	0				
	IN 105-105	2	66	31				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0			
UTERUS (42000)	) FA 65	1	1	0		1.0000	0.7367	0.7400
LEIOMYOMA (2030)	) FA 65	2	95	47				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0			
UTERUS (42000)	) IN 53-78	1	0	0		0.8111	0.8315	0.8322
POLYP (3250)	) IN 53-78	2	6	2				
	IN 79-91	1	0	0				
	IN 79-91	2	8	8				
	IN 105-105	1	3	4				
	IN 105-105	2	64	27				
	FA 66	1	1	0				
	FA 66	2	94	47				
	FA 92	1	1	0				
	FA 92	2	81	38				
Spontaneous tumor rate 5%	in ctrl.	- Total	-	5	4			
UTERUS (42000)	) FA 70	1	0	0		0.0484	0.0220	0.0223
SARCOMA (3460)	) FA 70	2	94	47				
	FA 104	1	0	0				
	FA 104	2	68	31				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	0	0			
UTERUS ENDOMETRIUM (42141)	) IN 105-105	1	0	1		0.3684	0.5093	0.5137
ADENOCARCINOMA (60)	) IN 105-105	2	67	30				
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	0	1			

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VAGINA	(46000 )	IN 105-105	1	0		1.0000	0.7189	0.7226
POLYP	(3250 )	IN 105-105	2	66	31			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	0			
VAGINA	(46000 )	IN 105-105	1	0	0	0.5592	0.7037	0.7074
SQUAMOUS CELL CARCINOMA	(3610 )	IN 105-105	2	67	31			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	0			
SKIN	(59000 )	IN 105-105	1	0	0	0.1645	0.0139	0.0142
FIBROMA	(1330 )	IN 105-105	2	67	31			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	0			
SKIN	(59000 )	IN 79-91	1	1	0	1.0000	0.7605	0.7638
LIPOSARCOMA	(2090 )	IN 79-91	2	7	8			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	0			
SKIN	(59000 )	FA 101	1	0	0	0.1882	0.0209	0.0214
OSTEOGENIC SARCOMA	(2725 )	FA 101	2	72	33			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	0			
SKIN	(59000 )	IN 105-105	1	0	1	0.3684	0.5093	0.5137
SCHWANNOMA	(3475 )	IN 105-105	2	67	30			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	1			
MAMMARY GLAND	(61000 )	IN 53-78	1	1	0	0.1864	0.1846	0.1850
FIBROADENOMA	(1320 )	IN 53-78	2	5	2			
		IN 79-91	1	1	1			
		IN 79-91	2	7	5			
		IN 92-104	1	6	1			
		IN 92-104	2	8	6			
		IN 105-105	1	27	17			
		IN 105-105	2	40	14			
		FA 70	1	1	0			
		FA 70	2	93	47			
		FA 83	1	0	1			
		FA 83	2	89	43			
		FA 90	1	0	1			
		FA 90	2	84	38			
		FA 91	1	0	0			
		FA 91	2	83	38			
		FA 101	1	0	0			
		FA 101	2	72	33			
		FA 102	1	1	0			
		FA 102	2	71	33			
Spontaneous tumor rate	37% in ctrl.	- Total	-	37	21			
MAMMARY GLAND	(61000 )	IN 53-78	1	0	1	0.9545	0.9480	0.9482
ADENOCARCINOMA	(60 )	IN 53-78	2	6	1			
		IN 79-91	1	1	1			
		IN 79-91	2	6	5			
		IN 92-104	1	3	1			
		IN 92-104	2	10	6			
		IN 105-105	1	8	1			
		IN 105-105	2	59	30			
		FA 50	1	0	0			
		FA 50	2	97	48			
		FA 77	1	1	0			
		FA 77	2	91	46			
		FA 83	1	1	0			
		FA 83	2	88	44			
		FA 86	1	0	1			
		FA 86	2	86	41			
		FA 88	1	0	1			
		FA 88	2	86	39			
		FA 102	1	2	0			
		FA 102	2	70	33			
Spontaneous tumor rate	16% in ctrl.	- Total	-	16	6			

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MAMMARY GLAND	(61000 )	IN 105-105 1	4	4	0.8356 0.8435 0.8445
ADENOMA	(70 )	IN 105-105 2	63	27	
Spontaneous tumor rate 4%		in ctrl. - Total	4	4	
BONE	(84000 )	FA 53 1	0	0	0.5975 0.7235 0.7269
OSTEOSARCOMA	(2770 )	FA 53 2	97	48	
Spontaneous tumor rate LE 1%		in ctrl. - Total	0	0	
BRAIN	(89000 )	IN 105-105 1	0	0	0.1645 0.0139 0.0142
GRANULAR CELL TUMOR	(1535 )	IN 105-105 2	67	31	
Spontaneous tumor rate LE 1%		in ctrl. - Total	0	0	
STOMACH NONGLANDULAR MUCO	(9027 )	IN 105-105 1	1	0	1.0000 0.7189 0.7226
KERATOACANTHOMA	(1970 )	IN 105-105 2	66	31	
Spontaneous tumor rate LE 1%		in ctrl. - Total	1	0	
PRIMARY SITE UNDETERMINED	(98000 )	IN 105-105 1	1	0	0.2934 0.3263 0.3282
HISTIOCYTIC SARCOMA	(1715 )	IN 105-105 2	66	31	
		FA 85 1	0	1	
		FA 85 2	86	42	
		FA 101 1	0	0	
		FA 101 2	72	33	
		FA 105 1	0	0	
		FA 105 2	67	31	
Spontaneous tumor rate LE 1%		in ctrl. - Total	1	1	
PRIMARY SITE UNDETERMINED	(98000 )	IN 105-105 1	1	0	0.6265 0.5730 0.5748
LYMPHOMA	(2150 )	IN 105-105 2	66	31	
		FA 11 1	1	0	
		FA 11 2	99	50	
		FA 35 1	0	0	
		FA 35 2	99	50	
		FA 84 1	1	0	
		FA 84 2	86	43	
		FA 92 1	0	0	
		FA 92 2	82	38	
Spontaneous tumor rate 3%		in ctrl. - Total	3	0	

