

NDA 20,987
Page 450

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143	FATES: ALL					PAGE 56
DAYS : ALL	SEX: FEMALE					
GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
	#	#	#	#	#	
adrenal 2	# Ex 46	50	49	50	50	
thrombosis	0	0	0	0	1	
purulent adenitis	0	0	0	0	1	
medullary hyperplasia	9	3	2	2	7	
leukocytostasis	0	0	2	2	2	
all organs	# Ex 14	25	30	23	28	
bacterial growth	1	0	0	0	0	
autolysis	14	25	30	23	28	
aorta	# Ex 50	50	50	50	49	
medial calcification	0	0	0	0	1	
peri- / vasculitis	0	1	0	1	2	
intravascular foreign material	0	0	0	0	1	
body openings	# Ex 0	0	0	0	0	
bone	# Ex 0	1	0	0	0	
healed fracture	0	1	0	0	0	
brain	# Ex 48	49	50	50	50	
Lympho-histiocytic infiltr.	0	1	2	1	0	
hemorrhage	1	1	0	2	0	
thalamic compression	6	2	4	2	3	
red malacia	0	0	0	2	0	
satellitosis	0	0	2	3	2	
neuronal / axonal degeneration	4	3	3	1	3	
hyperemia / congestion	2	2	0	0	0	
meningeal calcification	0	0	1	0	0	
neuronophagia	0	0	0	1	0	
pigment deposit(s)	0	0	0	1	0	
intravascular foreign material	0	0	0	0	1	
psammoma	0	0	1	0	0	

(Report Continued)

NDA 20,987
Page 451

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143		FATES: ALL					PAGE 57
DAYS : ALL		SEX: FEMALE					
GROUP:		-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:		50	50	50	50	50	
		#	#	#	#	#	
cecum	# Ex	48	49	50	50	50	
enteritis		1	0	0	0	0	
ulcer		1	0	1	0	0	
lymphocytic hyperplasia		0	0	0	2	0	
clitoral gland	# Ex	1	1	1	2	0	
colon	# Ex	48	50	50	50	50	
edema		0	0	0	1	0	
lymphocytic hyperplasia		1	0	0	0	0	
diaphragm	# Ex	0	0	0	0	0	
duodenum	# Ex	49	50	50	50	50	
mucosal pigment deposit(s)		0	0	0	1	0	
ear/auditory duct	# Ex	0	0	0	0	0	
esophagus	# Ex	50	50	50	50	49	
peri- / epi- / esophagitis		0	0	0	0	1	
traumatic separation		0	0	1	0	0	
dilatation		0	0	1	0	0	
residual ingesta		0	0	1	0	0	
lympho-histiocytic infiltr.		0	0	0	2	2	
purulent (traumatic) inflam.		0	0	1	0	1	
peri- / vasculitis		1	0	0	0	0	
extremities	# Ex	0	0	0	0	0	
eye 1	# Ex	45	47	48	47	47	
keratitis		0	0	1	1	0	
iritis		0	0	1	0	0	
conjunctivitis		0	0	0	0	1	

(Report Continued)

NDA 20,987
Page 452

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143
DAYS : ALL

FATES: ALL
SEX: FEMALE

PAGE 58

GROUP: -- mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
eye 1	# Ex 45	47	48	47	47
corneal dysplasia	0	0	1	0	0
uveitis	0	0	1	2	2
retinal degener. / atrophy	17	8	9	14	7
orbital inflammation	0	0	0	1	0
anterior chamber hemorrhage	0	0	1	1	0
granuloma	15	8	14	10	7
connective tissue calcific.	24	15	12	12	15
periobital blood	2	1	0	2	2
lympho-histiocytic infiltr.	1	1	0	0	0
degeneration of vitreous body	3	0	0	4	0
leukocytostasis	0	0	0	0	1
eye 2	# Ex 45	47	49	47	46
keratitis	1	1	1	0	0
uveitis	2	1	0	1	1
retinal degener. / atrophy	15	7	10	14	7
anterior chamber hemorrhage	0	1	0	0	0
granuloma	4	10	11	8	4
connective tissue calcific.	21	12	13	16	18
periobital blood	11	4	1	2	4
lympho-histiocytic infiltr.	3	0	0	0	0
degeneration of vitreous body	0	1	1	3	0
leukocytostasis	0	0	0	0	1
forestomach	# Ex 49	50	50	50	50
hyperkeratosis	1	0	0	0	0
subm. inflammation	3	0	0	0	0
erosion	1	0	0	0	0
ulcer	1	0	0	1	0
calcification, muscular	0	0	2	2	0
hyperplasia	3	1	0	1	4
squamous cell papilloma	0	1	0	0	0
general used preferred terms	# Ex 0	0	0	0	0

