CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019651/S005

PHARMACOLOGY REVIEW(S)

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Oncogenicity Study (24-Months) of 5-ASA in the Diet of Swiss Mice
Project No. 862.09.00-CD
Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS	TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC)											
		MALES						FEMALES					
		0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
ENDOCRINE SYSTEM:													
PITUITARY:		(47)	(50)	(49)	(48)			(48)	(47)	(50)	(49)		
Multifocal necrosis											1		
LYMPHOMA [M]		1	1					2	2				
Focal/multifocal hyperplasia		2	3		3			1	2	3	2		
Focal/multifocal cyst(s)		2		2	3			1	2	2	1		
Focal/multifocal/diffuse congestion								2	1	3	3		
Primary site: CARCINOMA [M]								1					
Autolysis											1		
Focal/multifocal angiectasis										1	2		
ADENOMA [B]		1			1			2	1	1	1		

Figures in brackets represent the number of animals from which this tissue was examined microscopically
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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
ENDOCRINE SYSTEM:-												
THYROID GLAND:	(47)	(50)	(45)	(48)			(46)	(47)	(49)	(49)		
No abnormality detected	23	26	24	26			20	24	21	28		
Metastatic site: HISTIOCYTIC SARCOMA [M]		2		1				1	1			
Multifocal capsular chronic inflammation							1					
Focal vasculitis	1		1	2				1				
LYMPHOMA [M]	2		1				2		2	1		
Focal/multifocal/NOS interstitial inflammation	8	3	4	4			6	6	7	7		
Focal/multifocal follicular hyperplasia			1					1				
Multifocal pericapsular hemorrhage		1										
Multifocal interstitial fibrosis	1											
Focal ectopia		1										

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OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
ENDOCRINE SYSTEM:-												
THYROID GLAND:	(47)	(50)	(45)	(48)			(46)	(47)	(49)	(49)		
Focal/multifocal follicular dilation	10	9	9	11			7	4	10	5		
Focal/multifocal cyst(s)		1	1				1					
Autolysis		3		1			1	2	1	2		
Diffuse/NOS follicular atrophy							1	1				
Multifocal/diffuse amyloidosis	5	12	7	8			13	14	9	10		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
BONE MARROW:	(50)	(49)	(50)	(50)			(50)	(50)	(50)	(50)		
No abnormality detected	40	36	34	33			31	25	32	34		
Metastatic site: HISTIOCYTIC SARCOMA [M]		2		1			1		1			
Primary site: GRANULOCYTIC LEUKEMIA [M]		1		1								

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OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	MALES 200 mg/kg	MALES 1000 mg/kg	MALES 2000 mg/kg	FEMALES 0 mg/kg	FEMALES 200 mg/kg	FEMALES 1000 mg/kg	FEMALES 2000 mg/kg
HEMATOPOIETIC AND LYMPHATIC SYSTEM:								
BONE MARROW:	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)
Multifocal acute inflammation								1
Multifocal necrosis		1	1	1			1	
Focal/multifocal myelofibrosis					2			2
LYMPHOMA [M]	2	2		2	2	2	2	
Multifocal/diffuse/NOS myeloid/granulocytic/erythrocytic/NOS hyperplasia	4	8	9	10	5	6	5	8
Multifocal hemosiderosis							1	
Focal hemorrhage		1	5					
Metastatic site: HEMANGIOSARCOMA [M]				1				
Metastatic site: CARCINOMA [M]					1			

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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
BONE MARROW:	(50)	(49)	(50)	(50)			(50)	(50)	(50)	(50)		
Autolysis			1							1		
Focal/multifocal/diffuse/NOS atrophy	3			1			9	17	9	5		
Multifocal angiectasis	1											
LYMPH NODE(S):	(1)	(1)	(4)	(2)			(4)	(2)	(1)	(1)		
Metastatic site: HISTIOCYTIC SARCOMA [M]									1			
Metastatic site: GRANULOCYTIC LEUKEMIA [M]				1								
Multifocal acute inflammation			1									
Medullary plasmacytosis							1					
LYMPHOMA [M]		1	1				2	1		1		