- 5 - (End of File)

APPEARS THIS WAY  
ON ORIGINAL

## APPENDIX B (Female-Rats)

## NDA 20-864 MAXALT

Analysis of Carcinogenic Potential in Female Rats  
Test of Dose-Response (Tumor) Positive Linear Trend

TABLE II.B (Female-Rats): Summary of Table I.B (Female-Rats)

42000	UTERUS	3460	SARCOMA	0.0484	0.0220	0.0223
31413	THYROID FOLLICULAR CELL	410	CARCINOMA	0.0937	0.0611	0.0620
89000	BRAIN	1535	GRANULAR CELL TUMOR	0.1645	0.0139	0.0142
59000	SKIN	1330	FIBROMA	0.1645	0.0139	0.0142
61000	MAMMARY GLAND	1320	FIBROADENOMA	0.1864	0.1846	0.1850
59000	SKIN	2725	OSTEOGENIC SARCOMA	0.1882	0.0209	0.0214
98000	PRIMARY SITE UNDETERMINED	1715	HISTIOCYTIC SARCOMA	0.2934	0.3263	0.3282
18014	PANCREAS ACINUS	70	ADENOMA	0.2955	0.0636	0.0647
59000	SKIN	3475	SCHWANNOMA	0.3684	0.5093	0.5137
42141	UTERUS ENDOMETRIUM	60	ADENOCARCINOMA	0.3684	0.5093	0.5137
40000	OVARY	1560	GRANULOSA CELL TUMOR	0.4031	0.3417	0.3439
46000	VAGINA	3610	SQUAMOUS CELL CARCINOMA	0.5592	0.7037	0.7074
14000	LIVER	1670	HEPATOCELLULAR CARCINOMA	0.5973	0.7660	0.7680
84000	BONE	2770	OSTEOSARCOMA	0.5975	0.7235	0.7269
31099	THYROID PARAFOLLICULAR CE	410	CARCINOMA	0.6200	0.6330	0.6347
98000	PRIMARY SITE UNDETERMINED	2150	LYMPHOMA	0.6265	0.5730	0.5748
18073	PANCREAS ISLET	70	ADENOMA	0.6374	0.7286	0.7306
22080	ADRENAL CORTEX	60	ADENOCARCINOMA	0.6590	0.7632	0.7660
27000	PARATHYROID	70	ADENOMA	0.6800	0.7471	0.7505
31099	THYROID PARAFOLLICULAR CE	70	ADENOMA	0.7496	0.7578	0.7586
29000	PITUITARY	70	ADENOMA	0.8110	0.8110	0.8113
42000	UTERUS	3250	POLYP	0.8111	0.8315	0.8322
61000	MAMMARY GLAND	70	ADENOMA	0.8356	0.8435	0.8445
14000	LIVER	1660	HEPATOCELLULAR ADENOMA	0.8642	0.8404	0.8416
61000	MAMMARY GLAND	60	ADENOCARCINOMA	0.9545	0.9480	0.9482
22000	ADRENAL	3060	PHEOCHROMOCYTOMA	1.0000	0.7189	0.7226
22080	ADRENAL CORTEX	70	ADENOMA	1.0000	0.8289	0.8307
33112	KIDNEY TUBULE	70	ADENOMA	1.0000	0.7189	0.7226
12000	LARGE INTESTINE	70	ADENOMA	1.0000	0.7189	0.7226
21000	PERITONEUM	1575	HEMANGIOPERICYTOMA	1.0000	0.7189	0.7226
59000	SKIN	2090	LIPOSARCOMA	1.0000	0.7605	0.7638
9027	STOMACH NONGLANDULAR MUCO	1970	KERATOACANTHOMA	1.0000	0.7189	0.7226
31413	THYROID FOLLICULAR CELL	70	ADENOMA	1.0000	0.7605	0.7638
42000	UTERUS	2030	LEIOMYOMA	1.0000	0.7367	0.7400
46000	VAGINA	3250	POLYP	1.0000	0.7189	0.7226

APPEARS THIS WAY  
ON ORIGINAL

## APPENDIX C (Male-Mice)

### NDA 20-864 MAXALT

#### Analysis of Carcinogenic Potential in Male Rats Test of Dose-Response (Tumor) Positive Linear Trend

Program Author: Ted Guo, PH.D, CDER/FDA

**Note:**

- Dose Levels Included: CTRL LOW MED HIGH (0 2 25 125)
- Missing value in Tumor-Caused Death is treated as tumor not causing death
- Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

**TABLE I.C (Male-Rats):**

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC CONTINGENCY -----TABLE-----	EXACT PROB	ASYMP TOTIC	ASYMP (CONTI NUITY CORR)	=PR (STATISTIC. GE. OBSERVED)
SMALL INTESTINE	(11000 )	IN 0-49	1	0	0			0.2353
ADENOCARCINOMA	(60 )	IN 0-49	2	6	4			0.0385
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	0			0.0393
LARGE INTESTINE CECUM	(12051 )	IN 99-99	1	0	1			0.3880
ADENOCARCINOMA	(60 )	IN 99-99	2	54	30			0.5072
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	1			0.5117
LIVER	(14000 )	IN 99-99	1	0	3			0.1230
HEMANGIOMA	(1570 )	IN 99-99	2	54	28			0.1324
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	3			0.1337
LIVER	(14000 )	FA 48	1	0	0			0.5095
HEMANGIOSARCOMA	(1580 )	FA 48	2	96	47			0.4487
		FA 87	1	1	0			0.4507
		FA 87	2	73	38			
		FA 90	1	1	0			
		FA 90	2	68	37			
		FA 93	1	0	0			
		FA 93	2	65	34			
Spontaneous tumor rate 2% in ctrl. - Total			-	2	0			
LIVER	(14000 )	IN 50-74	1	1	0			0.3896
HEPATOCELLULAR CARCINOMA	(1670 )	IN 50-74	2	8	2			0.4175
		IN 75-89	1	0	1			0.4186
		IN 75-89	2	16	6			
		IN 90-98	1	0	0			
		IN 90-98	2	15	5			
		IN 99-99	1	4	2			
		IN 99-99	2	50	29			
		FA 91	1	0	1			
		FA 91	2	68	36			
Spontaneous tumor rate 5% in ctrl. - Total			-	5	4			