(Report Continued)

NDA 30,987
Page 453

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143
DAYS : ALL

FATES: ALL
SEX: FEMALE

PAGE 59

GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg
NUMBER OF ANIMALS:	50	50	50	50	50

	#	#	#	#	#
glandular stomach (Grimelius) # Ex	35	23	17	25	20
GPC, diffuse	35	21	17	25	19
GPC, focal hyperplasia	0	1	4	4	2
GPC, chains	0	0	10	11	11
GPC, micronodules	0	0	0	2	4
GPC, submucosal growth	0	0	2	8	6
GPC, decreased	0	2	0	0	0
GPC, distribution	35	23	17	25	19
glandular stomach (antrum) # Ex	49	50	46	49	47
mucosal hyperplasia	2	1	4	15	12
erosion	4	0	1	1	0
epithelial hyperplasia	0	0	0	3	0
lymphfollicle	0	0	2	2	2
glandular stomach (fundus) # Ex	49	50	50	50	50
parietal cell vacuolation	0	1	0	0	1
mucosal hyperplasia/folding	10	3	41	39	42
gland. ectasia	23	16	40	39	29
cyst	4	5	4	11	2
erosion	16	8	1	2	1
ulcer	2	1	0	2	0
necrosis	0	0	0	0	3
eosinophilic chief cells	0	0	40	42	45
subm. mixed cell infiltration	0	1	0	1	0
subm. edema	0	3	0	0	3
gastritis	0	0	1	0	0
epithelial cyst	0	0	0	0	1
bleeding	0	0	1	0	1
basal fibrosis	1	0	5	16	11
vascular calcification	0	0	1	3	0
serositis	1	0	0	0	0
congestion/hyperemia	0	0	0	3	1
mucosal lymphfollicles	0	0	0	0	4
regenerative hyperplasia	0	0	0	1	5
eosinophilic infiltr.	0	0	5	11	8

(Report Continued)

NDA 20,987
Page 454

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143	FATES: ALL					PAGE 60
DAYS: ALL	SEX: FEMALE					
GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
haematopoetic system	# Ex 8	# 7	# 3	# 8	# 7	
harderian gland 1	# Ex 50	# 50	# 50	# 50	# 50	
chronic inflammation	11	6	4	11	9	
chronodacryorrhea	42	40	41	43	43	
intraglandular blood	1	2	3	2	3	
lympho-histiocytic infiltr.	18	17	27	18	15	
acute inflammation	1	0	1	2	0	
granuloma	1	2	1	2	0	
ductal hyperplasia	0	0	0	1	0	
hyperemia / congestion	0	0	0	1	0	
harderian gland 2	# Ex 50	# 50	# 50	# 50	# 50	
chronic inflammation	13	5	6	9	6	
chronodacryorrhea	39	42	46	43	48	
intraglandular blood	15	6	6	6	8	
lympho-histiocytic infiltr.	14	17	20	17	16	
acute inflammation	1	0	0	1	0	
granuloma	3	1	0	0	2	
acinar hyperplasia	0	0	0	1	1	
hyperemia / congestion	1	0	0	1	0	
heart	# Ex 49	# 50	# 50	# 50	# 50	
acute myocarditis	0	0	1	0	0	
chronic myocarditis	21	19	11	12	9	
myocardial hemosiderosis	2	0	1	4	2	
myocardial fibrosis	13	5	8	5	5	
peri- / vasculitis	3	6	0	1	2	
chondroid metaplasia	2	5	5	1	1	
myocardial degeneration	0	1	2	6	5	
lympho-histiocytic infiltr.	6	10	13	22	25	
vascular calcification	25	12	10	17	12	
leukocytostasis	0	0	0	0	1	
thrombosis	0	0	1	0	0	
hyperemia / congestion	0	1	0	0	0	
peri- / epicarditis	0	0	0	0	2	
intravascular foreign material	0	0	0	0	1	