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
LYMPH NODE(S):	(1)	(1)	(4)	(2)			(4)	(2)	(1)	(1)		
Lymphoid hyperplasia			1				1					
Medullary hemorrhage								1				
Multifocal amyloidosis	1		1	1								
MEDIASTINAL LYMPH NODE(S):	(2)			(2)				(1)	(1)	(3)		
Metastatic site: HISTIOCYTIC SARCOMA [M]										2		
Medullary plasmacytosis				1								
Metastatic site: MESOTHELIOMA [M]	1											
LYMPHOMA [M]	1			1				1	1			
Lymphoid hyperplasia										1		

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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
MESENTERIC LYMPH NODE(S):	(49)	(44)	(41)	(40)			(43)	(44)	(44)	(42)		
No abnormality detected	31	17	18	19			13	20	16	15		
Metastatic site: HISTIOCYTIC SARCOMA [M]		4		1			2	2	4	2		
Metastatic site: GRANULOCYTIC LEUKEMIA [M]		1										
Multifocal pericapsular acute/chronic inflammation			1							1		
Multifocal lymphocytolysis	1		1	2			1	1		1		
Multifocal pericapsular vasculitis							3					
Hematocyst(s)							1					
Multifocal granuloma(ta)			1									
Multifocal/NOS medullary plasmacytosis	1		2					2		1		

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
MESENTERIC LYMPH NODE(S):	(49)	(44)	(41)	(40)			(43)	(44)	(44)	(42)		
Multifocal edema	1											
Focal necrosis		1						1				
LYMPHOMA [M]	2	2	3	1			4	4	6	5		
Focal/multifocal/diffuse acute/chronic/chronic-active/pyogranulomatous inflammation/neutrophilic infiltration				1			1	2	1	2		
Lymphoid hyperplasia	2	2	2				5	3	4			
Focal histiocytic hyperplasia								1				
Diffuse/NOS sinus histiocytosis		2	1	1								
Multifocal hemosiderosis							1		1			
Multifocal/diffuse medullary hemorrhage			1					1				

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Oncogenicity Study (24-Months) of 5-ASA in the Diet of Swiss Mice
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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
MESENTERIC LYMPH NODE(S):	(49)	(44)	(41)	(40)			(43)	(44)	(44)	(42)		
Multifocal/NOS extramedullary hematopoiesis	4	1	3	2			4	2	1	3		
Metastatic site: HEMANGIOSARCOMA [M]	1											
HEMANGIOMA [B]							1					
Metastatic site: FIBROSARCOMA [M]										1		
Lymphoid depletion	1											
Focal/multifocal/diffuse/NOS congestion	3	3	4	4			2	2	6	9		
Autolysis	1	7		4			2	1	2	5		
Diffuse/NOS lymphoid atrophy		2		2			1		1			
Focal/multifocal angiectasis/vascular ectasia	1		2	3			3	2	1			

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Oncogenicity Study (24-Months) of 5-ASA in the Diet of Swiss Mice
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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
MESENTERIC LYMPH NODE(S):	(49)	(44)	(41)	(40)			(43)	(44)	(44)	(42)		
Multifocal amyloidosis	5	8	6	7			7	11	6	5		
SPLEEN:	(50)	(50)	(50)	(50)			(50)	(50)	(50)	(50)		
No abnormality detected	27	19	26	24			7	10	11	9		
Metastatic site: HISTIOCYTIC SARCOMA [M]		2		1			1	3	2	2		
Primary site: HISTIOCYTIC SARCOMA [M]		2							1	2		
Metastatic site: GRANULOCYTIC LEUKEMIA [M]		1		1								
Focal/multifocal capsular chronic inflammation	1		5					1				
Focal/multifocal acute/subacute inflammation			1						1			
Multifocal lymphocytolysis		1		1			1			2		

