

**TDMS No.** 20008 - 03  
**Test Type:** CHRONIC  
**Route:** DOSED FEED  
**Species/Strain:** RATS/F 344/N

**P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS**

Milk thistle extract  
**CAS Number:** 84604-20-6

**Date Report Requested:** 10/09/2008  
**Time Report Requested:** 11:00:55  
**First Dose M/F:** 03/04/03 / 03/04/03  
**Lab:** SRI

F1\_R2

**C Number:** C20008  
**Lock Date:** 06/29/2006  
**Cage Range:** ALL  
**Date Range:** ALL  
**Reasons For Removal:** ALL  
**Removal Date Range:** ALL  
**Treatment Groups:** Include ALL  
**Study Gender:** Both  
**TDMSE Version:** 2.0.0

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## HISTORICAL CONTROL STUDIES From October 2007 Report

### SAME ROUTE

88138-03 -- Benzophenone (ORAL FEED)  
99027-03 -- Chromium picolinate monohydrate (ORAL FEED)  
05174-05 -- Cresols (ORAL FEED)  
92012-05 -- 2-Methylimidazole (ORAL FEED)  
92013-05 -- 4-Methylimidazole (ORAL FEED)

### ALL ROUTES

88138-03 -- Benzophenone (ORAL FEED)  
99027-03 -- Chromium picolinate monohydrate (ORAL FEED)  
05174-05 -- Cresols (ORAL FEED)  
96011-05 -- Cumene (INHALATION AIR)  
97003-07 -- 1,2-Dibromo-2,4-dicyanobutane (SKIN ETHANOL)  
93020-07 -- Diisopropylcarbodiimide (SKIN ETHANOL)  
88004-05 -- Divinylbenzene (INHALATION AIR)  
88123-05 -- Formamide (GAVAGE WATER)  
95011-07 -- 5-(Hydroxymethyl)-2-furfural (GAVAGE WATER)  
88105-03 -- Isoeugenol (GAVAGE CORN OIL)  
97006-01 -- Methyl isobutyl ketone (INHALATION AIR)  
91005-07 -- Methylene blue trihydrate (GAVAGE METHYLCELLULOSE)  
92012-05 -- 2-Methylimidazole (ORAL FEED)  
92013-05 -- 4-Methylimidazole (ORAL FEED)  
88006-03 -- alpha-Methylstyrene (INHALATION AIR)  
99023-03 -- beta-Myrcene (GAVAGE CORN OIL)  
97008-05 -- Propargyl alcohol (INHALATION AIR)  
20114-07 -- Sodium dichromate dihydrate (VI) (ORAL WATER)  
96001-05 -- Stoddard solvent (type IIC) (INHALATION AIR)  
96019-05 -- Water disinfection byproducts (Bromochloroacetic acid) (ORAL WATER)

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**HISTORICAL CONTROL STUDIES**  
**From October 2007 Report**

96018-03 -- Water disinfection byproducts (Bromodichloromethane) (ORAL WATER)  
96017-05 -- Water disinfection byproducts (Dibromoacetic acid) (ORAL WATER)  
96015-05 -- Water disinfection byproducts (Dibromoacetonitrile) (ORAL WATER)  
96010-03 -- Water disinfection byproducts (Sodium chlorate) (ORAL WATER)

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**FOR ALL DOSES THE TUMOR RATES IN THE FOLLOWING TISSUES/ORGANS ARE BASED ON NUMBER OF TISSUES EXAMINED.  
IN OTHER TISSUES/ORGANS RATES ARE BASED ON THE NUMBER OF ANIMALS NECROPSIED.**

Adrenal Cortex  
Adrenal Medulla  
Brain  
Clitoral/Preputial Gland  
Heart  
Islets, Pancreatic  
Kidney  
Liver  
Lung  
Nose  
Ovary  
Pancreas  
Pituitary Gland  
Salivary Glands  
Testes  
Thymus  
Thyroid Gland

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## SUMMARY OF STATISTICALLY SIGNIFICANT ( $P \leq .05$ ) RESULTS IN THE ANALYSIS OF Milk thistle extract

### MALE RATS

<u>Organ</u>	<u>Morphology</u>
Adrenal Cortex	Adenoma
Clitoral/Preputial Gland	Adenoma
	Carcinoma or Adenoma
Skin	Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma
	Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma
	Squamous Cell Papilloma, Papilloma, or Keratoacanthoma
All Organs	Histiocytic Sarcoma
	Benign Tumors

### FEMALE RATS

<u>Organ</u>	<u>Morphology</u>
Clitoral/Preputial Gland	Adenoma
	Carcinoma or Adenoma
Islets, Pancreatic	Adenoma
	Carcinoma or Adenoma
Mammary Gland	Adenoma
	Fibroadenoma
	Fibroma, Fibroadenoma or Adenoma
	Fibroma, Fibroadenoma, Carcinoma, or Adenoma
Ovary	Granulosa Cell Tumor Malignant
Thyroid Gland: C-Cell	Carcinoma
	Carcinoma or Adenoma
All Organs	Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Cortex  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46.09	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	4.3%	0%	0%	0%
TERMINAL (d)	1/36 (3%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	613	---	---	---
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	6/1197 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.115N	P=0.239N	P=0.248N	P=0.232N
POLY 1.5	P=0.115N	P=0.238N	P=0.246N	P=0.234N
POLY 6	P=0.114N	P=0.240N	P=0.248N	P=0.229N
COCH-ARM / FISHERS	P=0.115N	P=0.247N	P=0.247N	P=0.247N
MAX-ISO-POLY-3	P=0.033N*	P=0.077N	P=0.086N	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Medulla  
 Pheochromocytoma Benign**

**TUMOR RATES**

OVERALL (a)	5/50 (10%)	10/49 (20%)	5/50 (10%)	6/50 (12%)
POLY-3 RATE (b)	5/45.75	10/44.93	5/44.28	6/47.35
POLY-3 PERCENT (g)	10.9%	22.3%	11.3%	12.7%
TERMINAL (d)	4/36 (11%)	9/36 (25%)	4/35 (11%)	4/38 (11%)
FIRST INCIDENCE	711	721	646	711
HC TUMORS SAME RTE	40/250 (16%)			
HC TUMORS ALL RTES	181/1196 (15%)			

**STATISTICAL TESTS**

POLY 3	P=0.441N	P=0.120	P=0.610	P=0.524
POLY 1.5	P=0.453N	P=0.121	P=0.610	P=0.514
POLY 6	P=0.424N	P=0.118	P=0.614	P=0.537
COCH-ARM / FISHERS	P=0.466N	P=0.122	P=0.630N	P=0.500
MAX-ISO-POLY-3	P=0.430N	P=0.073	P=0.477	P=0.397
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Medulla  
 Pheochromocytoma: Benign, Complex, Malignant, NOS**

**TUMOR RATES**

OVERALL (a)	6/50 (12%)	10/49 (20%)	6/50 (12%)	7/50 (14%)
POLY-3 RATE (b)	6/45.75	10/44.93	6/44.28	7/47.35
POLY-3 PERCENT (g)	13.1%	22.3%	13.6%	14.8%
TERMINAL (d)	5/36 (14%)	9/36 (25%)	5/35 (14%)	5/38 (13%)
FIRST INCIDENCE	711	721	646	711
HC TUMORS SAME RTE	45/250 (18%)			
HC TUMORS ALL RTES	209/1196 (18%)			

**STATISTICAL TESTS**

POLY 3	P=0.481N	P=0.193	P=0.598	P=0.526
POLY 1.5	P=0.494N	P=0.194	P=0.598	P=0.515
POLY 6	P=0.463N	P=0.190	P=0.603	P=0.541
COCH-ARM / FISHERS	P=0.508N	P=0.194	P=0.620N	P=0.500
MAX-ISO-POLY-3	P=0.499	P=0.127	P=0.475	P=0.408
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)



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**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Bone</b>				
<b>Osteosarcoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	0/250 (0%)			
HC TUMORS ALL RTES	8/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Bone  
 Osteosarcoma or Osteoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	2.2%	0%	0%	0%
TERMINAL (d)	1/36 (3%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	729 (T)	---	---	---
HC TUMORS SAME RTE	2/250 (1%)			
HC TUMORS ALL RTES	10/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.311N	P=0.500N	P=0.508N	P=0.493N
POLY 1.5	P=0.310N	P=0.500N	P=0.507N	P=0.496N
POLY 6	P=0.312N	P=0.500N	P=0.507N	P=0.490N
COCH-ARM / FISHERS	P=0.306N	P=0.500N	P=0.500N	P=0.500N
MAX-ISO-POLY-3	P=0.124N	P=0.159N	P=0.168N	P=0.159N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Brain  
 Astrocytoma Malignant**

**TUMOR RATES**

OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	1/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	2.3%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	1/35 (3%)	0/38 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	0/250 (0%)			
HC TUMORS ALL RTES	4/1198 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.710	(e)	P=0.492	(e)
POLY 1.5	P=0.704	(e)	P=0.493	(e)
POLY 6	P=0.717	(e)	P=0.493	(e)
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)
MAX-ISO-POLY-3	P=0.387	(e)	P=0.158	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Brain  
 Oligodendroglioma, Glioma, or Astrocytoma**

**TUMOR RATES**

OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	1/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	2.3%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	1/35 (3%)	0/38 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	0/250 (0%)			
HC TUMORS ALL RTES	8/1198 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.710	(e)	P=0.492	(e)
POLY 1.5	P=0.704	(e)	P=0.493	(e)
POLY 6	P=0.717	(e)	P=0.493	(e)
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)
MAX-ISO-POLY-3	P=0.387	(e)	P=0.158	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	6/49 (12%)	2/50 (4%)	3/50 (6%)
POLY-3 RATE (b)	1/45.68	6/45.88	2/44.01	3/47.21
POLY-3 PERCENT (g)	2.2%	13.1%	4.5%	6.4%
TERMINAL (d)	1/36 (3%)	4/36 (11%)	1/35 (3%)	3/38 (8%)
FIRST INCIDENCE	729 (T)	647	721	729 (T)
HC TUMORS SAME RTE	8/250 (3%)			
HC TUMORS ALL RTES	43/1193 (4%)			

**STATISTICAL TESTS**

POLY 3	P=0.523	P=0.056	P=0.487	P=0.317
POLY 1.5	P=0.514	P=0.055	P=0.488	P=0.312
POLY 6	P=0.534	P=0.058	P=0.488	P=0.323
COCH-ARM / FISHERS	P=0.504	P=0.053	P=0.500	P=0.309
MAX-ISO-POLY-3	P=0.209	P=0.025*	P=0.273	P=0.167
HISTCONT SAME RTE	P=0.253	P=0.027*	P=0.356	P=0.212
HISTCONT ALL RTES	P=0.240	P=0.025*	P=0.340	P=0.199

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Carcinoma**

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	3/49 (6%)	0/50 (0%)	1/50 (2%)
POLY-3 RATE (b)	2/46.26	3/45.74	0/43.97	1/47.21
POLY-3 PERCENT (g)	4.3%	6.6%	0%	2.1%
TERMINAL (d)	0/36 (0%)	2/36 (6%)	0/35 (0%)	1/38 (3%)
FIRST INCIDENCE	591	591	---	729 (T)
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	16/1193 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.240N	P=0.495	P=0.249N	P=0.493N
POLY 1.5	P=0.241N	P=0.493	P=0.247N	P=0.496N
POLY 6	P=0.238N	P=0.496	P=0.250N	P=0.490N
COCH-ARM / FISHERS	P=0.240N	P=0.490	P=0.247N	P=0.500N
MAX-ISO-POLY-3	P=0.192N	P=0.319	P=0.087N	P=0.277N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	3/50 (6%)	9/49 (18%)	2/50 (4%)	4/50 (8%)
POLY-3 RATE (b)	3/46.26	9/46.34	2/44.01	4/47.21
POLY-3 PERCENT (g)	6.5%	19.4%	4.5%	8.5%
TERMINAL (d)	1/36 (3%)	6/36 (17%)	1/35 (3%)	4/38 (11%)
FIRST INCIDENCE	591	591	721	729 (T)
HC TUMORS SAME RTE	9/250 (4%)			
HC TUMORS ALL RTES	57/1193 (5%)			