(Report Continued)

NDA 20,987
Page 455

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143	FATES: ALL					PAGE 61
DAYS : ALL	SEX: FEMALE					
GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
	#	#	#	#	#	
ileum	# Ex 48	49	50	49	50	
lymphocytic hyperplasia	6	11	5	6	3	
lymphoma / leukemia	0	0	0	1	0	
ischialic nerve	# Ex 50	50	48	48	47	
axonal degeneration	0	0	0	1	0	
intra-, interaxonal edema	0	0	0	1	0	
jejunum	# Ex 48	50	50	49	50	
lymphoma / leukemia	0	0	0	1	0	
lymphocytic hyperplasia	0	0	0	1	0	
joints	# Ex 0	0	0	0	0	
kidney 1	# Ex 47	50	49	50	50	
chron. progressive nephropathy	9	8	6	10	10	
pelvic epith. calcification	1	0	4	4	3	
interstitial nephritis	1	0	0	0	2	
pigment deposits	23	19	19	24	21	
tubular calcification	8	18	21	15	11	
tubular cell regeneration	1	1	0	0	4	
hyperemia / congestion	3	4	3	3	5	
lympho-histiocytic infiltr.	12	2	2	2	5	
leukocytostasis	0	0	0	0	1	
kidney 2	# Ex 47	50	49	50	50	
chron. progressive nephropathy	9	8	5	10	10	
pelvic epith. calcification	1	0	3	1	2	
urolithiasis	1	0	0	0	0	
interstitial nephritis	1	0	0	0	2	
pigment deposits	23	19	19	24	21	
tubular calcification	5	14	18	15	10	
tubular cell regeneration	0	0	0	0	3	
hyperemia / congestion	3	4	3	3	5	
lympho-histiocytic infiltr.	13	3	0	2	3	
leukocytostasis	0	0	0	0	1	

(Report Continued)

NDA 20,987

Page 456

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143		FATES: ALL					PAGE 62
DAYS : ALL		SEX: FEMALE					
GROUP:		-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:		50	50	50	50	50	
		#	#	#	#	#	
Liver	# Ex	50	50	50	50	50	
hepatitis		1	0	0	1	0	
bile duct proliferation		31	23	26	33	26	
clear cell focus		4	3	1	3	5	
eosinophilic cell focus		7	5	0	0	2	
basophilic cell focus		38	25	33	29	24	
necrosis		4	2	3	7	5	
hemorrhage		1	4	2	1	3	
activation of Kupffer-cells		0	0	0	2	0	
periductal fibrosis/inflammat.		31	16	25	26	22	
pigment deposits		5	5	3	13	2	
peliosis		0	0	0	1	1	
extramedullary hematopoiesis		0	0	0	1	0	
hepatocellular vacuolation		0	1	1	0	0	
hepatocell. fatty vacuolation		7	5	1	5	5	
leukocytostasis		4	1	1	2	3	
lympho-histiocytic infiltr.		10	13	19	17	12	
hyperemia / congestion		19	28	31	28	32	
apoptosis		1	9	16	8	14	
spongiosis		0	0	0	0	1	
regenerat. hepat. hyperplasia		12	4	3	3	6	
capsular fibrosis		0	0	0	0	1	
centrilobular hypertrophy		1	10	10	23	26	
Mallory bodies, intracytoplas.		1	0	0	0	0	
eosinophilic infiltr.		0	0	0	0	1	
intravascular foreign material		0	0	0	0	1	
organ parts absent (carnibal.)		1	0	0	0	0	
granuloma		15	7	5	6	5	
deformed, herniated lobe		0	1	0	1	0	
Lumb.spinal cord, bone m.	# Ex	48	49	48	48	48	
axon degeneration		14	9	7	9	2	
ectopic epidermoid cyst		0	0	1	0	0	
granulomatous inflammation		0	0	0	2	1	
red malacia		0	0	0	1	0	
bone marrow atrophy		0	1	0	0	1	
bone marrow depletion		0	0	0	0	1	
protozoal infection		0	0	0	1	0	
reactive hyperplasia.		0	0	0	3	0	