Statistical Reviewer: Kooros Mahjoob

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**Appendix C (Male-Mice): Page 2**

LIVER	(14000 )	IN 75-89	1	2	0	0.7291	0.7369	0.7377
ADENOMA	(70 )	IN 75-89	2	14	7			
		IN 90-98	1	0	1			
		IN 90-98	2	15	5			
		IN 99-99	1	12	5			
		IN 99-99	2	42	26			
Spontaneous tumor rate 14%		in ctrl. - Total	-	14	6			
GALLBLADDER	(16000 )	IN 99-99	1	2	0	1.0000	0.7978	0.8000
PAPILLOMA	(2910 )	IN 99-99	2	52	31			
Spontaneous tumor rate 2%		in ctrl. - Total	-	2	0			
PANCREAS ISLET	(18073 )	IN 99-99	1	0	0	0.1567	0.0120	0.0123
ADENOMA	(70 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	0	0			
PERITONEUM	(21000 )	IN 99-99	1	0	0	0.1567	0.0120	0.0123
SCHWANNOMA	(3475 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	0	0			
ADRENAL	(22000 )	IN 99-99	1	1	0	1.0000	0.7215	0.7253
PHEOCHROMOCYTOMA	(3060 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
ADRENAL CORTEX	(22080 )	IN 75-89	1	0	1	0.1386	0.1259	0.1265
ADENOMA	(70 )	IN 75-89	2	16	6			
		IN 99-99	1	4	2			
Spontaneous tumor rate 4%		in ctrl. - Total	-	4	3			
PITUITARY	(29000 )	IN 99-99	1	1	0	0.2899	0.1177	0.1193
ADENOMA	(70 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
THYROID FOLLICULAR CELL	(31413 )	IN 0-49	1	1	0	0.6742	0.7211	0.7235
ADENOMA	(70 )	IN 0-49	2	5	4			
		IN 75-89	1	0	1			
		IN 75-89	2	16	6			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	1			
KIDNEY	(33000 )	IN 99-99	1	1	0	1.0000	0.7215	0.7253
ADENOMA	(70 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
TESTIS LEYDIG CELL	(49157 )	IN 99-99	1	4	1	0.9375	0.8870	0.8878
ADENOMA	(70 )	IN 99-99	2	50	30			
Spontaneous tumor rate 4%		in ctrl. - Total	-	4	1			
TESTIS EPIDIDYMISS	(49159 )	IN 99-99	1	0	0	0.8368	0.7962	0.7983
SARCOMA	(3460 )	IN 99-99	2	54	31			
		FA 51	1	1	0			
		FA 51	2	93	46			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
TESTIS SPERMATIC CORD	(49162 )	IN 99-99	1	1	0	1.0000	0.7215	0.7253
LEIOMYOMA	(2030 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
SEMINAL VESICLE	(53000 )	IN 99-99	1	1	0	1.0000	0.7215	0.7253
ADENOMA	(70 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			
SKIN	(59000 )	IN 99-99	1	0	0	0.1567	0.0120	0.0123
FIBROMA	(1330 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	0	0			
SKIN	(59000 )	FA 82	1	1	0	1.0000	0.7304	0.7338
FIBROSARCOMA	(1350 )	FA 82	2	80	40			
Spontaneous tumor rate LE 1%		in ctrl. - Total	-	1	0			

Statistical Reviewer: Kooros Mahjoob



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Appendix C (Male-Mice): Page 3

SKIN	(59000 )	IN 99-99	1	0	0	0.5971	0.7060	0.7099
HEMANGIOMA	(1570 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	0			
SKIN	(59000 )	IN 75-89	1	1	0	1.0000	0.8513	0.8527
PAPILLOMA	(2910 )	IN 75-89	2	15	7			
		IN 99-99	1	2	0			
		IN 99-99	2	52	31			
Spontaneous tumor rate 3% in ctrl. - Total			-	3	0			
SKIN	(59000 )	FA 89	1	1	0	1.0000	0.7264	0.7299
SARCOMA	(3460 )	FA 89	2	70	37			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	0			
SKIN SEBACEOUS GLAND	(59173 )	IN 99-99	1	1	0	0.8394	0.7885	0.7908
ADENOMA	(70 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	0			
LUNG	(71000 )	IN 75-89	1	1	1	0.6264	0.6324	0.6327
ADENOCARCINOMA	(60 )	IN 75-89	2	13	6			
		IN 90-98	1	2	2			
		IN 90-98	2	8	4			
		IN 99-99	1	8	6			
		IN 99-99	2	46	25			
		FA 77	1	1	0			
		FA 77	2	83	41			
		FA 80	1	0	0			
		FA 80	2	81	40			
		FA 82	1	1	0			
		FA 82	2	80	40			
		FA 87	1	0	0			
		FA 87	2	74	38			
		FA 92	1	1	0			
		FA 92	2	65	34			
		FA 93	1	1	0			
		FA 93	2	64	34			
		FA 96	1	2	0			
		FA 96	2	57	33			
		FA 98	1	1	0			
		FA 98	2	55	32			
Spontaneous tumor rate 18% in ctrl. - Total			-	18	9			
LUNG	(71000 )	IN 50-74	1	2	0	0.4174	0.4233	0.4238
ADENOMA	(70 )	IN 50-74	2	7	2			
		IN 75-89	1	2	1			
		IN 75-89	2	14	6			
		IN 90-98	1	3	1			
		IN 90-98	2	12	5			
		IN 99-99	1	16	9			
		IN 99-99	2	38	22			
		FA 92	1	0	0			
		FA 92	2	66	34			
		FA 97	1	0	0			
		FA 97	2	56	32			
Spontaneous tumor rate 23% in ctrl. - Total			-	23	11			
SPLEEN	(77000 )	IN 99-99	1	0	0	0.5971	0.7060	0.7099
HEMANGIOSARCOMA	(1580 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	0			
LYMPH NODE	(79000 )	IN 99-99	1	0	1	0.3880	0.5072	0.5117
MASTOCYTOMA	(2200 )	IN 99-99	2	54	30			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	1			
BONE MARROW CRANIAL AND F	(83308 )	IN 99-99	1	0	0	0.5971	0.7060	0.7099
MASTOCYTOMA	(2200 )	IN 99-99	2	54	31			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	0			