**STATISTICAL TESTS**

POLY 3	P=0.388N	P=0.059	P=0.523N	P=0.511
POLY 1.5	P=0.393N	P=0.058	P=0.519N	P=0.507
POLY 6	P=0.383N	P=0.061	P=0.525N	P=0.516
COCH-ARM / FISHERS	P=0.397N	P=0.056	P=0.500N	P=0.500
MAX-ISO-POLY-3	P=0.238N	P=0.031*	P=0.347N	P=0.359
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Heart  
 Schwannoma Malignant**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/45.68	2/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	2.2%	4.4%	0%	0%
TERMINAL (d)	1/36 (3%)	2/36 (6%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	---	---
HC TUMORS SAME RTE	2/250 (1%)			
HC TUMORS ALL RTES	4/1199 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.186N	P=0.501	P=0.508N	P=0.493N
POLY 1.5	P=0.188N	P=0.501	P=0.507N	P=0.496N
POLY 6	P=0.184N	P=0.500	P=0.507N	P=0.490N
COCH-ARM / FISHERS	P=0.188N	P=0.500	P=0.500N	P=0.500N
MAX-ISO-POLY-3	P=0.173N	P=0.282	P=0.168N	P=0.159N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Islets, Pancreatic  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	3/50 (6%)	3/50 (6%)	1/50 (2%)	3/50 (6%)
POLY-3 RATE (b)	3/45.68	3/46.11	1/44.55	3/47.4
POLY-3 PERCENT (g)	6.6%	6.5%	2.2%	6.3%
TERMINAL (d)	3/36 (8%)	2/36 (6%)	0/35 (0%)	1/38 (3%)
FIRST INCIDENCE	729 (T)	643	549	702
HC TUMORS SAME RTE	6/249 (2%)			
HC TUMORS ALL RTES	73/1194 (6%)			

**STATISTICAL TESTS**

POLY 3	P=0.535N	P=0.658N	P=0.314N	P=0.645N
POLY 1.5	P=0.540N	P=0.659N	P=0.315N	P=0.652N
POLY 6	P=0.527N	P=0.656N	P=0.311N	P=0.635N
COCH-ARM / FISHERS	P=0.544N	P=0.661N	P=0.309N	P=0.661N
MAX-ISO-POLY-3	P=0.512N	P=0.495N	P=0.164N	P=0.481N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

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DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**Islets, Pancreatic  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	4/50 (8%)	3/50 (6%)	1/50 (2%)	3/50 (6%)
POLY-3 RATE (b)	4/45.68	3/46.11	1/44.55	3/47.4
POLY-3 PERCENT (g)	8.8%	6.5%	2.2%	6.3%
TERMINAL (d)	4/36 (11%)	2/36 (6%)	0/35 (0%)	1/38 (3%)
FIRST INCIDENCE	729 (T)	643	549	702
HC TUMORS SAME RTE	8/249 (3%)			
HC TUMORS ALL RTES	100/1194 (8%)			

**STATISTICAL TESTS**

POLY 3	P=0.389N	P=0.495N	P=0.186N	P=0.480N
POLY 1.5	P=0.394N	P=0.497N	P=0.187N	P=0.488N
POLY 6	P=0.381N	P=0.493N	P=0.183N	P=0.468N
COCH-ARM / FISHERS	P=0.397N	P=0.500N	P=0.181N	P=0.500N
MAX-ISO-POLY-3	P=0.305N	P=0.343N	P=0.091N	P=0.332N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

---

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Liver  
 Hepatocellular Adenoma**

**TUMOR RATES**

OVERALL (a)	3/50 (6%)	6/50 (12%)	5/50 (10%)	3/50 (6%)
POLY-3 RATE (b)	3/46.12	6/45.8	5/44.28	3/47.29
POLY-3 PERCENT (g)	6.5%	13.1%	11.3%	6.3%
TERMINAL (d)	2/36 (6%)	6/36 (17%)	4/35 (11%)	2/38 (5%)
FIRST INCIDENCE	600	729 (T)	646	711
HC TUMORS SAME RTE	3/250 (1%)			
HC TUMORS ALL RTES	10/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.432N	P=0.238	P=0.334	P=0.651N
POLY 1.5	P=0.440N	P=0.241	P=0.337	P=0.655N
POLY 6	P=0.421N	P=0.234	P=0.334	P=0.645N
COCH-ARM / FISHERS	P=0.449N	P=0.243	P=0.357	P=0.661N
MAX-ISO-POLY-3	P=0.415N	P=0.145	P=0.218	P=0.487N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Lung  
 Alveolar/Bronchiolar Adenoma**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	2/50 (4%)	2/50 (4%)	2/50 (4%)
POLY-3 RATE (b)	1/45.68	2/46.01	2/43.97	2/47.21
POLY-3 PERCENT (g)	2.2%	4.4%	4.6%	4.2%
TERMINAL (d)	1/36 (3%)	1/36 (3%)	2/35 (6%)	2/38 (5%)
FIRST INCIDENCE	729 (T)	672	729 (T)	729 (T)
HC TUMORS SAME RTE	7/250 (3%)			
HC TUMORS ALL RTES	31/1199 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.438	P=0.503	P=0.487	P=0.512
POLY 1.5	P=0.432	P=0.502	P=0.488	P=0.507
POLY 6	P=0.447	P=0.504	P=0.488	P=0.518
COCH-ARM / FISHERS	P=0.423	P=0.500	P=0.500	P=0.500
MAX-ISO-POLY-3	P=0.471	P=0.283	P=0.273	P=0.293
HISTCONT SAME RTE	P=0.571	P=0.369	P=0.355	P=0.382
HISTCONT ALL RTES	P=0.551	P=0.354	P=0.340	P=0.367

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Lung  
 Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	3/50 (6%)	2/50 (4%)	3/50 (6%)
POLY-3 RATE (b)	1/45.68	3/46.01	2/43.97	3/47.21
POLY-3 PERCENT (g)	2.2%	6.5%	4.6%	6.4%
TERMINAL (d)	1/36 (3%)	2/36 (6%)	2/35 (6%)	3/38 (8%)
FIRST INCIDENCE	729 (T)	672	729 (T)	729 (T)
HC TUMORS SAME RTE	9/250 (4%)			
HC TUMORS ALL RTES	46/1199 (4%)			

**STATISTICAL TESTS**

POLY 3	P=0.316	P=0.308	P=0.487	P=0.317
POLY 1.5	P=0.310	P=0.307	P=0.488	P=0.312
POLY 6	P=0.325	P=0.309	P=0.488	P=0.323
COCH-ARM / FISHERS	P=0.302	P=0.309	P=0.500	P=0.309
MAX-ISO-POLY-3	P=0.291	P=0.157	P=0.273	P=0.167
HISTCONT SAME RTE	P=0.354	P=0.199	P=0.355	P=0.212
HISTCONT ALL RTES	P=0.338	P=0.186	P=0.340	P=0.199

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Adenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	5/1199 (0%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Carcinoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	0/250 (0%)			
HC TUMORS ALL RTES	8/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

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DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

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**Mammary Gland  
 Carcinoma or Adenoma**

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TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	13/1199 (1%)			

**STATISTICAL TESTS**

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POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

---



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Fibroadenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)
POLY-3 RATE (b)	0/45.68	1/45.8	1/43.97	2/47.4
POLY-3 PERCENT (g)	0%	2.2%	2.3%	4.2%
TERMINAL (d)	0/36 (0%)	1/36 (3%)	1/35 (3%)	1/38 (3%)
FIRST INCIDENCE	---	729 (T)	729 (T)	682
HC TUMORS SAME RTE	7/250 (3%)			
HC TUMORS ALL RTES	43/1199 (4%)			

**STATISTICAL TESTS**

POLY 3	P=0.162	P=0.500	P=0.492	P=0.246
POLY 1.5	P=0.158	P=0.500	P=0.493	P=0.242
POLY 6	P=0.167	P=0.500	P=0.493	P=0.250
COCH-ARM / FISHERS	P=0.153	P=0.500	P=0.500	P=0.247
MAX-ISO-POLY-3	P=0.134	P=0.159	P=0.158	P=0.084
HISTCONT SAME RTE	P=0.162	P=0.202	P=0.201	P=0.103
HISTCONT ALL RTES	P=0.154	P=0.189	P=0.189	P=0.096

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Mammary Gland  
 Fibroma, Fibroadenoma or Adenoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)
POLY-3 RATE (b)	0/45.68	1/45.8	1/43.97	2/47.4
POLY-3 PERCENT (g)	0%	2.2%	2.3%	4.2%
TERMINAL (d)	0/36 (0%)	1/36 (3%)	1/35 (3%)	1/38 (3%)
FIRST INCIDENCE	---	729 (T)	729 (T)	682
HC TUMORS SAME RTE	8/250 (3%)			
HC TUMORS ALL RTES	49/1199 (4%)			

**STATISTICAL TESTS**

POLY 3	P=0.162	P=0.500	P=0.492	P=0.246
POLY 1.5	P=0.158	P=0.500	P=0.493	P=0.242
POLY 6	P=0.167	P=0.500	P=0.493	P=0.250
COCH-ARM / FISHERS	P=0.153	P=0.500	P=0.500	P=0.247
MAX-ISO-POLY-3	P=0.134	P=0.159	P=0.158	P=0.084
HISTCONT SAME RTE	P=0.162	P=0.202	P=0.201	P=0.103
HISTCONT ALL RTES	P=0.154	P=0.189	P=0.189	P=0.096

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Mammary Gland  
 Fibroma, Fibroadenoma, Carcinoma, or Adenoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)
POLY-3 RATE (b)	0/45.68	1/45.8	1/43.97	2/47.4
POLY-3 PERCENT (g)	0%	2.2%	2.3%	4.2%
TERMINAL (d)	0/36 (0%)	1/36 (3%)	1/35 (3%)	1/38 (3%)
FIRST INCIDENCE	---	729 (T)	729 (T)	682
HC TUMORS SAME RTE	8/250 (3%)			
HC TUMORS ALL RTES	55/1199 (5%)			

**STATISTICAL TESTS**

POLY 3	P=0.162	P=0.500	P=0.492	P=0.246
POLY 1.5	P=0.158	P=0.500	P=0.493	P=0.242
POLY 6	P=0.167	P=0.500	P=0.493	P=0.250
COCH-ARM / FISHERS	P=0.153	P=0.500	P=0.500	P=0.247
MAX-ISO-POLY-3	P=0.134	P=0.159	P=0.158	P=0.084
HISTCONT SAME RTE	P=0.162	P=0.202	P=0.201	P=0.103
HISTCONT ALL RTES	P=0.154	P=0.189	P=0.189	P=0.096

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Pancreas  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/45.75	1/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	4.4%	2.2%	0%	0%
TERMINAL (d)	1/36 (3%)	1/36 (3%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	711	729 (T)	---	---
HC TUMORS SAME RTE	2/247 (1%)			
HC TUMORS ALL RTES	21/1191 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.101N	P=0.500N	P=0.246N	P=0.230N
POLY 1.5	P=0.101N	P=0.500N	P=0.245N	P=0.233N
POLY 6	P=0.100N	P=0.501N	P=0.246N	P=0.227N
COCH-ARM / FISHERS	P=0.101N	P=0.500N	P=0.247N	P=0.247N
MAX-ISO-POLY-3	P=0.078N	P=0.280N	P=0.085N	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Pituitary Gland: Pars Distalis or Unspecified Site  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	13/50 (26%)	15/50 (30%)	8/50 (16%)	11/50 (22%)
POLY-3 RATE (b)	13/46.31	15/47.83	8/44.47	11/47.64
POLY-3 PERCENT (g)	28.1%	31.4%	18%	23.1%
TERMINAL (d)	10/36 (28%)	9/36 (25%)	6/35 (17%)	7/38 (18%)
FIRST INCIDENCE	599	587	637	682
HC TUMORS SAME RTE	65/249 (26%)			
HC TUMORS ALL RTES	541/1192 (45%)			