(Report Continued)

NDA 20,987
Page 457

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143
DAYS : ALL

FATES: ALL
SEX: FEMALE

PAGE 63

GROUP: -- mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
Lung	# Ex 50	50	50	50	50
hyperemia / congestion	34	41	42	39	39
lympho-histiocytic infiltr.	5	7	6	6	5
alveolar histiocytosis	16	9	15	20	19
purulent bronchopneumonia	0	0	0	3	2
foreign-body granuloma	0	1	0	1	0
intraalveolar blood	1	1	5	3	4
alveolar edema	0	1	1	0	3
vascular calcification	2	0	2	4	1
cholesterol clefts	0	0	0	0	1
atelectasis	1	0	0	0	0
emphysema	12	12	9	7	10
alveol. lipoproteinosis	3	0	0	0	0
granuloma	1	0	3	3	1
pigment in macrophages	6	0	4	9	6
bronchiolisation	0	0	1	0	0
bronch.-alv. hyperplasia	0	2	0	0	0
leukocytostasis	0	0	0	0	1
aspirated plant material	0	1	1	1	1
intravascular foreign material	0	0	0	0	1
Lung ass.(lym.no.(non-protocol)# Ex	13	11	9	18	19
erythrophagocytosis	2	2	3	4	5
capsular inflammation	0	0	0	1	0
pigment deposits	1	0	0	1	0
hemosiderosis	9	8	7	13	13
parafollicular hyperplasia	0	0	0	1	0
follicular hyperplasia	0	0	0	0	1
hyperemia / congestion	1	1	1	0	0
blood resorbtion	0	0	1	0	0
intravascular foreign material	0	0	0	0	1
histiocytic nodule / granuloma	0	1	0	0	0
necrosis	0	0	1	0	0
Lymph node mesent.	# Ex 47	50	48	49	50
sinus histiocytosis	6	1	10	9	12
erythrothagocytosis	3	1	2	1	0
hemosiderosis	0	0	1	0	0
hyperemia / congestion	0	1	3	0	0

(Report Continued)

NDA 20,987
Page 458

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KRD143
DAYS : ALL

FATES: ALL
SEX: FEMALE

PAGE 64

GROUP: -- mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
Lymph node mesent.	# Ex 47	50	48	49	50
mastocytosis	2	0	0	5	1
plasmacytosis	1	0	0	0	0
lymphoid atrophy	0	0	0	0	2
capsular inflammation	0	0	0	0	1
follicular hyperplasia	0	0	0	0	1
histiocytic nodule / granuloma	29	19	23	24	21
parafollicular hyperplasia	1	0	0	0	4
lymphoid depletion	0	0	0	0	1
reactive hyperplasia	0	0	0	2	1
intravascular foreign material	0	0	0	0	1
necrosis	0	0	0	0	1
Lymph node submand.	# Ex 48	46	48	47	44
erythrophagocytosis	2	1	1	2	3
hyperemia / congestion	4	2	5	2	5
hemosiderosis	13	7	10	12	11
plasmacytosis	18	6	7	10	10
follicular hyperplasia	6	2	2	2	2
parafollicular hyperplasia	3	2	1	0	4
sinus histiocytosis	2	1	1	1	2
hemorrhage	0	0	0	0	2
black pigment deposits	7	6	5	7	4
necrosis	0	0	1	0	0
reactive hyperplasia	0	0	2	2	0
histiocytic nodule / granuloma	0	0	0	1	0
intravascular foreign material	0	0	0	0	1
Lymph nodes (non-protocol)	# Ex 2	2	1	1	1
erythrophagocytosis	0	0	1	0	0
Mammary gland	# Ex 50	48	46	49	47
inflammation	1	0	0	0	0
galactocele	4	1	0	2	1
dilated ducts	4	0	0	2	2
epithelial hyperplasia	2	1	0	1	1