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Appendix C (Male-Mice): Page 4

STOMACH GLANDULAR MUCOSA	(9026 )	IN 99-99	1	1	0	1.0000	0.7215	0.7253
PAPILLOMA	(2910 )	IN 99-99	2	53	31			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	0			
EYE HARDERIAN GLAND	(95409 )	IN 50-74	1	1	0	0.1700	0.1619	0.1624
ADENOMA	(70 )	IN 50-74	2	8	2			
		IN 75-89	1	3	0			
		IN 75-89	2	13	7			
		IN 90-98	1	1	1			
		IN 90-98	2	14	5			
		IN 99-99	1	10	4			
		IN 99-99	2	44	27			
Spontaneous tumor rate 15%	in ctrl.	- Total	-	15	5			
EAR	(97000 )	FA 63	1	0	1	0.3911	0.5360	0.5402
SQUAMOUS CELL CARCINOMA	(3610 )	FA 63	2	92	44			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	1			
PRIMARY SITE UNDETERMINED	(98000 )	IN 99-99	1	0	1	0.3880	0.5072	0.5117
LEUKEMIA	(2050 )	IN 99-99	2	54	30			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	1			
PRIMARY SITE UNDETERMINED	(98000 )	IN 99-99	1	1	1	0.8375	0.8078	0.8088
LYMPHOMA	(2150 )	IN 99-99	2	53	30			
		FA 69	1	1	0			
		FA 69	2	90	44			
		FA 84	1	1	0			
		FA 84	2	78	38			
		FA 85	1	1	0			
		FA 85	2	77	38			
		FA 88	1	1	0			
		FA 88	2	72	38			
		FA 89	1	1	0			
		FA 89	2	70	37			
		FA 97	1	0	0			
		FA 97	2	56	32			
		FA 98	1	1	0			
		FA 98	2	55	32			
Spontaneous tumor rate 7%	in ctrl.	- Total	-	7	1			
PRIMARY SITE UNDETERMINED	(98000 )	IN 99-99	1	1	0	0.2174	0.2658	0.2671
SARCOMA	(3460 )	IN 99-99	2	53	31			
		FA 48	1	0	0			
		FA 48	2	96	47			
		FA 56	1	0	1			
		FA 56	2	93	45			
		FA 75	1	0	1			
		FA 75	2	85	43			
		FA 89	1	0	0			
		FA 89	2	71	37			
		FA 92	1	0	0			
		FA 92	2	66	34			
		FA 93	1	0	0			
		FA 93	2	65	34			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	2			

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## APPENDIX C (Male-Mice)

## NDA 20-864 MAXALT

**Analysis of Carcinogenic Potential in Male Mice**  
**Test of Dose-Response (Tumor) Positive Linear Trend**

TABLE II.C (Male-Mice): Summary of Table I.C (Male-Mice)

Organ Code	Organ Name	Tumor Code	Tumor Name	Exact-P	Asymp-P	AsyCor-P
14000	LIVER	1570	HEMANGIOMA	0.1230	0.1324	0.1337
22080	ADRENAL CORTEX	70	ADENOMA	0.1386	0.1259	0.1265
18073	PANCREAS ISLET	70	ADENOMA	0.1567	0.0120	0.0123
21000	PERITONEUM	3475	SCHWANNOMA	0.1567	0.0120	0.0123
59000	SKIN	1330	FIBROMA	0.1567	0.0120	0.0123
95409	EYE HARDERIAN GLAND	70	ADENOMA	0.1700	0.1619	0.1624
98000	PRIMARY SITE UNDETERMINED	3460	SARCOMA	0.2174	0.2658	0.2671
11000	SMALL INTESTINE	60	ADENOCARCINOMA	0.2353	0.0385	0.0393
29000	PITUITARY	70	ADENOMA	0.2899	0.1177	0.1193
12051	LARGE INTESTINE CECUM	60	ADENOCARCINOMA	0.3880	0.5072	0.5117
79000	LYMPH NODE	2200	MASTOCYTOMA	0.3880	0.5072	0.5117
98000	PRIMARY SITE UNDETERMINED	2050	LEUKEMIA	0.3880	0.5072	0.5117
14000	LIVER	1670	HEPATOCELLULAR CARCINOMA	0.3896	0.4175	0.4186
97000	EAR	3610	SQUAMOUS CELL CARCINOMA	0.3911	0.5360	0.5402
71000	LUNG	70	ADENOMA	0.4174	0.4233	0.4238
14000	LIVER	1580	HEMANGIOSARCOMA	0.5095	0.4487	0.4507
83308	BONE MARROW CRANIAL AND F	2200	MASTOCYTOMA	0.5971	0.7060	0.7099
59000	SKIN	1570	HEMANGIOMA	0.5971	0.7060	0.7099
77000	SPLEEN	1580	HEMANGIOSARCOMA	0.5971	0.7060	0.7099
71000	LUNG	60	ADENOCARCINOMA	0.6264	0.6324	0.6327
31413	THYROID FOLLICULAR CELL	70	ADENOMA	0.6742	0.7211	0.7235
14000	LIVER	70	ADENOMA	0.7291	0.7369	0.7377
49159	TESTIS EPIDIDYMIS	3460	SARCOMA	0.8368	0.7962	0.7983
98000	PRIMARY SITE UNDETERMINED	2150	LYMPHOMA	0.8375	0.8078	0.8088
59173	SKIN SEBACEOUS GLAND	70	ADENOMA	0.8394	0.7885	0.7908
49157	TESTIS LEYDIG CELL	70	ADENOMA	0.9375	0.8870	0.8878
22000	ADRENAL	3060	PHEOCHROMOCYTOMA	1.0000	0.7215	0.7253
16000	GALLBLADDER	2910	PAPILLOMA	1.0000	0.7978	0.8000
33000	KIDNEY	70	ADENOMA	1.0000	0.7215	0.7253
53000	SEMINAL VESICLE	70	ADENOMA	1.0000	0.7215	0.7253
59000	SKIN	1350	FIBROSARCOMA	1.0000	0.7304	0.7338
59000	SKIN	2910	PAPILLOMA	1.0000	0.8513	0.8527
59000	SKIN	3460	SARCOMA	1.0000	0.7264	0.7299
9026	STOMACH GLANDULAR MUCOSA	2910	PAPILLOMA	1.0000	0.7215	0.7253
49162	TESTIS SPERMATIC CORD	2030	LEIOMYOMA	1.0000	0.7215	0.7253

