Table 20 - 1 Histopathology - Incidence of microscopic neoplastic lesions in male mice
Terminal kill after 78 weeks of treatment

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	26	34	27	29
Hematopoietic & Lymphatic System					
General:	(N=)	(26)	(34)	(27)	(29)
(M) Malignant lymphoma		0	0	0	2
Respiratory System					
Lung:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		5	13	10	7
(M) Adenocarcinoma		0	0	4	1
Digestive System					
Liver:	(N=)	(26)	(34)	(27)	(29)
(B) Hepatocellular adenoma		8	13	9	5
(B) Hemangioma		1	0	0	0
(M) Hepatocellular carcinoma		0	0	2	0
Urinary System					
Kidney:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		0	0	0	2
Urinary bladder:	(N=)	(26)	(34)	(27)	(29)
(B) Transitional cell papilloma		0	2	0	0
Genital System					
Testis:	(N=)	(26)	(34)	(27)	(29)
(B) Interstitial cell tumor		0	1	0	0
Endocrine System					
Thyroid:	(N=)	(26)	(34)	(27)	(29)
(B) Follicular adenoma		0	1	0	0
Nervous System					
Cerebrum:	(N=)	(26)	(34)	(27)	(29)
(B) Lipoma		0	1	0	0
Musculo-Skeletal System					
Bone (others) :	(N=)	(3)	(1)	(4)	(1)
(B) Osteoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		2	4	0	2
Integumentary System					
Skin:	(N=)	(26)	(34)	(27)	(29)
(B) Papilloma		1	1	0	0
(M) Hemangiosarcoma		0	0	0	1
No. of benign neoplasms		17	36	20	16
No. of malignant neoplasms		0	0	6	4
No. of benign & malignant neoplasms		17	36	26	20
No. of animals with benign neoplasm(s)		13	25	17	14
No. of animals with malignant neoplasm(s)		0	0	6	4
No. of animals with neoplasm(s)		13	25	20	15

(N=) : Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm: (M), malignant neoplasm.

Table 20 - 2 Histopathology - Incidence of microscopic neoplastic lesions in male mice
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	24	16	23	21
Hematopoietic & Lymphatic System					
General:	(N=)	(24)	(16)	(23)	(21)
(M) Malignant lymphoma		2	2	0	4
Lymph nodes (mesenteric):	(N=)	(24)	(16)	(23)	(21)
(M) Malignant lymphoma		0	1	0	0
Spleen:	(N=)	(24)	(16)	(23)	(21)
(M) Histiocytic sarcoma		1	0	0	0
Respiratory System					
Nasal cavity:	(N=)	(0)	(0)	(0)	(1)
(M) Adenocarcinoma		–	–	–	1
Lung:	(N=)	(24)	(16)	(23)	(21)
(B) Adenoma		3	1	3	4
(M) Adenocarcinoma		1	1	2	3
Digestive System					
Small intestine:	(N=)	(24)	(16)	(23)	(21)
(B) Papillary adenoma		0	1	0	0
(M) Adenocarcinoma		0	0	0	1
Liver:	(N=)	(24)	(16)	(23)	(21)
(B) Hepatocellular adenoma		6	2	6	2
(M) Histiocytic sarcoma		1	0	0	0
(M) Hepatocellular carcinoma		0	1	1	1
Genital System					
Testis:	(N=)	(24)	(16)	(23)	(21)
(B) Hemangioma		1	0	0	0
Endocrine System					
Thyroid:	(N=)	(24)	(16)	(23)	(21)
(B) Follicular adenoma		0	1	0	0
Adrenal:	(N=)	(24)	(16)	(23)	(21)
(B) Benign B cell tumor		0	1	0	0
Musculo-Skeletal System					
Bone (others):	(N=)	(6)	(1)	(2)	(1)
(B) Osteoma		1	0	0	0
(M) Osteosarcoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(23)	(16)	(23)	(21)
(B) Adenoma		1	0	1	1
Integumentary System					
Skin:	(N=)	(24)	(16)	(23)	(21)
(M) Hemangiosarcoma		0	0	0	1
(M) Leiomyosarcoma		0	0	1	1
(M) Osteosarcoma		0	0	0	1