(Report Continued)

NDA 20,987

Page 459

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143 FATES: ALL PAGE 65
DAYS : ALL SEX: FEMALE

GROUP: -- mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
nasal/paranasal cavities	# Ex 49	49	49	49	49
purulent inflammation	8	4	6	7	5
inhaled foreign material	2	4	5	3	1
non-purulent inflammation	3	0	0	0	0
mucus accumulation	1	1	0	0	2
hyperemia / congestion	1	2	2	1	3
goblet-cell hyperplasia	1	23	17	13	10
squamous metaplasia	0	0	0	0	1
respir. epithel degen.	0	1	5	3	3
thrombosis	2	0	1	1	1
hemorrhage	0	1	1	0	2
mycotic infection	0	0	0	0	1
oral cavity (and teeth)	# Ex 50	48	48	49	49
orolaryngeal & oesoph. impact.	13	21	22	22	23
orolaryngeal granulomas	23	18	22	19	21
purulent laryngitis	6	7	0	8	4
lympho-histiocytic infiltr.	29	22	25	21	20
mucosal erosion	3	1	1	1	0
mucosal ulceration	0	1	1	0	0
cystic secretory duct dilat.	27	16	15	13	16
laryngeal cartilage degenerat.	9	21	17	19	7
laryngeal submucosal edema	6	7	11	11	13
ranula	0	0	1	0	0
goblet cell hyper-/metaplasia	1	0	0	0	0
squamous cell metaplasia	0	1	0	1	0
squamous cell hyper-/dysplasia	0	1	0	0	0
other tissues	# Ex 0	0	0	0	0
ovaries	# Ex 47	50	50	50	50
atrophy of funct. parenchym	9	8	6	9	6
sex cord hyperplasia	0	2	2	0	2
follicular cyst	0	0	1	0	2
bursal cyst	7	9	4	9	5
parenchymal cell degeneration	1	2	0	0	0
hyperemia / congestion	9	11	17	12	16
lympho-histiocytic infiltr.	0	0	0	0	0

(Report Continued)

NDA 20,987
Page 460

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KRO143	FATES: ALL					PAGE 66
DAYS : ALL	SEX: FEMALE					
GROUP:	50 mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
ovaries	# Ex 47	# 50	# 50	# 50	# 50	
intravascular foreign material	0	0	0	0	1	
pigment deposits	7	6	1	7	7	
granulomatous inflammation	1	2	1	1	0	
pancreas	# Ex 47	# 48	# 50	# 49	# 49	
lympho-histiocytic infiltr.	5	4	3	5	8	
increased apoptosis	0	0	0	0	1	
acinar cell atrophy	0	0	0	1	0	
islet hemosiderosis	0	0	1	0	0	
islet cell hyperplasia	0	0	1	1	0	
hyperemia / congestion	0	2	1	0	1	
basophilic focus	0	1	0	0	1	
edema	1	1	0	0	0	
chronic atrophic pancreatitis	12	8	10	7	8	
ductal cell regeneration	9	10	10	9	9	
necrosis	1	0	0	0	1	
intravascular foreign material	0	0	0	0	1	
ductal cyst	0	1	0	0	0	
acinar cell hypertrophy	0	0	1	2	0	
subac. necrot. pancreatitis	0	0	0	0	1	
parathyroid 1	# Ex 43	# 42	# 39	# 42	# 43	
hyperplasia	2	1	2	2	0	
fibrosis	0	0	3	0	0	
leukocytostasis	0	0	0	0	1	
parathyroid 2	# Ex 33	# 30	# 28	# 29	# 29	
hyperplasia	1	1	1	0	0	
hypertrophy	0	1	0	0	0	
leukocytostasis	0	0	0	0	1	
pituitary	# Ex 44	# 43	# 43	# 46	# 41	
hemoglobin /cholesterol clefts	1	0	0	1	0	
cavern / cyst	6	2	2	6	1	
nemosiderosis	10	0	2	2	3	
hemorrhage	3	0	2	0	1	