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HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
SPLEEN:	(50)	(50)	(50)	(50)			(50)	(50)	(50)	(50)		
Focal vasculitis	1											
Metastatic site: MESOTHELIOMA [M]	1											
LYMPHOMA [M]	3	2	1	2			7	5	5	5		
Lymphoid hyperplasia									1			
Multifocal hemosiderosis	2	1	1	1			5	11	10	11		
Focal hemorrhage	1	1										
Diffuse/NOS increased/NOS hematopoiesis	13	13	15	15			19	20	16	21		
Metastatic site: HEMANGIOSARCOMA [M]	1											
Primary site: HEMANGIOSARCOMA [M]	1	2		1			1		1			
Multifocal fibrosis									1			

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HEMATOPOIETIC AND LYMPHATIC SYSTEM:-								
SPLEEN:	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Multifocal sinusoidal ectasia	1							
Diffuse/NOS lymphoid depletion	1			1				
Diffuse/NOS congestion	1	1		1	2		1	1
Autolysis					5	4	1	2
Focal angiectasis						1		
Focal/multifocal/diffuse amyloidosis	4	10	3	5	11	9	7	5
SUBMANDIBULAR LYMPH NODE(S):	(38)	(41)	(46)	(44)	(40)	(47)	(45)	(44)
No abnormality detected	31	24	42	36	25	30	31	31
Metastatic site: HISTIOCYTIC SARCOMA (M)		2		1	1	1	2	1
Metastatic site: GRANULOCYTIC LEUKEMIA (M)		1		1				

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
SUBMANDIBULAR LYMPH NODE(S):	(38)	(41)	(46)	(44)			(40)	(47)	(45)	(44)		
Multifocal lymphocytolysis							1					
Diffuse/NOS medullary plasmacytosis	3	5	1	2			1	3		2		
Focal vascular mineralization	1											
LYMPHOMA [M]	2	2	1	1			3	2	3	3		
Multifocal neutrophilic infiltration				1								
Lymphoid hyperplasia			1				3	3	1			
Multifocal/diffuse hemosiderosis	1	4		1			5	4	7	7		
Lymphoid depletion								1				
Multifocal/diffuse/NOS congestion							1		1	2		
Autolysis		1						1		1		

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OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg	FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-								
SUBMANDIBULAR LYMPH NODE(S):	(38)	(41)	(46)	(44)	(40)	(47)	(45)	(44)
Focal/multifocal amyloidosis		2			1	2		
Abscess(es)			1					
THYMUS:	(22)	(16)	(24)	(23)	(25)	(31)	(35)	(30)
No abnormality detected	9	10	11	8	13	17	17	11
Metastatic site: HISTIOCYTIC SARCOMA [M]		2		1	3	2	2	3
Metastatic site: GRANULOCYTIC LEUKEMIA [M]				1				
Multifocal lymphocytolysis		2				1		2
Focal/multifocal vasculitis			2	1	1			
Multifocal vascular mineralization							1	
Multifocal mineralization					1			

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
HEMATOPOIETIC AND LYMPHATIC SYSTEM:-												
THYMUS:	(22)	(16)	(24)	(23)			(25)	(31)	(35)	(30)		
LYMPHOMA [M]	3	1	1	3			5	3	5	4		
Involution										1		
Focal pyogranulomatous inflammation										1		
Multifocal eosinophilic infiltration								1				
Lymphoid hyperplasia								1	1	1		
Focal/multifocal epithelial hyperplasia	2		3	3			1	1	2			
Focal/multifocal hemorrhage		1						2				
Focal fibrosis								1		1		
Focal/multifocal cyst(s)	9	1	9	8			2	4	6	4		
Multifocal/NOS congestion								1	2	2		

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HEMATOPOIETIC AND LYMPHATIC SYSTEM:-								
THYMUS:	(22)	(16)	(24)	(23)	(25)	(31)	(35)	(30)
Autolysis		1		1		1	2	2
Multifocal amyloidosis						1		
INTEGUMENTARY SYSTEM:-								
MAMMARY GLAND(S):	(10)	(6)	(5)	(5)	(50)	(49)	(49)	(49)
No abnormality detected	6	6	5	3	18	12	11	17
Focal mastocytosis						1		
Metastatic site: HISTIOCYTIC SARCOMA [M]					1		1	1
Focal/multifocal chronic inflammation	3				13	12	11	7
Focal cystic change					1			
LYMPHOMA [M]					1	2	3	3