**STATISTICAL TESTS**

POLY 3	P=0.227N	P=0.451	P=0.186N	P=0.376N
POLY 1.5	P=0.234N	P=0.434	P=0.184N	P=0.389N
POLY 6	P=0.217N	P=0.474	P=0.183N	P=0.358N
COCH-ARM / FISHERS	P=0.240N	P=0.412	P=0.163N	P=0.408N
MAX-ISO-POLY-3	P=0.252N	P=0.365	P=0.131N	P=0.293N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

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DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

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**Pituitary Gland: Pars Distalis or Unspecified Site  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	13/50 (26%)	15/50 (30%)	9/50 (18%)	11/50 (22%)
POLY-3 RATE (b)	13/46.31	15/47.83	9/44.47	11/47.64
POLY-3 PERCENT (g)	28.1%	31.4%	20.2%	23.1%
TERMINAL (d)	10/36 (28%)	9/36 (25%)	7/35 (20%)	7/38 (18%)
FIRST INCIDENCE	599	587	637	682
HC TUMORS SAME RTE	65/249 (26%)			
HC TUMORS ALL RTES	547/1192 (46%)			

**STATISTICAL TESTS**

POLY 3	P=0.236N	P=0.451	P=0.266N	P=0.376N
POLY 1.5	P=0.244N	P=0.434	P=0.263N	P=0.389N
POLY 6	P=0.226N	P=0.474	P=0.263N	P=0.358N
COCH-ARM / FISHERS	P=0.251N	P=0.412	P=0.235N	P=0.408N
MAX-ISO-POLY-3	P=0.305N	P=0.365	P=0.197N	P=0.293N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

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DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

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**Skin**  
 Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthoma, Trichoepithelioma

---

TUMOR RATES	#	#	#	#
OVERALL (a)	6/50 (12%)	2/50 (4%)	4/50 (8%)	3/50 (6%)
POLY-3 RATE (b)	6/46.34	2/45.8	4/44.14	3/47.28
POLY-3 PERCENT (g)	13%	4.4%	9.1%	6.4%
TERMINAL (d)	4/36 (11%)	2/36 (6%)	3/35 (9%)	2/38 (5%)
FIRST INCIDENCE	613	729 (T)	687	714
HC TUMORS SAME RTE	21/250 (8%)			
HC TUMORS ALL RTES	112/1199 (9%)			

**STATISTICAL TESTS**

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POLY 3	P=0.268N	P=0.137N	P=0.401N	P=0.232N
POLY 1.5	P=0.273N	P=0.135N	P=0.395N	P=0.237N
POLY 6	P=0.261N	P=0.140N	P=0.403N	P=0.228N
COCH-ARM / FISHERS	P=0.278N	P=0.134N	P=0.370N	P=0.243N
MAX-ISO-POLY-3	P=0.196N	P=0.072N	P=0.284N	P=0.142N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibroma**

TUMOR RATES	#	#	#	#
OVERALL (a)	3/50 (6%)	7/50 (14%)	2/50 (4%)	1/50 (2%)
POLY-3 RATE (b)	3/45.75	7/45.9	2/43.97	1/47.21
POLY-3 PERCENT (g)	6.6%	15.3%	4.6%	2.1%
TERMINAL (d)	2/36 (6%)	6/36 (17%)	2/35 (6%)	1/38 (3%)
FIRST INCIDENCE	711	702	729 (T)	729 (T)
HC TUMORS SAME RTE	20/250 (8%)			
HC TUMORS ALL RTES	121/1199 (10%)			

**STATISTICAL TESTS**

POLY 3	P=0.086N	P=0.158	P=0.518N	P=0.294N
POLY 1.5	P=0.090N	P=0.159	P=0.516N	P=0.299N
POLY 6	P=0.082N	P=0.157	P=0.518N	P=0.288N
COCH-ARM / FISHERS	P=0.095N	P=0.159	P=0.500N	P=0.309N
MAX-ISO-POLY-3	P=0.076N	P=0.091	P=0.343N	P=0.150N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	4/50 (8%)	8/50 (16%)	3/50 (6%)	1/50 (2%)
POLY-3 RATE (b)	4/46.2	8/45.9	3/44.9	1/47.21
POLY-3 PERCENT (g)	8.7%	17.4%	6.7%	2.1%
TERMINAL (d)	2/36 (6%)	7/36 (19%)	2/35 (6%)	1/38 (3%)
FIRST INCIDENCE	599	702	310	729 (T)
HC TUMORS SAME RTE	24/250 (10%)			
HC TUMORS ALL RTES	146/1199 (12%)			

**STATISTICAL TESTS**

POLY 3	P=0.050N*	P=0.173	P=0.516N	P=0.172N
POLY 1.5	P=0.052N	P=0.176	P=0.514N	P=0.175N
POLY 6	P=0.048N*	P=0.169	P=0.517N	P=0.169N
COCH-ARM / FISHERS	P=0.056N	P=0.178	P=0.500N	P=0.181N
MAX-ISO-POLY-3	P=0.046N*	P=0.105	P=0.363N	P=0.082N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibrosarcoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	1/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	2.2%	0%	0%
TERMINAL (d)	0/36 (0%)	1/36 (3%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	729 (T)	---	---
HC TUMORS SAME RTE	2/250 (1%)			
HC TUMORS ALL RTES	14/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.568N	P=0.500	(e)	(e)
POLY 1.5	P=0.568N	P=0.500	(e)	(e)
POLY 6	P=0.567N	P=0.500	(e)	(e)
COCH-ARM / FISHERS	P=0.567N	P=0.500	(e)	(e)
MAX-ISO-POLY-3	P=0.388N	P=0.159	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	1/46.13	1/45.8	1/44.9	0/47.21
POLY-3 PERCENT (g)	2.2%	2.2%	2.2%	0%
TERMINAL (d)	0/36 (0%)	1/36 (3%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	599	729 (T)	310	---
HC TUMORS SAME RTE	4/250 (2%)			
HC TUMORS ALL RTES	26/1199 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.308N	P=0.759	P=0.755	P=0.495N
POLY 1.5	P=0.310N	P=0.760	P=0.755	P=0.497N
POLY 6	P=0.305N	P=0.758	P=0.755	P=0.493N
COCH-ARM / FISHERS	P=0.311N	P=0.753N	P=0.753N	P=0.500N
MAX-ISO-POLY-3	P=0.330N	P=0.497	P=0.492	P=0.159N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

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DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

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**Skin  
 Keratoacanthoma**

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TUMOR RATES	#	#	#	#
OVERALL (a)	4/50 (8%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
POLY-3 RATE (b)	4/46.09	1/45.8	2/43.97	3/47.28
POLY-3 PERCENT (g)	8.7%	2.2%	4.6%	6.4%
TERMINAL (d)	3/36 (8%)	1/36 (3%)	2/35 (6%)	2/38 (5%)
FIRST INCIDENCE	613	729 (T)	729 (T)	714
HC TUMORS SAME RTE	16/250 (6%)			
HC TUMORS ALL RTES	71/1199 (6%)			

**STATISTICAL TESTS**

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POLY 3	P=0.537N	P=0.181N	P=0.359N	P=0.486N
POLY 1.5	P=0.541N	P=0.180N	P=0.356N	P=0.492N
POLY 6	P=0.530N	P=0.182N	P=0.360N	P=0.479N
COCH-ARM / FISHERS	P=0.544N	P=0.181N	P=0.339N	P=0.500N
MAX-ISO-POLY-3	P=0.293N	P=0.085N	P=0.223N	P=0.337N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

---

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin**  
 Squamous Cell Carcinoma, Basal Cell Carcinoma, Basosquamous Tumor (malignant or NOS), or Carcinoma

TUMOR RATES	#	#	#	#
OVERALL (a)	2/50 (4%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	2/45.94	0/45.8	1/44.14	0/47.21
POLY-3 PERCENT (g)	4.4%	0%	2.3%	0%
TERMINAL (d)	1/36 (3%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	660	---	687	---
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	9/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.186N	P=0.238N	P=0.514N	P=0.231N
POLY 1.5	P=0.187N	P=0.237N	P=0.512N	P=0.234N
POLY 6	P=0.183N	P=0.239N	P=0.514N	P=0.228N
COCH-ARM / FISHERS	P=0.188N	P=0.247N	P=0.500N	P=0.247N
MAX-ISO-POLY-3	P=0.077N	P=0.077N	P=0.296N	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	6/50 (12%)	1/50 (2%)	3/50 (6%)	3/50 (6%)
POLY-3 RATE (b)	6/46.34	1/45.8	3/44.14	3/47.28
POLY-3 PERCENT (g)	13%	2.2%	6.8%	6.4%
TERMINAL (d)	4/36 (11%)	1/36 (3%)	2/35 (6%)	2/38 (5%)
FIRST INCIDENCE	613	729 (T)	687	714
HC TUMORS SAME RTE	18/250 (7%)			
HC TUMORS ALL RTES	91/1199 (8%)			

**STATISTICAL TESTS**

POLY 3	P=0.288N	P=0.058N	P=0.266N	P=0.232N
POLY 1.5	P=0.293N	P=0.057N	P=0.263N	P=0.237N
POLY 6	P=0.282N	P=0.059N	P=0.268N	P=0.228N
COCH-ARM / FISHERS	P=0.297N	P=0.056N	P=0.243N	P=0.243N
MAX-ISO-POLY-3	P=0.108N	P=0.025N*	P=0.171N	P=0.142N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Squamous Cell Papilloma, Papilloma, or Keratoacanthoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	5/50 (10%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
POLY-3 RATE (b)	5/46.09	1/45.8	2/43.97	3/47.28
POLY-3 PERCENT (g)	10.9%	2.2%	4.6%	6.4%
TERMINAL (d)	4/36 (11%)	1/36 (3%)	2/35 (6%)	2/38 (5%)
FIRST INCIDENCE	613	729 (T)	729 (T)	714
HC TUMORS SAME RTE	17/250 (7%)			
HC TUMORS ALL RTES	87/1199 (7%)			

**STATISTICAL TESTS**

POLY 3	P=0.390N	P=0.103N	P=0.235N	P=0.343N
POLY 1.5	P=0.394N	P=0.102N	P=0.233N	P=0.349N
POLY 6	P=0.383N	P=0.104N	P=0.236N	P=0.335N
COCH-ARM / FISHERS	P=0.397N	P=0.102N	P=0.218N	P=0.357N
MAX-ISO-POLY-3	P=0.150N	P=0.046N*	P=0.138N	P=0.223N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

Testes  
 Adenoma

**TUMOR RATES**

OVERALL (a)	46/50 (92%)	44/50 (88%)	41/50 (82%)	44/50 (88%)
POLY-3 RATE (b)	46/49.45	44/48.37	41/46.71	44/48.53
POLY-3 PERCENT (g)	93%	91%	87.8%	90.7%
TERMINAL (d)	34/36 (94%)	34/36 (94%)	31/35 (89%)	37/38 (97%)
FIRST INCIDENCE	477	501	549	591
HC TUMORS SAME RTE	234/250 (94%)			
HC TUMORS ALL RTES	1035/1199 (86%)			

**STATISTICAL TESTS**

POLY 3	P=0.394N	P=0.499N	P=0.290N	P=0.476N
POLY 1.5	P=0.363N	P=0.436N	P=0.244N	P=0.424N
POLY 6	P=0.447N	P=0.600N	P=0.318N	P=0.565N
COCH-ARM / FISHERS	P=0.319N	P=0.370N	P=0.117N	P=0.370N
MAX-ISO-POLY-3	P=0.398N	P=0.344N	P=0.186N	P=0.325N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: C-Cell  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	5/48 (10%)	6/49 (12%)	2/50 (4%)	7/49 (14%)
POLY-3 RATE (b)	5/43.86	6/45.27	2/44.44	7/46.68
POLY-3 PERCENT (g)	11.4%	13.3%	4.5%	15%
TERMINAL (d)	4/35 (11%)	6/36 (17%)	1/35 (3%)	7/38 (18%)
FIRST INCIDENCE	702	729 (T)	591	729 (T)
HC TUMORS SAME RTE	41/245 (17%)			
HC TUMORS ALL RTES	151/1185 (13%)			