## APPENDIX D (Female-Mice)

NDA 20-864 MAXALT

### Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend

Program Author: Ted Guo, PH.D. CDER/FDA

**Note:**

- Dose Levels Included: CTRL LOW MED HIGH (0 2 25 125)
- Missing value in Tumor-Caused Death is treated as tumor not causing death
- Tumor Type: IN: Incidental (nonfatal) tumor, FA: Fatal tumor.

**TABLE I.D (Female-Mice):**

ORGAN/TISSUE NAME AND TUMOR NAME	(ORG#) (TMR#)	TUMOR TIME TYPES STRATA	ROW NO.	2xC -----TABLE-----	CONTINGENCY	EXACT PROB	ASYMP TOTIC	ASYMP(CONTI NUITY CORR)
SMALL INTESTINE HEMANGIOMA	(11000 ) (1570 )	IN 99-99 IN 99-99	1 2	1 48	0 24	1.0000	0.7484	0.7515
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	0			
SMALL INTESTINE HEMANGIOSARCOMA	(11000 ) (1580 )	IN 99-99 IN 99-99	1 2	0 49	0 24	0.6111	0.7357	0.7388
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	0			
SMALL INTESTINE ADENOCARCINOMA	(11000 ) (60 )	IN 90-98 IN 90-98	1 2	1 9	0 7	1.0000	0.7320	0.7356
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	1	0			
LIVER HEMANGIOMA	(14000 ) (1570 )	IN 90-98 IN 90-98	1 2	1 9	0 7	0.6519	0.7171	0.7183
		IN 99-99	1	1	2			
		IN 99-99	2	48	22			
Spontaneous tumor rate 2%	in ctrl.	- Total	-	2	2			
LIVER HEMANGIOSARCOMA	(14000 ) (1580 )	IN 99-99 IN 99-99	1 2	0 49	0 24	0.4952	0.7009	0.7034
		FA 76	1	0	1			
		FA 76	2	81	40			
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	1			
LIVER HISTIOCYTIC SARCOMA	(14000 ) (1715 )	IN 99-99 IN 99-99	1 2	0 49	1 23	0.4207	0.5699	0.5737
Spontaneous tumor rate LE	1% in ctrl.	- Total	-	0	1			
LIVER ADENOMA	(14000 ) (70 )	IN 75-89 IN 75-89	1 2	1 21	1 10	0.3656	0.3137	0.3157
		IN 99-99	1	1	0			
		IN 99-99	2	48	24			
Spontaneous tumor rate 2%	in ctrl.	- Total	-	2	1			

Statistical Reviewer: Kooros Mahjoob

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Appendix D (Female-Mice): Page 2

PANCREAS ISLET	(18073 )	IN 99-99	1	1	1	0.6663	0.7258	0.7282
ADENOMA	(70 )	IN 99-99	2	48	23			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	1			
ADRENAL	(22000 )	IN 50-74	1	1	0	1.0000	0.7425	0.7456
PHEOCHROMOCYTOMA	(3060 )	IN 50-74	2	13	5			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	0			
ADRENAL	(22000 )	IN 75-89	1	0	1	0.8739	0.8449	0.8462
SPINDLE CELL TUMOR	(3585 )	IN 75-89	2	22	10			
		IN 99-99	1	3	0			
		IN 99-99	2	46	24			
Spontaneous tumor rate 3% in ctrl. - Total			-	3	1			
ADRENAL CORTEX	(22080 )	IN 99-99	1	0	0	0.2302	0.0361	0.0369
CARCINOMA	(410 )	IN 99-99	2	49	24			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	0	0			
ADRENAL CORTEX	(22080 )	IN 99-99	1	2	0	1.0000	0.8291	0.8309
ADENOMA	(70 )	IN 99-99	2	47	24			
Spontaneous tumor rate 2% in ctrl. - Total			-	2	0			
PARATHYROID	(27000 )	IN 90-98	1	1	0	1.0000	0.7320	0.7356
ADENOMA	(70 )	IN 90-98	2	9	7			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	0			
PITUITARY	(29000 )	IN 75-89	1	2	0	0.7573	0.7479	0.7490
ADENOMA	(70 )	IN 75-89	2	20	11			
		IN 99-99	1	2	1			
		IN 99-99	2	47	23			
Spontaneous tumor rate 4% in ctrl. - Total			-	4	1			
OVARY	(40000 )	IN 90-98	1	1	0	0.5107	0.3654	0.3675
GRANULOSA CELL TUMOR	(1560 )	IN 90-98	2	9	7			
		IN 99-99	1	1	0			
		IN 99-99	2	48	24			
Spontaneous tumor rate 2% in ctrl. - Total			-	2	0			
OVARY	(40000 )	IN 90-98	1	1	0	0.3629	0.1771	0.1789
LUTEOMA	(2095 )	IN 90-98	2	9	7			
		IN 99-99	1	0	0			
		IN 99-99	2	49	24			
Spontaneous tumor rate LE 1% in ctrl. - Total			-	1	0			
OVARY	(40000 )	IN 75-89	1	0	0	0.7278	0.6973	0.6988
CYSTADENOMA	(780 )	IN 75-89	2	22	11			
		IN 90-98	1	1	0			
		IN 90-98	2	9	7			
		IN 99-99	1	3	1			
		IN 99-99	2	46	23			
Spontaneous tumor rate 4% in ctrl. - Total			-	4	1			
UTERUS	(42000 )	IN 75-89	1	0	0	0.9901	0.9239	0.9246
HEMANGIOMA	(1570 )	IN 75-89	2	22	11			
		IN 99-99	1	4	0			
		IN 99-99	2	45	24			
Spontaneous tumor rate 4% in ctrl. - Total			-	4	0			
UTERUS	(42000 )	IN 75-89	1	1	0	0.8178	0.7852	0.7875
HEMANGIOSARCOMA	(1580 )	IN 75-89	2	21	11			
		FA 92	1	0	0			
		FA 92	2	58	29			