(N=) : Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

Table 20 - 3 Histopathology - Incidence of microscopic neoplastic lesions in male mice
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	24	16	23	21
No. of benign neoplasms		12	6	10	7
No. of malignant neoplasms		5	5	5	13
No. of benign & malignant neoplasms		17	11	15	20
No. of animals with benign neoplasm(s)		10	5	8	6
No. of animals with malignant neoplasm(s)		5	5	5	12
No. of animals with neoplasm(s)		12	9	10	15

Table 20 - 4 Histopathology - Incidence of microscopic neoplastic lesions in male mice
All animals examined

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Hematopoietic & Lymphatic System					
General:	(N=)	(50)	(50)	(50)	(50)
(M) Malignant lymphoma		2	2	0	6
Lymph nodes (mesenteric):	(N=)	(50)	(50)	(50)	(50)
(M) Malignant lymphoma		0	1	0	0
Spleen:	(N=)	(50)	(50)	(50)	(50)
(M) Histiocytic sarcoma		1	0	0	0
Respiratory System					
Nasal cavity:	(N=)	(0)	(0)	(0)	(1)
(M) Adenocarcinoma		–	–	–	1
Lung:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		8	14	13	11
(M) Adenocarcinoma		1	1	6	4
Digestive System					
Small intestine:	(N=)	(50)	(50)	(50)	(50)
(B) Papillary adenoma		0	1	0	0
(M) Adenocarcinoma		0	0	0	1
Liver:	(N=)	(50)	(50)	(50)	(50)
(B) Hepatocellular adenoma		14	15	15	7
(B) Hemangioma		1	0	0	0
(M) Histiocytic sarcoma		1	0	0	0
(M) Hepatocellular carcinoma		0	1	3	1
Urinary System					
Kidney:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	0	0	2
Urinary bladder:	(N=)	(50)	(50)	(50)	(50)
(B) Transitional cell papilloma		0	2	0	0
Genital System					
Testis:	(N=)	(50)	(50)	(50)	(50)
(B) Interstitial cell tumor		0	1	0	0
(B) Hemangioma		1	0	0	0
Endocrine System					
Thyroid:	(N=)	(50)	(50)	(50)	(50)
(B) Follicular adenoma		0	2	0	0
Adrenal:	(N=)	(50)	(50)	(50)	(50)
(B) Benign B cell tumor		0	1	0	0
Nervous System					
Cerebrum:	(N=)	(50)	(50)	(50)	(50)
(B) Lipoma		0	1	0	0
Musculo-Skeletal System					
Bone (others):	(N=)	(9)	(2)	(6)	(2)
(B) Osteoma		1	0	1	0
(M) Osteosarcoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(49)	(50)	(50)	(50)
(B) Adenoma		3	4	1	3
Integumentary System					
Skin:	(N=)	(50)	(50)	(50)	(50)
(B) Papilloma		1	1	0	0
(M) Hemangiosarcoma		0	0	0	2

(N=): Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

Table 20 - 5 Histopathology - Incidence of microscopic neoplastic lesions in male mice
All animals examined

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Integumentary System《cont.》					
Skin《cont.》:	(N=)	(50)	(50)	(50)	(50)
(M) Leiomyosarcoma		0	0	1	1
(M) Osteosarcoma		0	0	0	1
No. of benign neoplasms		29	42	30	23
No. of malignant neoplasms		5	5	11	17
No. of benign & malignant neoplasms		34	47	41	40
No. of animals with benign neoplasm(s)		23	30	25	20
No. of animals with malignant neoplasm(s)		5	5	11	16
No. of animals with neoplasm(s)		25	34	30	30

Malignancy: (M), malignant neoplasm.

Table 21 - 1 Histopathology - Incidence of microscopic neoplastic lesions in female mice
Terminal kill after 78 weeks of treatment