**STATISTICAL TESTS**

POLY 3	P=0.405	P=0.522	P=0.210N	P=0.423
POLY 1.5	P=0.396	P=0.519	P=0.211N	P=0.411
POLY 6	P=0.418	P=0.524	P=0.207N	P=0.438
COCH-ARM / FISHERS	P=0.387	P=0.515	P=0.201N	P=0.394
MAX-ISO-POLY-3	P=0.351	P=0.395	P=0.116N	P=0.313
HISTCONT SAME RTE	P=0.427	P=0.517	P=1.000	P=0.409
HISTCONT ALL RTES	P=0.408	P=0.502	P=1.000	P=0.393

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: C-Cell  
 Carcinoma**

**TUMOR RATES**

OVERALL (a)	1/48 (2%)	1/49 (2%)	2/50 (4%)	1/49 (2%)
POLY-3 RATE (b)	1/43.83	1/45.27	2/43.97	1/46.68
POLY-3 PERCENT (g)	2.3%	2.2%	4.6%	2.1%
TERMINAL (d)	0/35 (0%)	1/36 (3%)	2/35 (6%)	1/38 (3%)
FIRST INCIDENCE	711	729 (T)	729 (T)	729 (T)
HC TUMORS SAME RTE	7/245 (3%)			
HC TUMORS ALL RTES	38/1185 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.615	P=0.753N	P=0.501	P=0.746N
POLY 1.5	P=0.607	P=0.754N	P=0.502	P=0.750N
POLY 6	P=0.623N	P=0.753N	P=0.502	P=0.742N
COCH-ARM / FISHERS	P=0.597	P=0.747N	P=0.515	P=0.747N
MAX-ISO-POLY-3	P=0.598	P=0.490N	P=0.283	P=0.482N
HISTCONT SAME RTE	P=0.718	P=1.000	P=0.369	P=1.000
HISTCONT ALL RTES	P=0.704	P=1.000	P=0.353	P=1.000

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: C-Cell  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	6/48 (13%)	7/49 (14%)	4/50 (8%)	8/49 (16%)
POLY-3 RATE (b)	6/43.94	7/45.27	4/44.44	8/46.68
POLY-3 PERCENT (g)	13.7%	15.5%	9%	17.1%
TERMINAL (d)	4/35 (11%)	7/36 (19%)	3/35 (9%)	8/38 (21%)
FIRST INCIDENCE	702	729 (T)	591	729 (T)
HC TUMORS SAME RTE	48/245 (20%)			
HC TUMORS ALL RTES	188/1185 (16%)			

**STATISTICAL TESTS**

POLY 3	P=0.409	P=0.523	P=0.362N	P=0.434
POLY 1.5	P=0.398	P=0.521	P=0.362N	P=0.421
POLY 6	P=0.424	P=0.524	P=0.358N	P=0.449
COCH-ARM / FISHERS	P=0.386	P=0.516	P=0.344N	P=0.403
MAX-ISO-POLY-3	P=0.443	P=0.404	P=0.247N	P=0.328
HISTCONT SAME RTE	P=0.539	P=0.528	P=1.000	P=0.429
HISTCONT ALL RTES	P=0.519	P=0.515	P=1.000	P=0.413

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: Follicular Cell  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	0/48 (0%)	2/49 (4%)	0/50 (0%)	0/49 (0%)
POLY-3 RATE (b)	0/43.76	2/45.74	0/43.97	0/46.68
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/35 (0%)	1/36 (3%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	591	---	---
HC TUMORS SAME RTE	5/245 (2%)			
HC TUMORS ALL RTES	15/1185 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.392N	P=0.247	(e)	(e)
POLY 1.5	P=0.396N	P=0.245	(e)	(e)
POLY 6	P=0.386N	P=0.249	(e)	(e)
COCH-ARM / FISHERS	P=0.401N	P=0.253	(e)	(e)
MAX-ISO-POLY-3	P=0.256N	P=0.084	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: Follicular Cell  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	0/48 (0%)	2/49 (4%)	0/50 (0%)	0/49 (0%)
POLY-3 RATE (b)	0/43.76	2/45.74	0/43.97	0/46.68
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/35 (0%)	1/36 (3%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	591	---	---
HC TUMORS SAME RTE	5/245 (2%)			
HC TUMORS ALL RTES	27/1185 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.392N	P=0.247	(e)	(e)
POLY 1.5	P=0.396N	P=0.245	(e)	(e)
POLY 6	P=0.386N	P=0.249	(e)	(e)
COCH-ARM / FISHERS	P=0.401N	P=0.253	(e)	(e)
MAX-ISO-POLY-3	P=0.256N	P=0.084	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Histiocytic Sarcoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	3/50 (6%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	3/46.87	1/45.83	0/43.97	0/47.21
POLY-3 PERCENT (g)	6.4%	2.2%	0%	0%
TERMINAL (d)	1/36 (3%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	477	721	---	---
HC TUMORS SAME RTE	0/250 (0%)			
HC TUMORS ALL RTES	8/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.043N*	P=0.313N	P=0.131N	P=0.117N
POLY 1.5	P=0.043N*	P=0.310N	P=0.128N	P=0.118N
POLY 6	P=0.043N*	P=0.318N	P=0.132N	P=0.116N
COCH-ARM / FISHERS	P=0.044N*	P=0.309N	P=0.121N	P=0.121N
MAX-ISO-POLY-3	P=0.023N*	P=0.163N	P=0.048N*	P=0.038N*
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs**  
**Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated**

TUMOR RATES	#	#	#	#
OVERALL (a)	17/50 (34%)	17/50 (34%)	17/50 (34%)	16/50 (32%)
POLY-3 RATE (b)	17/48.19	17/47.7	17/47.28	16/49.06
POLY-3 PERCENT (g)	35.3%	35.6%	36%	32.6%
TERMINAL (d)	8/36 (22%)	8/36 (22%)	6/35 (17%)	8/38 (21%)
FIRST INCIDENCE	600	638	86	591
HC TUMORS SAME RTE	91/250 (36%)			
HC TUMORS ALL RTES	465/1199 (39%)			

**STATISTICAL TESTS**

POLY 3	P=0.420N	P=0.570	P=0.557	P=0.475N
POLY 1.5	P=0.433N	P=0.576	P=0.561	P=0.484N
POLY 6	P=0.406N	P=0.561	P=0.561	P=0.466N
COCH-ARM / FISHERS	P=0.450N	P=0.583N	P=0.583N	P=0.500N
MAX-ISO-POLY-3	P=0.594N	P=0.485	P=0.471	P=0.391N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>All Organs</b>				
<b>Osteosarcoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/36 (0%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	1/250 (0%)			
HC TUMORS ALL RTES	11/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Osteosarcoma or Osteoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/45.68	0/45.8	0/43.97	0/47.21
POLY-3 PERCENT (g)	2.2%	0%	0%	0%
TERMINAL (d)	1/36 (3%)	0/36 (0%)	0/35 (0%)	0/38 (0%)
FIRST INCIDENCE	729 (T)	---	---	---
HC TUMORS SAME RTE	3/250 (1%)			
HC TUMORS ALL RTES	13/1199 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.311N	P=0.500N	P=0.508N	P=0.493N
POLY 1.5	P=0.310N	P=0.500N	P=0.507N	P=0.496N
POLY 6	P=0.312N	P=0.500N	P=0.507N	P=0.490N
COCH-ARM / FISHERS	P=0.306N	P=0.500N	P=0.500N	P=0.500N
MAX-ISO-POLY-3	P=0.124N	P=0.159N	P=0.168N	P=0.159N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Benign Tumors**

TUMOR RATES	#	#	#	#
OVERALL (a)	50/50 (100%)	49/50 (98%)	45/50 (90%)	48/50 (96%)
POLY-3 RATE (b)	50/50	49/50	45/47.05	48/49.36
POLY-3 PERCENT (g)	100%	98%	95.7%	97.2%
TERMINAL (d)	36/36 (100%)	35/36 (97%)	34/35 (97%)	38/38 (100%)
FIRST INCIDENCE	477	501	549	546
HC TUMORS SAME RTE	247/250 (99%)			
HC TUMORS ALL RTES	1166/1199 (97%)			

**STATISTICAL TESTS**

POLY 3	P=0.250N	P=0.500N	P=0.190N	P=0.349N
POLY 1.5	P=0.194N	P=0.500N	P=0.112N	P=0.286N
POLY 6	P=0.370N	P=0.500N	P=0.274N	P=0.537N
COCH-ARM / FISHERS	P=0.165N	P=0.500N	P=0.028N*	P=0.247N
MAX-ISO-POLY-3	P=0.149N	P=0.159N	P=0.052N	P=0.078N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>All Organs</b>				
<b>Malignant Tumors</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	26/50 (52%)	26/50 (52%)	25/50 (50%)	20/50 (40%)
POLY-3 RATE (b)	26/50	26/48.47	25/49.43	20/49.06
POLY-3 PERCENT (g)	52%	53.6%	50.6%	40.8%
TERMINAL (d)	12/36 (33%)	15/36 (42%)	11/35 (31%)	12/38 (32%)
FIRST INCIDENCE	477	591	86	591
HC TUMORS SAME RTE	127/250 (51%)			
HC TUMORS ALL RTEs	686/1199 (57%)			

**STATISTICAL TESTS**

POLY 3	P=0.121N	P=0.515	P=0.523N	P=0.179N
POLY 1.5	P=0.117N	P=0.541	P=0.514N	P=0.170N
POLY 6	P=0.129N	P=0.485	P=0.533N	P=0.193N
COCH-ARM / FISHERS	P=0.111N	P=0.579N	P=0.500N	P=0.158N
MAX-ISO-POLY-3	P=0.187N	P=0.435	P=0.443N	P=0.134N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTEs	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Males			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Malignant and Benign Tumors**

TUMOR RATES	#	#	#	#
OVERALL (a)	50/50 (100%)	49/50 (98%)	49/50 (98%)	50/50 (100%)
POLY-3 RATE (b)	50/50	49/50	49/50	50/50
POLY-3 PERCENT (g)	100%	98%	98%	100%
TERMINAL (d)	36/36 (100%)	35/36 (97%)	34/35 (97%)	38/38 (100%)
FIRST INCIDENCE	477	501	86	546
HC TUMORS SAME RTE	250/250 (100%)			
HC TUMORS ALL RTES	1195/1199 (100%)			

**STATISTICAL TESTS**

POLY 3	P=0.594	P=0.500N	P=0.500N	(e)
POLY 1.5	P=0.594	P=0.500N	P=0.500N	(e)
POLY 6	P=0.594	P=0.500N	P=0.500N	(e)
COCH-ARM / FISHERS	P=0.595	P=0.500N	P=0.500N	(e)
MAX-ISO-POLY-3	P=0.407N	P=0.159N	P=0.159N	(e)
HISTCONT SAME RTE	P=0.496	P=1.000	P=1.000	(e)
HISTCONT ALL RTES	P=0.475	P=1.000	P=1.000	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Cortex  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	0/48 (0%)	1/48 (2%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/43.73	1/43.34	0/43.08	0/46.62
POLY-3 PERCENT (g)	0%	2.3%	0%	0%
TERMINAL (d)	0/38 (0%)	1/35 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	729 (T)	---	---
HC TUMORS SAME RTE	8/199 (4%)			
HC TUMORS ALL RTES	17/1098 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.562N	P=0.498	(e)	(e)
POLY 1.5	P=0.560N	P=0.501	(e)	(e)
POLY 6	P=0.567N	P=0.493	(e)	(e)
COCH-ARM / FISHERS	P=0.561N	P=0.500	(e)	(e)
MAX-ISO-POLY-3	P=0.383N	P=0.159	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Medulla  
 Pheochromocytoma Benign**