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
INTEGUMENTARY SYSTEM:-												
MAMMARY GLAND(S):	(10)	(6)	(5)	(5)			(50)	(49)	(49)	(49)		
Multifocal lymphangiectasia									1			
Multifocal/diffuse lobular hyperplasia							2			1		
Multifocal ductular/NOS epithelial hyperplasia								2		1		
Focal/multifocal/NOS ductular dilation	2			2			19	27	29	25		
Multifocal congestion							1					
Autolysis							1	4	2			
ADENOMA [B]							1					
Primary site: ADENOCARCINOMA [M]							2		1	1		

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Oncogenicity Study (24-Months) of 5-ASA in the Diet of Swiss Mice
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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)									
	MALES					FEMALES				
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg	
INTEGUMENTARY SYSTEM:-										
PREPUTIAL/CLITORAL GLAND(S):	(48)	(46)	(50)	(49)		(43)	(39)	(42)	(37)	
Metastatic site: HISTIOCYTIC SARCOMA [M]						1			1	
Metastatic site: GRANULOCYTIC LEUKEMIA [M]		1								
Focal/multifocal/diffuse/NOS acute/subacute/chronic inflammation	23	17	28	22		25	21	25	19	
One examined		1		1						
LYMPHOMA [M]	1	1	1	1				4	1	
Multifocal lymphangiectasis	2	2	8	5		3	5	4	2	
Focal/multifocal/diffuse/NOS ductular dilation	48	45	49	48		43	39	41	35	
Multifocal/diffuse/NOS acinar atrophy	10	13	16	14		10	8	8	8	
Multifocal amyloidosis								1		

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OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)									
	MALES					FEMALES				
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg	
INTEGUMENTARY SYSTEM:-										
PREPUTIAL/CLITORAL GLAND(S):	(48)	(46)	(50)	(49)		(43)	(39)	(42)	(37)	
Focal/NOS abscess(es)	4	4	2	3			2	1	1	
SKIN/SUBCUTIS:	(49)	(50)	(49)	(49)		(50)	(50)	(50)	(50)	
No abnormality detected	32	29	37	26		33	33	31	37	
Primary site: mass (1): HISTIOCYTIC SARCOMA (M)							1			
Metastatic site: HISTIOCYTIC SARCOMA (M)		1				2				
Metastatic site: GRANULOCYTIC LEUKEMIA (M)		1								
LIPOMA (B)				1						
Primary site: BASOSQUAMOUS CARCINOMA (M)									1	
Focal/multifocal ulceration(s)		4	2	1			3	1		

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified

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Oncogenicity Study (24-Months) of 5-ASA in the Diet of Swiss Mice
Project No. 862.09.00-CD
Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg	FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg
INTEGUMENTARY SYSTEM:-								
SKIN/SUBCUTIS:	(49)	(50)	(49)	(49)	(50)	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA (M)							1	
PAPILLOMA (B)				1				
Diffuse/NOS subcutaneous/dermal edema	1	4	1	2	2	4	1	1
Focal/diffuse necrosis			1					1
LYMPHOMA (M)	1	1	1	1			2	1
Multifocal subcutaneous lymphangiectasis	1							
Focal/multifocal/diffuse acute/subacute/chronic/chronic-active inflammation	6	7	6	11	4	3	3	3
Multifocal papillary hyperplasia							1	
Focal/multifocal/diffuse hyperkeratosis		2	2	1	1	5	4	3

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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
INTEGUMENTARY SYSTEM:-												
SKIN/SUBCUTIS:	(49)	(50)	(49)	(49)			(50)	(50)	(50)	(50)		
Hematoma	1											
Metastatic site: HEMANGIOSARCOMA (M)				1								
Primary site: HEMANGIOSARCOMA (M)	1						1					
HEMANGIOMA (B)	1		1									
Focal/multifocal dermal fibrosis									1	1		
Primary site: FIBROSARCOMA (M)								1		1		
Focal subcutaneous fibroplasia									1			
Focal glandular ectasia			1									
Multifocal follicular dilation	2		2	1			1		1			
Focal/multifocal/diffuse acute/NOS ulcerative dermatitis	2	5	2	4			1		3	2		