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	32	36	40	35
Hematopoietic & Lymphatic System					
General:	(N=)	(32)	(36)	(40)	(35)
(M) Malignant lymphoma		4	0*	5	3
Thymus:	(N=)	(32)	(35)	(40)	(35)
(M) Malignant lymphoma		0	0	1	0
Spleen:	(N=)	(32)	(36)	(40)	(35)
(B) Hemangioma		0	0	1	0
Respiratory System					
Lung:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		7	4	12	4
(M) Adenocarcinoma		1	1	3	0
Digestive System					
Small intestine:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		0	0	1	0
Liver:	(N=)	(32)	(36)	(40)	(35)
(B) Hepatocellular adenoma		1	1	1	0
Urinary System					
Urinary bladder:	(N=)	(32)	(36)	(40)	(35)
(B) Leiomyoma		0	0	1	1
Genital System					
Uterus:	(N=)	(32)	(36)	(40)	(35)
(B) Endometrial stromal polyp		0	2	0	0
(B) Hemangioma		0	0	1	2
(B) Leiomyoma		1	0	2	1
(M) Histiocytic sarcoma		0	1	0	0
(M) Leiomyosarcoma		2	1	0	0
Endocrine System					
Pituitary:	(N=)	(32)	(36)	(40)	(35)
(B) Anterior adenoma		0	1	0	0
Thyroid:	(N=)	(32)	(36)	(40)	(35)
(B) Follicular adenoma		0	1	0	0
Adrenal:	(N=)	(32)	(36)	(40)	(35)
(B) Benign A cell tumor		0	1	2	0
(B) Pheochromocytoma		0	2	0	0
Sense Organs					
Harderian gland:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		1	3	0	3
Integumentary System					
Skin:	(N=)	(32)	(36)	(40)	(35)
(B) Papilloma		1	0	0	0
(B) Lipoma		1	0	1	0
(M) Liposarcoma		0	0	0	1
Mammary gland:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		0	1	0	0
(M) Adenocarcinoma		0	2	0	0
Body Cavities					
Abdominal cavity:	(N=)	(5)	(4)	(3)	(4)
(B) Hemangioma		0	0	0	1

(N=): Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.
*: Significantly different from the control at 5 % level of probability.

Table 21 - 2 Histopathology - Incidence of microscopic neoplastic lesions in female mice
Terminal kill after 78 weeks of treatment

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	32	36	40	35
No. of benign neoplasms		12	16	22	12
No. of malignant neoplasms		7	5	9	4
No. of benign & malignant neoplasms		19	21	31	16
No. of animals with benign neoplasm(s)		11	12	18	11
No. of animals with malignant neoplasm(s)		7	5	9	4
No. of animals with neoplasm(s)		16	16	21	12

Table 21 - 3 Histopathology - Incidence of microscopic neoplastic lesions in female mice
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	18	14	10	15
Hematopoietic & Lymphatic System					
General:	(N=)	(18)	(14)	(10)	(15)
(M) Myeloid leukemia		0	0	0	1
(M) Malignant lymphoma		2	4	3	4
Spleen:	(N=)	(18)	(14)	(10)	(15)
(M) Hemangiosarcoma		0	0	1	0
(M) Histiocytic sarcoma		0	0	0	1
Respiratory System					
Lung:	(N=)	(18)	(14)	(10)	(15)
(B) Adenoma		1	1	0	1
(M) Adenocarcinoma		0	1	0	1
< Nodule/mass not in section >		0	0	1	0
Digestive System					
Liver:	(N=)	(18)	(14)	(10)	(15)
(B) Hemangioma		0	0	0	1
Genital System					
Ovary:	(N=)	(18)	(14)	(10)	(15)
(B) Hemangioma		0	0	0	1
Uterus:	(N=)	(18)	(14)	(10)	(15)
(M) Leiomyosarcoma		0	0	0	1
Endocrine System					
Thyroid:	(N=)	(18)	(14)	(10)	(15)
(B) Follicular adenoma		0	1	0	0
Musculo-Skeletal System					
Bone (femur) :	(N=)	(18)	(14)	(10)	(15)
(B) Osteoma		0	0	0	1
Skeletal muscle (others) :	(N=)	(0)	(3)	(3)	(1)
(M) Rhabdomyosarcoma		-	1	2	0
Sense Organs					
Harderian gland:	(N=)	(18)	(14)	(10)	(15)
(B) Adenoma		0	0	0	2
Integumentary System					
Skin:	(N=)	(18)	(14)	(10)	(15)
(M) Basal cell carcinoma		0	1	0	0
(M) Hemangiosarcoma		0	0	1	0
Mammary gland:	(N=)	(18)	(14)	(10)	(15)
(M) Adenocarcinoma		0	1	1	0
Body Cavities					
Thoracic cavity:	(N=)	(2)	(4)	(4)	(7)
(M) Osteosarcoma		0	0	0	1
Abdominal cavity:	(N=)	(3)	(5)	(6)	(5)
(M) Osteosarcoma		0	0	0	1