**TUMOR RATES**

OVERALL (a)	1/48 (2%)	1/48 (2%)	4/48 (8%)	1/50 (2%)
POLY-3 RATE (b)	1/43.73	1/43.34	4/42.35	1/46.64
POLY-3 PERCENT (g)	2.3%	2.3%	9.4%	2.1%
TERMINAL (d)	1/38 (3%)	1/35 (3%)	3/34 (9%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	676	722
HC TUMORS SAME RTE	3/197 (2%)			
HC TUMORS ALL RTES	27/1091 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.561	P=0.759	P=0.169	P=0.746N
POLY 1.5	P=0.560	P=0.759N	P=0.173	P=0.745N
POLY 6	P=0.555	P=0.753	P=0.163	P=0.750N
COCH-ARM / FISHERS	P=0.542	P=0.753N	P=0.181	P=0.742N
MAX-ISO-POLY-3	P=0.343	P=0.497	P=0.081	P=0.481N
HISTCONT SAME RTE	P=0.324	P=0.521	P=0.076	P=0.548
HISTCONT ALL RTES	P=0.314	P=0.628	P=0.022*	P=1.000

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Adrenal Medulla  
 Pheochromocytoma: Benign, Complex, Malignant, NOS**

**TUMOR RATES**

OVERALL (a)	2/48 (4%)	1/48 (2%)	4/48 (8%)	1/50 (2%)
POLY-3 RATE (b)	2/43.73	1/43.34	4/42.35	1/46.64
POLY-3 PERCENT (g)	4.6%	2.3%	9.4%	2.1%
TERMINAL (d)	2/38 (5%)	1/35 (3%)	3/34 (9%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	676	722
HC TUMORS SAME RTE	6/197 (3%)			
HC TUMORS ALL RTES	36/1091 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.467N	P=0.503N	P=0.322	P=0.477N
POLY 1.5	P=0.469N	P=0.498N	P=0.329	P=0.477N
POLY 6	P=0.471N	P=0.513N	P=0.313	P=0.484N
COCH-ARM / FISHERS	P=0.482N	P=0.500N	P=0.339	P=0.485N
MAX-ISO-POLY-3	P=0.374N	P=0.284N	P=0.192	P=0.266N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Bone</b>				
<b>Osteosarcoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	2/45.31	0/44.06	0/46.62
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	619	---	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	5/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.399N	P=0.239	(e)	(e)
POLY 1.5	P=0.398N	P=0.240	(e)	(e)
POLY 6	P=0.404N	P=0.235	(e)	(e)
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)
MAX-ISO-POLY-3	P=0.252N	P=0.077	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Bone  
 Osteosarcoma or Osteoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	2/45.31	0/44.06	0/46.62
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	619	---	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	5/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.399N	P=0.239	(e)	(e)
POLY 1.5	P=0.398N	P=0.240	(e)	(e)
POLY 6	P=0.404N	P=0.235	(e)	(e)
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)
MAX-ISO-POLY-3	P=0.252N	P=0.077	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Brain  
 Astrocytoma Malignant**

**TUMOR RATES**

OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	0/44.93	2/44.06	0/46.62
POLY-3 PERCENT (g)	0%	0%	4.5%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	2/34 (6%)	0/37 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	0/200 (0%)			
HC TUMORS ALL RTES	1/1098 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.617	(e)	P=0.232	(e)
POLY 1.5	P=0.613	(e)	P=0.234	(e)
POLY 6	P=0.616	(e)	P=0.229	(e)
COCH-ARM / FISHERS	P=0.595	(e)	P=0.247	(e)
MAX-ISO-POLY-3	P=0.254	(e)	P=0.076	(e)
HISTCONT SAME RTE	P=0.305	(e)	P=0.050*	(e)
HISTCONT ALL RTES	P=0.093	(e)	P<0.001**	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Brain  
 Oligodendroglioma, Glioma, or Astrocytoma**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	0/50 (0%)	2/50 (4%)	0/50 (0%)
POLY-3 RATE (b)	1/45.28	0/44.93	2/44.06	0/46.62
POLY-3 PERCENT (g)	2.2%	0%	4.5%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	2/34 (6%)	0/37 (0%)
FIRST INCIDENCE	660	---	729 (T)	---
HC TUMORS SAME RTE	0/200 (0%)			
HC TUMORS ALL RTES	5/1098 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.450N	P=0.502N	P=0.491	P=0.494N
POLY 1.5	P=0.452N	P=0.499N	P=0.495	P=0.494N
POLY 6	P=0.449N	P=0.507N	P=0.484	P=0.497N
COCH-ARM / FISHERS	P=0.461N	P=0.500N	P=0.500	P=0.500N
MAX-ISO-POLY-3	P=0.327N	P=0.161N	P=0.275	P=0.159N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	11/50 (22%)	8/49 (16%)	4/50 (8%)	6/50 (12%)
POLY-3 RATE (b)	11/45.74	8/44.68	4/44.06	6/46.62
POLY-3 PERCENT (g)	24.1%	17.9%	9.1%	12.9%
TERMINAL (d)	8/38 (21%)	7/36 (19%)	4/34 (12%)	6/37 (16%)
FIRST INCIDENCE	618	637	729 (T)	729 (T)
HC TUMORS SAME RTE	26/200 (13%)			
HC TUMORS ALL RTES	104/1096 (10%)			

**STATISTICAL TESTS**

POLY 3	P=0.084N	P=0.324N	P=0.051N	P=0.131N
POLY 1.5	P=0.084N	P=0.315N	P=0.048N*	P=0.130N
POLY 6	P=0.088N	P=0.343N	P=0.056N	P=0.140N
COCH-ARM / FISHERS	P=0.091N	P=0.323N	P=0.045N*	P=0.143N
MAX-ISO-POLY-3	P=0.068N	P=0.239N	P=0.029N*	P=0.084N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Carcinoma**

**TUMOR RATES**

OVERALL (a)	3/50 (6%)	5/49 (10%)	1/50 (2%)	1/50 (2%)
POLY-3 RATE (b)	3/45.02	5/44.6	1/44.36	1/46.62
POLY-3 PERCENT (g)	6.7%	11.2%	2.3%	2.2%
TERMINAL (d)	3/38 (8%)	4/36 (11%)	0/34 (0%)	1/37 (3%)
FIRST INCIDENCE	729 (T)	660	647	729 (T)
HC TUMORS SAME RTE	6/200 (3%)			
HC TUMORS ALL RTES	29/1096 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.105N	P=0.351	P=0.310N	P=0.293N
POLY 1.5	P=0.106N	P=0.354	P=0.308N	P=0.294N
POLY 6	P=0.107N	P=0.344	P=0.313N	P=0.296N
COCH-ARM / FISHERS	P=0.113N	P=0.346	P=0.309N	P=0.309N
MAX-ISO-POLY-3	P=0.126N	P=0.227	P=0.160N	P=0.149N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Clitoral/Preputial Gland  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	14/50 (28%)	11/49 (22%)	5/50 (10%)	7/50 (14%)
POLY-3 RATE (b)	14/45.74	11/44.93	5/44.36	7/46.62
POLY-3 PERCENT (g)	30.6%	24.5%	11.3%	15%
TERMINAL (d)	11/38 (29%)	9/36 (25%)	4/34 (12%)	7/37 (19%)
FIRST INCIDENCE	618	637	647	729 (T)
HC TUMORS SAME RTE	32/200 (16%)			
HC TUMORS ALL RTES	133/1096 (12%)			

**STATISTICAL TESTS**

POLY 3	P=0.029N*	P=0.338N	P=0.021N*	P=0.060N
POLY 1.5	P=0.029N*	P=0.330N	P=0.020N*	P=0.059N
POLY 6	P=0.031N*	P=0.357N	P=0.023N*	P=0.065N
COCH-ARM / FISHERS	P=0.034N*	P=0.343N	P=0.020N*	P=0.070N
MAX-ISO-POLY-3	P=0.027N*	P=0.258N	P=0.012N*	P=0.037N*
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Heart  
 Schwannoma Malignant**

**TUMOR RATES**

OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	0/44.93	1/44.06	0/46.62
POLY-3 PERCENT (g)	0%	0%	2.3%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	1/34 (3%)	0/37 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	4/1099 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.710	(e)	P=0.496	(e)
POLY 1.5	P=0.707	(e)	P=0.498	(e)
POLY 6	P=0.709	(e)	P=0.493	(e)
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)
MAX-ISO-POLY-3	P=0.390	(e)	P=0.158	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Islets, Pancreatic  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	0/48 (0%)	0/48 (0%)	3/49 (6%)	0/49 (0%)
POLY-3 RATE (b)	0/43.73	0/43.68	3/43.08	0/45.86
POLY-3 PERCENT (g)	0%	0%	7%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	3/34 (9%)	0/37 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	2/198 (1%)			
HC TUMORS ALL RTES	21/1092 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.567	(e)	P=0.116	(e)
POLY 1.5	P=0.565	(e)	P=0.119	(e)
POLY 6	P=0.562	(e)	P=0.111	(e)
COCH-ARM / FISHERS	P=0.545	(e)	P=0.125	(e)
MAX-ISO-POLY-3	P=0.171	(e)	P=0.039*	(e)
HISTCONT SAME RTE	P=0.211	(e)	P=0.046*	(e)
HISTCONT ALL RTES	P=0.198	(e)	P=0.041*	(e)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Islets, Pancreatic  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	0/48 (0%)	0/48 (0%)	3/49 (6%)	0/49 (0%)
POLY-3 RATE (b)	0/43.73	0/43.68	3/43.08	0/45.86
POLY-3 PERCENT (g)	0%	0%	7%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	3/34 (9%)	0/37 (0%)
FIRST INCIDENCE	---	---	729 (T)	---
HC TUMORS SAME RTE	4/198 (2%)			
HC TUMORS ALL RTES	25/1092 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.567	(e)	P=0.116	(e)
POLY 1.5	P=0.565	(e)	P=0.119	(e)
POLY 6	P=0.562	(e)	P=0.111	(e)
COCH-ARM / FISHERS	P=0.545	(e)	P=0.125	(e)
MAX-ISO-POLY-3	P=0.171	(e)	P=0.039*	(e)
HISTCONT SAME RTE	P=0.211	(e)	P=0.046*	(e)
HISTCONT ALL RTES	P=0.198	(e)	P=0.041*	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

Liver  
 Hepatocellular Adenoma

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	1/50 (2%)	3/49 (6%)	0/50 (0%)
POLY-3 RATE (b)	2/45.09	1/44.93	3/43.74	0/46.62
POLY-3 PERCENT (g)	4.4%	2.2%	6.9%	0%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	2/34 (6%)	0/37 (0%)
FIRST INCIDENCE	710	729 (T)	507	---
HC TUMORS SAME RTE	3/200 (2%)			
HC TUMORS ALL RTES	14/1099 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.230N	P=0.501N	P=0.486	P=0.230N
POLY 1.5	P=0.233N	P=0.497N	P=0.488	P=0.230N
POLY 6	P=0.230N	P=0.509N	P=0.481	P=0.232N
COCH-ARM / FISHERS	P=0.243N	P=0.500N	P=0.490	P=0.247N
MAX-ISO-POLY-3	P=0.188N	P=0.282N	P=0.313	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Lung  
 Alveolar/Bronchiolar Adenoma**

**TUMOR RATES**

OVERALL (a)	0/50 (0%)	0/50 (0%)	2/49 (4%)	1/50 (2%)
POLY-3 RATE (b)	0/45.02	0/44.93	2/43.08	1/46.62
POLY-3 PERCENT (g)	0%	0%	4.6%	2.2%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	2/34 (6%)	1/37 (3%)
FIRST INCIDENCE	---	---	729 (T)	729 (T)
HC TUMORS SAME RTE	5/200 (3%)			
HC TUMORS ALL RTES	24/1099 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.261	(e)	P=0.227	P=0.507
POLY 1.5	P=0.258	(e)	P=0.230	P=0.506
POLY 6	P=0.260	(e)	P=0.224	P=0.505
COCH-ARM / FISHERS	P=0.246	(e)	P=0.242	P=0.500
MAX-ISO-POLY-3	P=0.172	(e)	P=0.075	P=0.167
HISTCONT SAME RTE	P=0.212	(e)	P=0.093	P=0.217
HISTCONT ALL RTES	P=0.198	(e)	P=0.085	P=0.200