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Spontaneous tumor rate LE 1% in ctrl. - Total		-	1	0	0	
UTERUS	(42000 )	IN 75-89	1	0	1	0.6139 0.7546 0.7561
LEIOMYOMA	(2030 )	IN 75-89	2	22	10	
		IN 99-99	1	0	1	
		IN 99-99	2	49	23	
		FA 95	1	0	0	
		FA 95	2	54	27	
Spontaneous tumor rate LE 1% in ctrl. - Total		-	0	2	2	
UTERUS	(42000 )	FA 62	1	1	0	0.4991 0.3528 0.3549
LEIOMYOSARCOMA	(2040 )	FA 62	2	89	44	
		FA 83	1	0	0	
		FA 83	2	73	36	
		FA 95	1	1	0	
		FA 95	2	53	27	
Spontaneous tumor rate 2% in ctrl. - Total		-	2	0	0	
UTERUS	(42000 )	IN 50-74	1	0	1	0.5338 0.5511 0.5521
POLYP	(3250 )	IN 50-74	2	14	4	
		IN 75-89	1	1	1	
		IN 75-89	2	21	10	
		IN 99-99	1	5	1	
		IN 99-99	2	44	23	
Spontaneous tumor rate 6% in ctrl. - Total		-	6	3	3	
UTERUS	(42000 )	IN 75-89	1	2	0	0.3424 0.2914 0.2926
SARCOMA	(3460 )	IN 75-89	2	20	11	
		IN 99-99	1	2	1	
		IN 99-99	2	47	23	
		FA 91	1	0	0	
		FA 91	2	58	31	
Spontaneous tumor rate 4% in ctrl. - Total		-	4	1	1	
UTERUS OVIDUCT	(42146 )	IN 50-74	1	1	0	1.0000 0.7425 0.7456
LEIOMYOSARCOMA	(2040 )	IN 50-74	2	13	5	
Spontaneous tumor rate LE 1% in ctrl. - Total		-	1	0	0	
VAGINA	(46000 )	IN 99-99	1	1	0	1.0000 0.7484 0.7515
LEIOMYOMA	(2030 )	IN 99-99	2	48	24	
Spontaneous tumor rate LE 1% in ctrl. - Total		-	1	0	0	
VAGINA CERVIX	(46140 )	FA 89	1	1	0	1.0000 0.7428 0.7460
POLYP	(3250 )	FA 89	2	60	32	
Spontaneous tumor rate LE 1% in ctrl. - Total		-	1	0	0	
VAGINA CERVIX	(46140 )	IN 90-98	1	0	0	0.1724 0.0163 0.0168
SARCOMA	(3460 )	IN 90-98	2	10	7	
Spontaneous tumor rate LE 1% in ctrl. - Total		-	0	0	0	
SKIN	(59000 )	IN 75-89	1	1	0	0.6915 0.7520 0.7534
FIBROSARCOMA	(1350 )	IN 75-89	2	21	11	
		IN 90-98	1	1	0	
		IN 90-98	2	9	5	
		IN 99-99	1	0	1	
		IN 99-99	2	49	23	
		FA 91	1	0	2	
		FA 91	2	58	29	
Spontaneous tumor rate 2% in ctrl. - Total		-	2	3	3	
SKIN	(59000 )	FA 83	1	1	0	1.0000 0.8176 0.8195
MYXOSARCOMA	(2440 )	FA 83	2	72	36	
		FA 93	1	1	0	
		FA 93	2	54	29	

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Appendix D (Female-Mice): Page 4