(N=) : Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

Table 21 - 4 Histopathology - Incidence of microscopic neoplastic lesions in female mice
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	18	14	10	15
No. of benign neoplasms		1	2	0	6
No. of malignant neoplasms		2	8	8	10
No. of benign & malignant neoplasms		3	10	8	16
No. of animals with benign neoplasm(s)		1	1	0	5
No. of animals with malignant neoplasm(s)		2	8	7	9
No. of animals with neoplasm(s)		3	8	7	11

Table 21 - 5 Histopathology - Incidence of microscopic neoplastic lesions in female mice
All animals examined

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Hematopoietic & Lymphatic System					
General:	(N=)	(50)	(50)	(50)	(50)
(M) Myeloid leukemia		0	0	0	1
(M) Malignant lymphoma		6	4	8	7
Thymus:	(N=)	(49)	(49)	(50)	(50)
(M) Malignant lymphoma		0	0	1	0
Spleen:	(N=)	(50)	(50)	(50)	(50)
(B) Hemangioma		0	0	1	0
(M) Hemangiosarcoma		0	0	1	0
(M) Histiocytic sarcoma		0	0	0	1
Respiratory System					
Lung:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		8	5	12	5
(M) Adenocarcinoma		1	2	3	1
< Nodule/mass not in section >		0	0	1	0
Digestive System					
Small intestine:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	0	1	0
Liver:	(N=)	(50)	(50)	(50)	(50)
(B) Hepatocellular adenoma		1	1	1	0
(B) Hemangioma		0	0	0	1
Urinary System					
Urinary bladder:	(N=)	(50)	(50)	(50)	(50)
(B) Leiomyoma		0	0	1	1
Genital System					
Ovary:	(N=)	(50)	(50)	(50)	(50)
(B) Hemangioma		0	0	0	1
Uterus:	(N=)	(50)	(50)	(50)	(50)
(B) Endometrial stromal polyp		0	2	0	0
(B) Hemangioma		0	0	1	2
(B) Leiomyoma		1	0	2	1
(M) Histiocytic sarcoma		0	1	0	0
(M) Leiomyosarcoma		2	1	0	1
Endocrine System					
Pituitary:	(N=)	(50)	(50)	(50)	(50)
(B) Anterior adenoma		0	1	0	0
Thyroid:	(N=)	(50)	(50)	(50)	(50)
(B) Follicular adenoma		0	2	0	0
Adrenal:	(N=)	(50)	(50)	(50)	(50)
(B) Benign A cell tumor		0	1	2	0
(B) Pheochromocytoma		0	2	0	0
Musculo-Skeletal System					
Bone (femur) :	(N=)	(50)	(50)	(50)	(50)
(B) Osteoma		0	0	0	1
Skeletal muscle (others) :	(N=)	(0)	(3)	(4)	(3)
(M) Rhabdomyosarcoma		-	1	2	0
Sense Organs					
Harderian gland:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		1	3	0	5

(N=) : Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

Table 21 - 6 Histopathology - Incidence of microscopic neoplastic lesions in female mice
All animals examined

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Integumentary System					
Skin:	(N=)	(50)	(50)	(50)	(50)
(B) Papilloma		1	0	0	0
(B) Lipoma		1	0	1	0
(M) Basal cell carcinoma		0	1	0	0
(M) Liposarcoma		0	0	0	1
(M) Hemangiosarcoma		0	0	1	0
Mammary gland:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	1	0	0
(M) Adenocarcinoma		0	3	1	0
Body Cavities					
Thoracic cavity:	(N=)	(4)	(6)	(5)	(10)
(M) Osteosarcoma		0	0	0	1
Abdominal cavity:	(N=)	(8)	(9)	(9)	(9)
(B) Hemangioma		0	0	0	1
(M) Osteosarcoma		0	0	0	1
No. of benign neoplasms		13	18	22	18
No. of malignant neoplasms		9	13	17	14
No. of benign & malignant neoplasms		22	31	39	32
No. of animals with benign neoplasm(s)		12	13	18	16
No. of animals with malignant neoplasm(s)		9	13	16	13
No. of animals with neoplasm(s)		19	24	28	23

(N=): Number of animals examined microscopically at the site.
Malignancy: (B), benign neoplasm; (M), malignant neoplasm.