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Lung  
 Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma**

**TUMOR RATES**

OVERALL (a)	1/50 (2%)	0/50 (0%)	3/49 (6%)	1/50 (2%)
POLY-3 RATE (b)	1/45.02	0/44.93	3/43.08	1/46.62
POLY-3 PERCENT (g)	2.2%	0%	7%	2.2%
TERMINAL (d)	1/38 (3%)	0/36 (0%)	3/34 (9%)	1/37 (3%)
FIRST INCIDENCE	729 (T)	---	729 (T)	729 (T)
HC TUMORS SAME RTE	5/200 (3%)			
HC TUMORS ALL RTES	29/1099 (3%)			

**STATISTICAL TESTS**

POLY 3	P=0.490	P=0.500N	P=0.289	P=0.753N
POLY 1.5	P=0.485	P=0.498N	P=0.293	P=0.753N
POLY 6	P=0.490	P=0.505N	P=0.284	P=0.755N
COCH-ARM / FISHERS	P=0.469	P=0.500N	P=0.301	P=0.753N
MAX-ISO-POLY-3	P=0.270	P=0.159N	P=0.147	P=0.489N
HISTCONT SAME RTE	P=0.332	(e)	P=0.190	P=1.000
HISTCONT ALL RTES	P=0.313	(e)	P=0.175	P=1.000

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Adenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 RATE (b)	0/45.02	0/44.93	0/44.06	2/46.62
POLY-3 PERCENT (g)	0%	0%	0%	4.3%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	0/34 (0%)	2/37 (5%)
FIRST INCIDENCE	---	---	---	729 (T)
HC TUMORS SAME RTE	3/200 (2%)			
HC TUMORS ALL RTES	15/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.047*	(e)	(e)	P=0.245
POLY 1.5	P=0.046*	(e)	(e)	P=0.244
POLY 6	P=0.047*	(e)	(e)	P=0.243
COCH-ARM / FISHERS	P=0.046*	(e)	(e)	P=0.247
MAX-ISO-POLY-3	P=0.039*	(e)	(e)	P=0.083
HISTCONT SAME RTE	P=0.047*	(e)	(e)	P=0.105
HISTCONT ALL RTES	P=0.044*	(e)	(e)	P=0.096

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Carcinoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	4/50 (8%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
POLY-3 RATE (b)	4/45.02	1/44.93	2/44.06	3/46.88
POLY-3 PERCENT (g)	8.9%	2.2%	4.5%	6.4%
TERMINAL (d)	4/38 (11%)	1/36 (3%)	2/34 (6%)	1/37 (3%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	667
HC TUMORS SAME RTE	6/200 (3%)			
HC TUMORS ALL RTES	60/1100 (6%)			

**STATISTICAL TESTS**

POLY 3	P=0.531N	P=0.179N	P=0.347N	P=0.478N
POLY 1.5	P=0.535N	P=0.176N	P=0.343N	P=0.481N
POLY 6	P=0.527N	P=0.185N	P=0.353N	P=0.480N
COCH-ARM / FISHERS	P=0.544N	P=0.181N	P=0.339N	P=0.500N
MAX-ISO-POLY-3	P=0.288N	P=0.084N	P=0.210N	P=0.331N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Carcinoma or Adenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	4/50 (8%)	1/50 (2%)	2/50 (4%)	5/50 (10%)
POLY-3 RATE (b)	4/45.02	1/44.93	2/44.06	5/46.88
POLY-3 PERCENT (g)	8.9%	2.2%	4.5%	10.7%
TERMINAL (d)	4/38 (11%)	1/36 (3%)	2/34 (6%)	3/37 (8%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	667
HC TUMORS SAME RTE	9/200 (5%)			
HC TUMORS ALL RTES	75/1100 (7%)			

**STATISTICAL TESTS**

POLY 3	P=0.286	P=0.179N	P=0.347N	P=0.525
POLY 1.5	P=0.282	P=0.176N	P=0.343N	P=0.522
POLY 6	P=0.289	P=0.185N	P=0.353N	P=0.523
COCH-ARM / FISHERS	P=0.273	P=0.181N	P=0.339N	P=0.500
MAX-ISO-POLY-3	P=0.242	P=0.084N	P=0.210N	P=0.388
HISTCONT SAME RTE	P=0.154	P=1.000	P=1.000	P=0.135
HISTCONT ALL RTES	P=0.280	P=1.000	P=1.000	P=0.436

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Fibroadenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	28/50 (56%)	27/50 (54%)	17/50 (34%)	18/50 (36%)
POLY-3 RATE (b)	28/45.92	27/46.66	17/45.68	18/47.46
POLY-3 PERCENT (g)	61%	57.9%	37.2%	37.9%
TERMINAL (d)	26/38 (68%)	21/36 (58%)	11/34 (32%)	14/37 (38%)
FIRST INCIDENCE	575	592	477	647
HC TUMORS SAME RTE	106/200 (53%)			
HC TUMORS ALL RTEs	574/1100 (52%)			

**STATISTICAL TESTS**

POLY 3	P=0.006N**	P=0.462N	P=0.017N*	P=0.019N*
POLY 1.5	P=0.007N**	P=0.459N	P=0.017N*	P=0.021N*
POLY 6	P=0.005N**	P=0.475N	P=0.016N*	P=0.018N*
COCH-ARM / FISHERS	P=0.012N*	P=0.500N	P=0.022N*	P=0.035N*
MAX-ISO-POLY-3	P=0.008N**	P=0.378N	P=0.010N**	P=0.012N*
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTEs	(h)	(h)	(h)	(h)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Fibroma, Fibroadenoma or Adenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	28/50 (56%)	27/50 (54%)	17/50 (34%)	18/50 (36%)
POLY-3 RATE (b)	28/45.92	27/46.66	17/45.68	18/47.46
POLY-3 PERCENT (g)	61%	57.9%	37.2%	37.9%
TERMINAL (d)	26/38 (68%)	21/36 (58%)	11/34 (32%)	14/37 (38%)
FIRST INCIDENCE	575	592	477	647
HC TUMORS SAME RTE	108/200 (54%)			
HC TUMORS ALL RTEs	583/1100 (53%)			

**STATISTICAL TESTS**

POLY 3	P=0.006N**	P=0.462N	P=0.017N*	P=0.019N*
POLY 1.5	P=0.007N**	P=0.459N	P=0.017N*	P=0.021N*
POLY 6	P=0.005N**	P=0.475N	P=0.016N*	P=0.018N*
COCH-ARM / FISHERS	P=0.012N*	P=0.500N	P=0.022N*	P=0.035N*
MAX-ISO-POLY-3	P=0.008N**	P=0.378N	P=0.010N**	P=0.012N*
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTEs	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Mammary Gland Fibroma, Fibroadenoma, Carcinoma, or Adenoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	28/50 (56%)	27/50 (54%)	19/50 (38%)	20/50 (40%)
POLY-3 RATE (b)	28/45.92	27/46.66	19/45.68	20/47.5
POLY-3 PERCENT (g)	61%	57.9%	41.6%	42.1%
TERMINAL (d)	26/38 (68%)	21/36 (58%)	13/34 (38%)	15/37 (41%)
FIRST INCIDENCE	575	592	477	647
HC TUMORS SAME RTE	111/200 (56%)			
HC TUMORS ALL RTES	619/1100 (56%)			

**STATISTICAL TESTS**

POLY 3	P=0.022N*	P=0.462N	P=0.046N*	P=0.049N*
POLY 1.5	P=0.025N*	P=0.459N	P=0.047N*	P=0.054N
POLY 6	P=0.021N*	P=0.475N	P=0.045N*	P=0.048N*
COCH-ARM / FISHERS	P=0.038N*	P=0.500N	P=0.054N	P=0.080N
MAX-ISO-POLY-3	P=0.033N*	P=0.378N	P=0.029N*	P=0.033N*
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Ovary  
 Granulosa Cell Tumor Malignant**

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	0/49 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46	0/44.34	0/44.06	0/46.62
POLY-3 PERCENT (g)	4.4%	0%	0%	0%
TERMINAL (d)	1/38 (3%)	0/36 (0%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	200	---	---	---
HC TUMORS SAME RTE	0/200 (0%)			
HC TUMORS ALL RTES	1/1098 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.113N	P=0.245N	P=0.247N	P=0.234N
POLY 1.5	P=0.114N	P=0.243N	P=0.244N	P=0.234N
POLY 6	P=0.112N	P=0.249N	P=0.250N	P=0.236N
COCH-ARM / FISHERS	P=0.115N	P=0.253N	P=0.247N	P=0.247N
MAX-ISO-POLY-3	P=0.033N*	P=0.083N	P=0.085N	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Ovary  
 Granulosa Cell Tumor: Benign, Malignant, NOS**

**TUMOR RATES**

OVERALL (a)	2/50 (4%)	1/49 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46	1/44.34	0/44.06	0/46.62
POLY-3 PERCENT (g)	4.4%	2.3%	0%	0%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	200	729 (T)	---	---
HC TUMORS SAME RTE	0/200 (0%)			
HC TUMORS ALL RTES	3/1098 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.100N	P=0.513N	P=0.247N	P=0.234N
POLY 1.5	P=0.101N	P=0.509N	P=0.244N	P=0.234N
POLY 6	P=0.100N	P=0.519N	P=0.250N	P=0.236N
COCH-ARM / FISHERS	P=0.100N	P=0.508N	P=0.247N	P=0.247N
MAX-ISO-POLY-3	P=0.078N	P=0.294N	P=0.085N	P=0.076N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Pancreas</b>				
<b>Adenoma</b>				
<b>TUMOR RATES</b>				
OVERALL (a)	0/48 (0%)	0/48 (0%)	0/49 (0%)	0/49 (0%)
POLY-3 RATE (b)	0/43.73	0/43.68	0/43.08	0/45.86
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	0/198 (0%)			
HC TUMORS ALL RTES	3/1093 (0%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Pituitary Gland: Pars Distalis or Unspecified Site  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	20/50 (40%)	20/50 (40%)	18/50 (36%)	28/50 (56%)
POLY-3 RATE (b)	20/45.99	20/46.11	18/44.34	28/48.2
POLY-3 PERCENT (g)	43.5%	43.4%	40.6%	58.1%
TERMINAL (d)	17/38 (45%)	17/36 (47%)	15/34 (44%)	22/37 (60%)
FIRST INCIDENCE	575	592	703	619
HC TUMORS SAME RTE	93/197 (47%)			
HC TUMORS ALL RTES	613/1093 (56%)			

**STATISTICAL TESTS**

POLY 3	P=0.070	P=0.579N	P=0.474N	P=0.110
POLY 1.5	P=0.066	P=0.564N	P=0.450N	P=0.105
POLY 6	P=0.071	P=0.561	P=0.508N	P=0.109
COCH-ARM / FISHERS	P=0.056	P=0.581N	P=0.418N	P=0.080
MAX-ISO-POLY-3	P=0.101	P=0.495N	P=0.390N	P=0.080
HISTCONT SAME RTE	P=0.124	P=1.000	P=1.000	P=0.100
HISTCONT ALL RTES	P=0.115	P=1.000	P=1.000	P=0.092

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Pituitary Gland: Pars Distalis or Unspecified Site  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	21/50 (42%)	20/50 (40%)	18/50 (36%)	28/50 (56%)
POLY-3 RATE (b)	21/45.99	20/46.11	18/44.34	28/48.2
POLY-3 PERCENT (g)	45.7%	43.4%	40.6%	58.1%
TERMINAL (d)	18/38 (47%)	17/36 (47%)	15/34 (44%)	22/37 (60%)
FIRST INCIDENCE	575	592	703	619
HC TUMORS SAME RTE	96/197 (49%)			
HC TUMORS ALL RTES	626/1093 (57%)			