Spontaneous tumor rate 2%	in ctrl.	-	Total	-	2	0	
SKIN	(59000	)	IN 75-89	1	0	0	0.1006 0.1183 0.1195
SARCOMA	(3460	)	IN 75-89	2	22	10	
			FA 80	1	0	1	
			FA 80	2	76	38	
			FA 93	1	0	1	
			FA 93	2	55	28	
Spontaneous tumor rate LE 1%	in ctrl.	-	Total	-	0	2	
SKIN	(59000	)	FA 49	1	1	0	1.0000 0.7345 0.7379
TRICHOEPITHELIOMA	(3860	)	FA 49	2	95	47	
Spontaneous tumor rate LE 1%	in ctrl.	-	Total	-	1	0	
MAMMARY GLAND	(61000	)	IN 99-99	1	1	0	1.0000 0.7484 0.7515
FIBROADENOMA	(1320	)	IN 99-99	2	48	24	
Spontaneous tumor rate LE 1%	in ctrl.	-	Total	-	1	0	
MAMMARY GLAND	(61000	)	IN 75-89	1	1	0	0.6134 0.6491 0.6522
ADENOACANTHOMA	(55	)	IN 75-89	2	21	11	
			IN 90-98	1	0	1	
			IN 90-98	2	10	6	
Spontaneous tumor rate LE 1%	in ctrl.	-	Total	-	1	1	
MAMMARY GLAND	(61000	)	IN 50-74	1	0	0	0.2679 0.2977 0.2985
ADENOCARCINOMA	(60	)	IN 50-74	2	14	4	
			IN 90-98	1	0	0	
			IN 90-98	2	10	7	
			IN 99-99	1	2	1	
			IN 99-99	2	47	23	
			FA 72	1	0	0	
			FA 72	2	81	43	
			FA 73	1	0	1	
			FA 73	2	81	42	
			FA 75	1	0	1	
			FA 75	2	81	41	
			FA 90	1	0	0	
			FA 90	2	59	31	
			FA 92	1	0	0	
			FA 92	2	58	29	
Spontaneous tumor rate 2%	in ctrl.	-	Total	-	2	3	
MAMMARY GLAND	(61000	)	IN 99-99	1	1	0	1.0000 0.7484 0.7515
ADENOMA	(70	)	IN 99-99	2	48	24	
Spontaneous tumor rate LE 1%	in ctrl.	-	Total	-	1	0	
LUNG	(71000	)	IN 50-74	1	0	0	0.8751 0.8428 0.8436
ADENOCARCINOMA	(60	)	IN 50-74	2	14	5	
			IN 75-89	1	2	0	
			IN 75-89	2	18	11	
			IN 99-99	1	3	1	
			IN 99-99	2	46	23	
			FA 82	1	1	0	
			FA 82	2	75	36	
			FA 84	1	1	0	
			FA 84	2	71	34	
			FA 98	1	0	0	
			FA 98	2	50	24	
Spontaneous tumor rate 7%	in ctrl.	-	Total	-	7	1	
LUNG	(71000	)	IN 0-49	1	0	0	0.3351 0.3398 0.3407
ADENOMA	(70	)	IN 0-49	2	5	3	
			IN 50-74	1	1	0	
			IN 50-74	2	13	5	
			IN 75-89	1	2	0	

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		IN 75-89	2	20	11	
		IN 90-98	1	4	0	
		IN 90-98	2	6	7	
		IN 99-99	1	10	2	
		IN 99-99	2	39	22	
Spontaneous tumor rate 17%	in ctrl.	- Total	-	17	2	
SPLEEN	(77000 )	IN 99-99	1	0	0	0.0516 0.0054 0.0054
HEMANGIOMA	(1570 )	IN 99-99	2	49	24	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	0	0	
SPLEEN	(77000 )	IN 90-98	1	1	0	0.0948 0.0543 0.0548
HEMANGIOSARCOMA	(1580 )	IN 90-98	2	9	7	
		IN 99-99	1	0	0	
		IN 99-99	2	49	24	
		FA 83	1	0	1	
		FA 83	2	73	35	
		FA 91	1	0	0	
		FA 91	2	58	31	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	1	
BONE CRANIAL AND FACIAL B	(84308 )	IN 99-99	1	0	0	0.2302 0.0361 0.0369
OSTEOMA	(2730 )	IN 99-99	2	49	24	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	0	0	
SKELETAL MUSCLE	(87000 )	IN 99-99	1	1	0	0.8506 0.8219 0.8237
RHABDOMYOSARCOMA	(3420 )	IN 99-99	2	48	24	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0	
STOMACH GLANDULAR MUCOSA	(9026 )	IN 75-89	1	1	0	0.6134 0.6491 0.6522
PAPILLOMA	(2910 )	IN 75-89	2	21	11	
		IN 90-98	1	0	1	
		IN 90-98	2	10	6	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	1	
STOMACH NONGLANDULAR MUCO	(9027 )	IN 99-99	1	1	1	0.6663 0.7258 0.7282
PAPILLOMA	(2910 )	IN 99-99	2	48	23	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	1	
STOMACH PYLORUS	(9038 )	IN 99-99	1	1	0	1.0000 0.7484 0.7515
CARCINOMA	(410 )	IN 99-99	2	48	24	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0	
EYE HARDERIAN GLAND	(95409 )	IN 50-74	1	2	0	0.9815 0.9736 0.9738
ADENOMA	(70 )	IN 50-74	2	12	5	
		IN 75-89	1	1	0	
		IN 75-89	2	21	11	
		IN 90-98	1	0	1	
		IN 90-98	2	10	6	
		IN 99-99	1	2	3	
		IN 99-99	2	47	21	
Spontaneous tumor rate 5%	in ctrl.	- Total	-	5	4	
PRIMARY SITE UNDETERMINED	(98000 )	FA 67	1	1	0	1.0000 0.7349 0.7383
LEUKEMIA	(2050 )	FA 67	2	85	44	
Spontaneous tumor rate LE 1%	in ctrl.	- Total	-	1	0	
PRIMARY SITE UNDETERMINED	(98000 )	IN 99-99	1	3	2	0.8928 0.8867 0.8868
LYMPHOMA	(2150 )	IN 99-99	2	45	22	
		FA 54	1	0	1	
		FA 54	2	95	46	
		FA 63	1	1	0	
		FA 63	2	88	44	
		FA 69	1	1	0	
		FA 69	2	83	44	
		FA 72	1	0	0	



FA 72	2	81	43	
FA 76	1	1	0	
FA 76	2	80	41	
FA 79	1	2	0	
FA 79	2	77	39	
FA 84	1	0	1	
FA 84	2	72	33	
FA 85	1	0	0	
FA 85	2	69	33	
FA 86	1	0	1	
FA 86	2	69	32	
FA 87	1	2	0	
FA 87	2	65	32	
FA 89	1	1	1	
FA 89	2	60	31	
FA 90	1	1	0	
FA 90	2	58	31	
FA 92	1	1	0	
FA 92	2	57	29	
FA 93	1	0	0	
FA 93	2	55	29	
FA 94	1	0	1	
FA 94	2	54	27	
FA 95	1	1	0	
FA 95	2	53	27	
FA 96	1	1	0	
FA 96	2	51	26	
FA 97	1	0	1	
FA 97	2	50	25	
FA 99	1	1	0	
FA 99	2	48	24	
Spontaneous tumor rate 16% in ctrl. - Total	-	16	8	
PRIMARY SITE UNDETERMINED (98000 ) FA 69	1	0	0	0.6997
SARCOMA (3460 ) FA 69	2	84	44	0.7610
FA 78	1	0	1	0.7624
FA 78	2	79	39	
FA 81	1	0	1	
FA 81	2	76	36	
FA 84	1	1	0	
FA 84	2	71	34	
FA 97	1	0	1	
FA 97	2	50	25	
Spontaneous tumor rate LE 1% in ctrl. - Total	-	1	3	
PRIMARY SITE UNDETERMINED (98000 ) FA 82	1	1	0	1.0000
SCHWANNOMA (3475 ) FA 82	2	75	36	0.7357
Spontaneous tumor rate LE 1% in ctrl. - Total	-	1	0	0.7391