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OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
INTEGUMENTARY SYSTEM:-												
SKIN/SUBCUTIS:	(49)	(50)	(49)	(49)			(50)	(50)	(50)	(50)		
Focal follicular cyst(s)							2		1	1		
Autolysis		2						2				
Focal/multifocal/diffuse adnexal atrophy	3	3	3	3			4	3	4	1		
Focal angiectasis				1								
Multifocal amyloidosis		1								1		
Mass (1): ADENOCARCINOMA [M]									1			
Focal acanthosis	1	1		1								
Focal abscess(es)	1	1		2								
: See TAIL	1											
: See TAIL									1			

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Project No. 862.09.00-CD
Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
INTEGUMENTARY SYSTEM:-												
ZYMBAL'S GLAND(S):	(41)	(39)	(41)	(44)			(42)	(42)	(40)	(41)		
No abnormality detected			2	1					1	1		
Metastatic site: HISTIOCYTIC SARCOMA [M]				1			1		1	1		
Metastatic site: GRANULOCYTIC LEUKEMIA [M]		1										
Focal/multifocal/diffuse chronic inflammation	22	19	17	17			14	19	11	14		
Focal vasculitis	1											
One examined	23	19	23	18			23	12	16	19		
Focal basal cell proliferation								1				
LYMPHOMA [M]	3	2	1				2	1	2	1		
Focal fibrosis							1			1		

Figures in brackets represent the number of animals from which this tissue was examined microscopically
the absence of a numeral indicates that the lesion specified was not identified

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Summary of all Histomorphologic Findings

OBSERVATIONS / TREATMENT	INCIDENCE OF OBSERVATION (NUMERIC) MALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg	FEMALES 0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg
INTEGUMENTARY SYSTEM:-								
ZYMBAL'S GLAND(S):	(41)	(39)	(41)	(44)	(42)	(42)	(40)	(41)
Focal/multifocal ductular dilation	38	38	35	39	39	41	39	38
Focal/multifocal/diffuse acinar atrophy	2	2	5	3	1			1
Multifocal/diffuse amyloidosis	6	10	8	8	13	11	5	5
MUSCULOSKELETAL SYSTEM:-								
BONE:	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
No abnormality detected	39	38	43	39	32	29	27	34
Metastatic site: HISTIOCYTIC SARCOMA [M]		1		1			1	1
Focal/multifocal periosteal/NOS acute/subacute/chronic inflammation	1		1				1	2
Focal cartilage retention				1				
Focal/multifocal fibrous osteodystrophy	5	4	1	2	15	17	15	11

Figures in brackets represent the number of animals from which this tissue was examined microscopically
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Pathology Table 7
Summary of all Histomorphologic Findings

OBSERVATIONS	INCIDENCE OF OBSERVATION (NUMERIC)											
	MALES						FEMALES					
TREATMENT	0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg			0 mg/kg	200 mg/kg	1000 mg/kg	2000 mg/kg		
MUSCULOSKELETAL SYSTEM:-												
BONE:	(50)	(50)	(50)	(50)			(50)	(50)	(50)	(50)		
Focal/multifocal necrosis	2	4	3	4			4	5	2	2		
LYMPHOMA [M]	2	1		1					1			
Focal/multifocal/NOS hyperostosis								2	1	1		
Focal periosteal hematopoiesis		1										
Metastatic site: HEMANGIOSARCOMA [M]				1								
Multifocal fracture									1			
Focal/multifocal fibrosis	1							1	3			
Metastatic site: FIBROSARCOMA [M]										1		
Focal dental dysplasia			1	1			1					
Sternal dislocation			1									

Figures in brackets represent the number of animals from which this tissue was examined microscopically
The absence of a numeral indicates that the lesion specified was not identified