**STATISTICAL TESTS**

POLY 3	P=0.097	P=0.495N	P=0.392N	P=0.156
POLY 1.5	P=0.092	P=0.481N	P=0.369N	P=0.148
POLY 6	P=0.099	P=0.525N	P=0.425N	P=0.155
COCH-ARM / FISHERS	P=0.077	P=0.500N	P=0.341N	P=0.115
MAX-ISO-POLY-3	P=0.116	P=0.410N	P=0.316N	P=0.116
HISTCONT SAME RTE	P=0.143	P=1.000	P=1.000	P=0.148
HISTCONT ALL RTES	P=0.133	P=1.000	P=1.000	P=0.136

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin**  
 Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthoma, Trichoepithelioma

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	2/50 (4%)	0/50 (0%)
POLY-3 RATE (b)	1/45.02	2/44.93	2/44.22	0/46.62
POLY-3 PERCENT (g)	2.2%	4.5%	4.5%	0%
TERMINAL (d)	1/38 (3%)	2/36 (6%)	1/34 (3%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	687	---
HC TUMORS SAME RTE	7/200 (4%)			
HC TUMORS ALL RTES	24/1100 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.284N	P=0.499	P=0.494	P=0.493N
POLY 1.5	P=0.285N	P=0.503	P=0.496	P=0.494N
POLY 6	P=0.286N	P=0.492	P=0.490	P=0.495N
COCH-ARM / FISHERS	P=0.296N	P=0.500	P=0.500	P=0.500N
MAX-ISO-POLY-3	P=0.228N	P=0.280	P=0.277	P=0.158N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Skin Fibroma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 RATE (b)	1/45.02	0/44.93	0/44.06	2/47.2
POLY-3 PERCENT (g)	2.2%	0%	0%	4.2%
TERMINAL (d)	1/38 (3%)	0/36 (0%)	0/34 (0%)	1/37 (3%)
FIRST INCIDENCE	729 (T)	---	---	546
HC TUMORS SAME RTE	5/200 (3%)			
HC TUMORS ALL RTES	19/1100 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.252	P=0.500N	P=0.504N	P=0.516
POLY 1.5	P=0.249	P=0.498N	P=0.502N	P=0.514
POLY 6	P=0.254	P=0.505N	P=0.507N	P=0.516
COCH-ARM / FISHERS	P=0.246	P=0.500N	P=0.500N	P=0.500
MAX-ISO-POLY-3	P=0.155	P=0.159N	P=0.164N	P=0.298
HISTCONT SAME RTE	P=0.191	(e)	(e)	P=0.395
HISTCONT ALL RTES	P=0.179	(e)	(e)	P=0.275

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	1/50 (2%)	2/50 (4%)
POLY-3 RATE (b)	1/45.02	2/45.37	1/44.13	2/47.2
POLY-3 PERCENT (g)	2.2%	4.4%	2.3%	4.2%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	0/34 (0%)	1/37 (3%)
FIRST INCIDENCE	729 (T)	599	711	546
HC TUMORS SAME RTE	6/200 (3%)			
HC TUMORS ALL RTES	25/1100 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.463	P=0.503	P=0.756	P=0.516
POLY 1.5	P=0.459	P=0.505	P=0.758	P=0.514
POLY 6	P=0.463	P=0.497	P=0.754	P=0.516
COCH-ARM / FISHERS	P=0.444	P=0.500	P=0.753N	P=0.500
MAX-ISO-POLY-3	P=0.477	P=0.283	P=0.494	P=0.298
HISTCONT SAME RTE	P=0.585	P=0.374	P=0.637	P=0.395
HISTCONT ALL RTES	P=0.561	P=0.354	P=0.624	P=0.375

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Skin</b>				
<b>Fibrosarcoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	1/45.02	2/45.37	1/44.13	0/46.62
POLY-3 PERCENT (g)	2.2%	4.4%	2.3%	0%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	599	711	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	5/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.240N	P=0.503	P=0.756	P=0.493N
POLY 1.5	P=0.241N	P=0.505	P=0.758	P=0.494N
POLY 6	P=0.242N	P=0.497	P=0.754	P=0.495N
COCH-ARM / FISHERS	P=0.247N	P=0.500	P=0.753N	P=0.500N
MAX-ISO-POLY-3	P=0.231N	P=0.283	P=0.494	P=0.158N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	1/45.02	2/45.37	1/44.13	0/46.62
POLY-3 PERCENT (g)	2.2%	4.4%	2.3%	0%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	599	711	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	6/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.240N	P=0.503	P=0.756	P=0.493N
POLY 1.5	P=0.241N	P=0.505	P=0.758	P=0.494N
POLY 6	P=0.242N	P=0.497	P=0.754	P=0.495N
COCH-ARM / FISHERS	P=0.247N	P=0.500	P=0.753N	P=0.500N
MAX-ISO-POLY-3	P=0.231N	P=0.283	P=0.494	P=0.158N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Skin</b>				
<b>Keratoacanthoma</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	1/44.93	1/44.06	0/46.62
POLY-3 PERCENT (g)	0%	2.2%	2.3%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	1/34 (3%)	0/37 (0%)
FIRST INCIDENCE	---	729 (T)	729 (T)	---
HC TUMORS SAME RTE	3/200 (2%)			
HC TUMORS ALL RTES	8/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.586N	P=0.500	P=0.496	(e)
POLY 1.5	P=0.586N	P=0.502	P=0.498	(e)
POLY 6	P=0.588N	P=0.495	P=0.493	(e)
COCH-ARM / FISHERS	P=0.595N	P=0.500	P=0.500	(e)
MAX-ISO-POLY-3	P=0.404N	P=0.159	P=0.158	(e)
HISTCONT SAME RTE	(h)	(h)	(h)	(e)
HISTCONT ALL RTES	(h)	(h)	(h)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin**  
 Squamous Cell Carcinoma, Basal Cell Carcinoma, Basosquamous Tumor (malignant or NOS), or Carcinoma

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/45.02	0/44.93	0/44.06	0/46.62
POLY-3 PERCENT (g)	2.2%	0%	0%	0%
TERMINAL (d)	1/38 (3%)	0/36 (0%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	---	---	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	4/1100 (0%)			

**STATISTICAL TESTS**

POLY 3	P=0.310N	P=0.500N	P=0.504N	P=0.493N
POLY 1.5	P=0.311N	P=0.498N	P=0.502N	P=0.494N
POLY 6	P=0.308N	P=0.505N	P=0.507N	P=0.495N
COCH-ARM / FISHERS	P=0.306N	P=0.500N	P=0.500N	P=0.500N
MAX-ISO-POLY-3	P=0.124N	P=0.159N	P=0.164N	P=0.158N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	1/45.02	1/44.93	1/44.06	0/46.62
POLY-3 PERCENT (g)	2.2%	2.2%	2.3%	0%
TERMINAL (d)	1/38 (3%)	1/36 (3%)	1/34 (3%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	---
HC TUMORS SAME RTE	4/200 (2%)			
HC TUMORS ALL RTES	12/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.306N	P=0.760	P=0.756	P=0.493N
POLY 1.5	P=0.307N	P=0.759N	P=0.758	P=0.494N
POLY 6	P=0.306N	P=0.756	P=0.753	P=0.495N
COCH-ARM / FISHERS	P=0.311N	P=0.753N	P=0.753N	P=0.500N
MAX-ISO-POLY-3	P=0.332N	P=0.499	P=0.493	P=0.158N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Skin  
 Squamous Cell Papilloma, Papilloma, or Keratoacanthoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	1/44.93	1/44.06	0/46.62
POLY-3 PERCENT (g)	0%	2.2%	2.3%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	1/34 (3%)	0/37 (0%)
FIRST INCIDENCE	---	729 (T)	729 (T)	---
HC TUMORS SAME RTE	4/200 (2%)			
HC TUMORS ALL RTES	11/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.586N	P=0.500	P=0.496	(e)
POLY 1.5	P=0.586N	P=0.502	P=0.498	(e)
POLY 6	P=0.588N	P=0.495	P=0.493	(e)
COCH-ARM / FISHERS	P=0.595N	P=0.500	P=0.500	(e)
MAX-ISO-POLY-3	P=0.404N	P=0.159	P=0.158	(e)
HISTCONT SAME RTE	(h)	(h)	(h)	(e)
HISTCONT ALL RTES	(h)	(h)	(h)	(e)



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

---

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**Thyroid Gland: C-Cell  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	2/47 (4%)	3/49 (6%)	6/49 (12%)	2/50 (4%)
POLY-3 RATE (b)	2/43.91	3/44.73	6/43.18	2/46.62
POLY-3 PERCENT (g)	4.6%	6.7%	13.9%	4.3%
TERMINAL (d)	1/38 (3%)	2/36 (6%)	5/34 (15%)	2/37 (5%)
FIRST INCIDENCE	618	619	703	729 (T)
HC TUMORS SAME RTE	26/195 (13%)			
HC TUMORS ALL RTES	124/1086 (11%)			

**STATISTICAL TESTS**

POLY 3	P=0.565N	P=0.508	P=0.127	P=0.672N
POLY 1.5	P=0.559N	P=0.517	P=0.135	P=0.668N
POLY 6	P=0.574	P=0.495	P=0.117	P=0.682N
COCH-ARM / FISHERS	P=0.567N	P=0.520	P=0.148	P=0.668N
MAX-ISO-POLY-3	P=0.346	P=0.331	P=0.069	P=0.475N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: C-Cell  
 Carcinoma**

**TUMOR RATES**

OVERALL (a)	0/47 (0%)	3/49 (6%)	1/49 (2%)	2/50 (4%)
POLY-3 RATE (b)	0/43.52	3/44.34	1/43.08	2/46.95
POLY-3 PERCENT (g)	0%	6.8%	2.3%	4.3%
TERMINAL (d)	0/38 (0%)	3/36 (8%)	1/34 (3%)	1/37 (3%)
FIRST INCIDENCE	---	729 (T)	729 (T)	638
HC TUMORS SAME RTE	2/195 (1%)			
HC TUMORS ALL RTES	18/1086 (2%)			

**STATISTICAL TESTS**

POLY 3	P=0.360	P=0.122	P=0.498	P=0.254
POLY 1.5	P=0.363	P=0.126	P=0.502	P=0.256
POLY 6	P=0.351	P=0.116	P=0.492	P=0.250
COCH-ARM / FISHERS	P=0.355	P=0.129	P=0.510	P=0.263
MAX-ISO-POLY-3	P=0.197	P=0.039*	P=0.161	P=0.089
HISTCONT SAME RTE	P=0.242	P=0.047*	P=0.209	P=0.112
HISTCONT ALL RTES	P=0.207	P=0.042*	P=0.192	P=0.102

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

---

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**Thyroid Gland: C-Cell  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	2/47 (4%)	6/49 (12%)	7/49 (14%)	4/50 (8%)
POLY-3 RATE (b)	2/43.91	6/44.73	7/43.18	4/46.95
POLY-3 PERCENT (g)	4.6%	13.4%	16.2%	8.5%
TERMINAL (d)	1/38 (3%)	5/36 (14%)	6/34 (18%)	3/37 (8%)
FIRST INCIDENCE	618	619	703	638
HC TUMORS SAME RTE	28/195 (14%)			
HC TUMORS ALL RTES	141/1086 (13%)			

**STATISTICAL TESTS**

POLY 3	P=0.430	P=0.138	P=0.074	P=0.369
POLY 1.5	P=0.436	P=0.145	P=0.080	P=0.373
POLY 6	P=0.412	P=0.128	P=0.067	P=0.358
COCH-ARM / FISHERS	P=0.423	P=0.148	P=0.090	P=0.369
MAX-ISO-POLY-3	P=0.171	P=0.072	P=0.038*	P=0.229
HISTCONT SAME RTE	P=0.212	P=0.090	P=0.045*	P=0.301
HISTCONT ALL RTES	P=0.198	P=0.082	P=0.041*	P=0.282