- 6 - (End of File)

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## APPENDIX D (Female-Mice)

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Analysis of Carcinogenic Potential in Female Mice  
Test of Dose-Response (Tumor) Positive Linear Trend

TABLE II.D (Female-Mice): Summary of Table I.D (Female-Mice)

Organ Code	Organ Name	Tumor Code	Tumor Name	Exact-P	Asymp-P	AsyCor-P
77000	SPLEEN	1570	HEMANGIOMA	0.0516	0.0054	
77000	SPLEEN	1580	HEMANGIOSARCOMA	0.0948	0.0543	0.0054
59000	SKIN	3460	SARCOMA	0.1006	0.1183	0.0548
46140	VAGINA CERVIX	3460	SARCOMA	0.1724	0.0163	0.1185
22080	ADRENAL CORTEX	410	CARCINOMA	0.2302	0.0361	0.0168
84308	BONE CRANIAL AND FACIAL B	2730	OSTEOMA	0.2302	0.0361	0.0369
61000	MAMMARY GLAND	60	ADENOCARCINOMA	0.2679	0.2977	0.0369
71000	LUNG	70	ADENOMA	0.3351	0.3398	0.2985
42000	UTERUS	3460	SARCOMA	0.3424	0.2914	0.3407
40000	OVARY	2095	LUTEOMA	0.3629	0.1771	0.2926
14000	LIVER	70	ADENOMA	0.3656	0.3137	0.1789
14000	LIVER	1715	HISTIOCYTIC SARCOMA	0.4207	0.5699	0.3157
14000	LIVER	1580	HEMANGIOSARCOMA	0.4952	0.7009	0.5737
42000	UTERUS	2040	LEIOMYOSARCOMA	0.4991	0.3528	0.7034
40000	OVARY	1560	GRANULOSA CELL TUMOR	0.5107	0.3654	0.3549
42000	UTERUS	3250	POLYP	0.5338	0.5511	0.3675
11000	SMALL INTESTINE	1580	HEMANGIOSARCOMA	0.6111	0.7357	0.5521
61000	MAMMARY GLAND	55	ADENOACANTHOMA	0.6134	0.6491	0.7388
9026	STOMACH GLANDULAR MUCOSA	2910	PAPILLOMA	0.6134	0.6491	0.6522
42000	UTERUS	2030	LEIOMYOMA	0.6139	0.7546	0.6522
14000	LIVER	1570	HEMANGIOMA	0.6519	0.7171	0.7561
18073	PANCREAS ISLET	70	ADENOMA	0.6663	0.7258	0.7183
9027	STOMACH NONGLANDULAR MUCO	2910	PAPILLOMA	0.6663	0.7258	0.7282
59000	SKIN	1350	FIBROSARCOMA	0.6915	0.7520	0.7282
98000	PRIMARY SITE UNDETERMINED	3460	SARCOMA	0.6997	0.7610	0.7534
40000	OVARY	780	CYSTADENOMA	0.7278	0.6973	0.7624
29000	PITUITARY	70	ADENOMA	0.7573	0.7479	0.6988
42000	UTERUS	1580	HEMANGIOSARCOMA	0.7573	0.7479	0.7490
87000	SKELETAL MUSCLE	3420	RHABDOMYOSARCOMA	0.8178	0.7852	0.7875
22000	ADRENAL	3585	SPINDLE CELL TUMOR	0.8506	0.8219	0.8237
71000	LUNG	60	ADENOCARCINOMA	0.8739	0.8449	0.8462
98000	PRIMARY SITE UNDETERMINED	2150	LYMPHOMA	0.8751	0.8428	0.8436
95409	EYE HARDERIAN GLAND	70	ADENOMA	0.8928	0.8867	0.8868
42000	UTERUS	1570	HEMANGIOMA	0.9815	0.9736	0.9738
22000	ADRENAL	3060	PHEOCHROMOCYTOMA	0.9901	0.9239	0.9246
22080	ADRENAL CORTEX	70	ADENOMA	1.0000	0.7425	0.7456
61000	MAMMARY GLAND	70	ADENOMA	1.0000	0.8291	0.8309
61000	MAMMARY GLAND	1320	FIBROADENOMA	1.0000	0.7484	0.7515
27000	PARATHYROID	70	ADENOMA	1.0000	0.7484	0.7515
98000	PRIMARY SITE UNDETERMINED	2050	LEUKEMIA	1.0000	0.7320	0.7356
98000	PRIMARY SITE UNDETERMINED	3475	SCHWANNOMA	1.0000	0.7349	0.7383
59000	SKIN	2440	MYXOSARCOMA	1.0000	0.7357	0.7391
59000	SKIN	3860	TRICHOEPITHELIOMA	1.0000	0.8176	0.8195
11000	SMALL INTESTINE	60	ADENOCARCINOMA	1.0000	0.7345	0.7379
11000	SMALL INTESTINE	1570	HEMANGIOMA	1.0000	0.7320	0.7356
9038	STOMACH PYLORUS	410	CARCINOMA	1.0000	0.7484	0.7515
42146	UTERUS OVIDUCT	2040	LEIOMYOSARCOMA	1.0000	0.7484	0.7515
46000	VAGINA	2030	LEIOMYOMA	1.0000	0.7425	0.7456
46140	VAGINA CERVIX	3250	POLYP	1.0000	0.7484	0.7515
				1.0000	0.7428	0.7460

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