---

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

---

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**Thyroid Gland: Follicular Cell  
 Adenoma**

**TUMOR RATES**

OVERALL (a)	0/47 (0%)	0/49 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/43.52	0/44.34	0/43.08	0/46.62
POLY-3 PERCENT (g)	0%	0%	0%	0%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	---	---	---
HC TUMORS SAME RTE	2/195 (1%)			
HC TUMORS ALL RTES	5/1086 (1%)			

**STATISTICAL TESTS**

POLY 3	(e)	(e)	(e)	(e)
POLY 1.5	(e)	(e)	(e)	(e)
POLY 6	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)
MAX-ISO-POLY-3	(e)	(e)	(e)	(e)
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

---

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**Thyroid Gland: Follicular Cell  
 Carcinoma or Adenoma**

**TUMOR RATES**

OVERALL (a)	1/47 (2%)	0/49 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/43.52	0/44.34	0/43.08	0/46.62
POLY-3 PERCENT (g)	2.3%	0%	0%	0%
TERMINAL (d)	1/38 (3%)	0/36 (0%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	729 (T)	---	---	---
HC TUMORS SAME RTE	3/195 (2%)			
HC TUMORS ALL RTES	10/1086 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.300N	P=0.496N	P=0.502N	P=0.486N
POLY 1.5	P=0.302N	P=0.492N	P=0.498N	P=0.485N
POLY 6	P=0.296N	P=0.502N	P=0.508N	P=0.491N
COCH-ARM / FISHERS	P=0.299N	P=0.490N	P=0.490N	P=0.485N
MAX-ISO-POLY-3	P=0.118N	P=0.156N	P=0.164N	P=0.155N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Uterus</b>				
<b>Polyp Stromal</b>				
<b>TUMOR RATES</b>	#	#	#	#
OVERALL (a)	10/50 (20%)	12/50 (24%)	16/50 (32%)	16/50 (32%)
POLY-3 RATE (b)	10/46.18	12/45.55	16/44.8	16/47.94
POLY-3 PERCENT (g)	21.7%	26.4%	35.7%	33.4%
TERMINAL (d)	8/38 (21%)	9/36 (25%)	13/34 (38%)	10/37 (27%)
FIRST INCIDENCE	434	619	567	613
HC TUMORS SAME RTE	40/200 (20%)			
HC TUMORS ALL RTES	203/1100 (19%)			

**STATISTICAL TESTS**

POLY 3	P=0.110	P=0.389	P=0.103	P=0.148
POLY 1.5	P=0.105	P=0.404	P=0.112	P=0.145
POLY 6	P=0.114	P=0.367	P=0.094	P=0.149
COCH-ARM / FISHERS	P=0.089	P=0.405	P=0.127	P=0.127
MAX-ISO-POLY-3	P=0.136	P=0.301	P=0.070	P=0.105
HISTCONT SAME RTE	P=0.117	P=0.398	P=0.087	P=0.133
HISTCONT ALL RTES	P=0.013*	P=0.340	P=0.078	P=0.100

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Histiocytic Sarcoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 RATE (b)	0/45.02	0/44.93	0/44.06	1/46.62
POLY-3 PERCENT (g)	0%	0%	0%	2.2%
TERMINAL (d)	0/38 (0%)	0/36 (0%)	0/34 (0%)	1/37 (3%)
FIRST INCIDENCE	---	---	---	729 (T)
HC TUMORS SAME RTE	3/200 (2%)			
HC TUMORS ALL RTES	9/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.204	(e)	(e)	P=0.507
POLY 1.5	P=0.203	(e)	(e)	P=0.506
POLY 6	P=0.204	(e)	(e)	P=0.505
COCH-ARM / FISHERS	P=0.198	(e)	(e)	P=0.500
MAX-ISO-POLY-3	P=0.136	(e)	(e)	P=0.167
HISTCONT SAME RTE	(e)	(e)	(e)	(e)
HISTCONT ALL RTES	(e)	(e)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs**  
**Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated**

TUMOR RATES	#	#	#	#
OVERALL (a)	6/50 (12%)	9/50 (18%)	13/50 (26%)	9/50 (18%)
POLY-3 RATE (b)	6/46.48	9/46.6	13/46.65	9/47.98
POLY-3 PERCENT (g)	12.9%	19.3%	27.9%	18.8%
TERMINAL (d)	1/38 (3%)	4/36 (11%)	5/34 (15%)	3/37 (8%)
FIRST INCIDENCE	434	459	484	613
HC TUMORS SAME RTE	43/200 (22%)			
HC TUMORS ALL RTES	265/1100 (24%)			

**STATISTICAL TESTS**

POLY 3	P=0.290	P=0.289	P=0.061	P=0.311
POLY 1.5	P=0.285	P=0.296	P=0.061	P=0.309
POLY 6	P=0.291	P=0.276	P=0.060	P=0.308
COCH-ARM / FISHERS	P=0.259	P=0.288	P=0.062	P=0.288
MAX-ISO-POLY-3	P=0.168	P=0.202	P=0.035*	P=0.224
HISTCONT SAME RTE	P=0.207	P=0.264	P=0.041*	P=0.293
HISTCONT ALL RTES	P=0.194	P=0.246	P=0.038*	P=0.274



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Osteosarcoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	2/45.31	0/44.06	0/46.62
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	619	---	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	5/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.399N	P=0.239	(e)	(e)
POLY 1.5	P=0.398N	P=0.240	(e)	(e)
POLY 6	P=0.404N	P=0.235	(e)	(e)
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)
MAX-ISO-POLY-3	P=0.252N	P=0.077	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Osteosarcoma or Osteoma**

TUMOR RATES	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/45.02	2/45.31	0/44.06	0/46.62
POLY-3 PERCENT (g)	0%	4.4%	0%	0%
TERMINAL (d)	0/38 (0%)	1/36 (3%)	0/34 (0%)	0/37 (0%)
FIRST INCIDENCE	---	619	---	---
HC TUMORS SAME RTE	1/200 (1%)			
HC TUMORS ALL RTES	5/1100 (1%)			

**STATISTICAL TESTS**

POLY 3	P=0.399N	P=0.239	(e)	(e)
POLY 1.5	P=0.398N	P=0.240	(e)	(e)
POLY 6	P=0.404N	P=0.235	(e)	(e)
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)
MAX-ISO-POLY-3	P=0.252N	P=0.077	(e)	(e)
HISTCONT SAME RTE	(h)	(h)	(e)	(e)
HISTCONT ALL RTES	(h)	(h)	(e)	(e)

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

---

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**All Organs  
 Benign Tumors**

**TUMOR RATES**

	#	#	#	#
OVERALL (a)	39/50 (78%)	42/50 (84%)	41/50 (82%)	43/50 (86%)
POLY-3 RATE (b)	39/47.42	42/47.28	41/48.04	43/49.86
POLY-3 PERCENT (g)	82.3%	88.8%	85.3%	86.2%
TERMINAL (d)	33/38 (87%)	33/36 (92%)	29/34 (85%)	31/37 (84%)
FIRST INCIDENCE	434	592	451	546
HC TUMORS SAME RTE	178/200 (89%)			
HC TUMORS ALL RTES	966/1100 (88%)			

**STATISTICAL TESTS**

POLY 3	P=0.428	P=0.258	P=0.447	P=0.395
POLY 1.5	P=0.354	P=0.304	P=0.427	P=0.347
POLY 6	P=0.506	P=0.200	P=0.465	P=0.440
COCH-ARM / FISHERS	P=0.216	P=0.306	P=0.402	P=0.218
MAX-ISO-POLY-3	P=0.419	P=0.170	P=0.339	P=0.297
HISTCONT SAME RTE	P=0.515	P=0.220	P=0.448	P=0.392
HISTCONT ALL RTES	P=0.488	P=0.203	P=0.426	P=0.370

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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

---

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

---

**All Organs  
 Malignant Tumors**

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TUMOR RATES	#	#	#	#
OVERALL (a)	18/50 (36%)	20/50 (40%)	23/50 (46%)	16/50 (32%)
POLY-3 RATE (b)	18/47.72	20/48.41	23/47.36	16/48.58
POLY-3 PERCENT (g)	37.7%	41.3%	48.6%	32.9%
TERMINAL (d)	11/38 (29%)	11/36 (31%)	11/34 (32%)	7/37 (19%)
FIRST INCIDENCE	200	459	484	613
HC TUMORS SAME RTE	73/200 (37%)			
HC TUMORS ALL RTES	428/1100 (39%)			

**STATISTICAL TESTS**

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POLY 3	P=0.332N	P=0.440	P=0.194	P=0.391N
POLY 1.5	P=0.338N	P=0.437	P=0.192	P=0.397N
POLY 6	P=0.327N	P=0.436	P=0.202	P=0.389N
COCH-ARM / FISHERS	P=0.356N	P=0.418	P=0.208	P=0.417N
MAX-ISO-POLY-3	P=0.274N	P=0.360	P=0.143	P=0.314N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
 Milk thistle extract  
 CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

**STATISTICAL ANALYSIS OF PRIMARY TUMORS IN RATS(F 344/N)  
 TERMINAL SACRIFICE AT 105 WEEKS**

DOSE	Females			
	0 PPM	12500 PPM	25000 PPM	50000 PPM

**All Organs  
 Malignant and Benign Tumors**

TUMOR RATES	#	#	#	#
OVERALL (a)	46/50 (92%)	48/50 (96%)	46/50 (92%)	44/50 (88%)
POLY-3 RATE (b)	46/49.07	48/50	46/49	44/50
POLY-3 PERCENT (g)	93.7%	96%	93.9%	88%
TERMINAL (d)	35/38 (92%)	34/36 (94%)	31/34 (91%)	31/37 (84%)
FIRST INCIDENCE	200	459	451	546
HC TUMORS SAME RTE	186/200 (93%)			
HC TUMORS ALL RTES	1039/1100 (95%)			

**STATISTICAL TESTS**

POLY 3	P=0.119N	P=0.478	P=0.652	P=0.261N
POLY 1.5	P=0.132N	P=0.445	P=0.628	P=0.282N
POLY 6	P=0.115N	P=0.490	P=0.661	P=0.254N
COCH-ARM / FISHERS	P=0.189N	P=0.339	P=0.643N	P=0.370N
MAX-ISO-POLY-3	P=0.148N	P=0.307	P=0.488	P=0.164N
HISTCONT SAME RTE	(h)	(h)	(h)	(h)
HISTCONT ALL RTES	(h)	(h)	(h)	(h)

TDMS No. 20008 - 03  
Test Type: CHRONIC  
Route: DOSED FEED  
Species/Strain: RATS/F 344/N

P08: STATISTICAL ANALYSIS OF PRIMARY TUMORS  
Milk thistle extract  
CAS Number: 84604-20-6

Date Report Requested: 10/09/2008  
Time Report Requested: 11:00:55  
First Dose M/F: 03/04/03 / 03/04/03  
Lab: SRI

## LEGEND

- (a) Number of tumor-bearing animals/number of animals examined at site.
  - (b) Number of tumor-bearing animals/Poly-3 number
  - (d) Observed incidence at terminal kill.
  - (e) Value of Statistic cannot be computed.
  - (f) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group.
  - (g) Poly-3 adjusted lifetime tumor incidence.
  - (h) Value of Historical Controls statistic is only calculated when Poly-3 trend is positive and when there is more than one tumor in the treatment groups.
  - (I) Interim sacrifice
  - (T) Terminal sacrifice
  - # Tumor rates based on numbers of animals necropsied.
  - \* To the right of any statistical result, indicates significance at ( $P \leq 0.05$ ).
  - \*\* To the right of any statistical result, indicates significance at ( $P \leq 0.01$ ).
  - N Indicates a negative trend for all tests
- The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates.

\*\*\* END OF REPORT \*\*\*