(Report Continued)

NDA 20,987
Page 461

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143	FATES: ALL					PAGE 67
DAYS : ALL	SEX: FEMALE					
GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
pituitary	# Ex 44	# 43	# 43	# 46	# 41	
pars distalis hyperplasia	3	8	5	5	4	
pars distalis adenoma	0	0	0	1	0	
hyperemia / congestion	0	0	1	0	1	
leukocytostasis	0	0	0	0	1	
rectum	# Ex 48	50	50	50	50	
nematodes	1	0	0	0	0	
lymphocytic hyperplasia	1	0	0	0	0	
lymphoma / leukemia	0	0	0	1	0	
salivary gland, parot.	# Ex 48	50	49	48	50	
interstitial fibrosis	1	0	0	0	0	
lobular atrophy	2	0	0	0	0	
edema	0	0	0	0	1	
lympho-histiocytic infiltr.	2	1	0	0	0	
sialoadenitis	0	1	0	2	0	
acinar hyperplasia	0	1	0	1	0	
basophilic focus	1	0	1	0	0	
acinar cell degeneration	0	0	2	3	1	
nuclear polymorphism	0	0	0	1	1	
acinar cell hypertrophy	0	0	0	0	1	
salivary gland, submand.	# Ex 48	50	50	50	50	
edema	0	0	0	0	1	
lympho-histiocytic infiltr.	0	0	0	1	0	
hyperemia / congestion	0	0	1	0	0	
mucous acinar hyperplasia	0	1	0	0	2	
serous acinar hyperplasia	1	0	0	2	0	
basophilic focus	1	0	0	0	0	
skeletal muscle quadriceps	# Ex 50	50	50	50	50	
myodegeneration	0	0	0	1	0	
lympho-histiocytic infiltr.	1	0	0	0	0	

(Report Continued)

NDA 20,987
Page 462

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KRO143	FATES: ALL					PAGE 68
DAYS : ALL	SEX: FEMALE					
GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg	
NUMBER OF ANIMALS:	50	50	50	50	50	
skin	# Ex 50	# 50	# 48	# 48	# 49	
dermatitis	1	0	1	0	1	
dermal fibrosis/calcif.	0	0	0	0	1	
acanthosis	0	0	1	0	0	
ulcer	1	0	0	0	2	
abscess	2	0	0	0	0	
epithelial cell hyperplasia	0	0	1	0	0	
lympho-histiocytic infiltr.	0	0	0	0	1	
ostitis / osteomyelitis	1	0	0	0	0	
epithelial dysplasia	0	0	0	0	1	
epidermal cyst	0	0	1	0	0	
spleen	# Ex 49	# 50	# 50	# 50	# 50	
extramedullary hematopoiesis	24	19	17	23	14	
hemosiderosis	42	43	47	43	40	
chronic perisplenitis	0	2	3	2	0	
fibrosis	3	6	0	3	1	
hemorrhagic necrosis	1	1	0	1	1	
lymphoid atrophy	1	0	1	2	2	
follicular hyperplasia	0	0	0	0	2	
parafollicular hyperplasia	0	1	0	2	1	
hyperemia / congestion	9	17	26	25	27	
reactive hyperplasia	0	0	0	2	1	
granuloma	0	0	1	1	0	
serosal cyst	2	0	0	0	0	
intravascular foreign material	0	0	0	0	1	
tail	# Ex 0	# 0	# 0	# 0	# 0	
thorac.spinal cord, bone m.	# Ex 49	# 50	# 50	# 50	# 49	
red malacia	0	0	1	0	0	
hemorrhage	0	0	0	1	0	
bone marrow atrophy	0	1	0	0	1	
bone marrow depletion	0	0	0	0	1	
reactive hyperplasia	0	0	0	3	0	

(Report Continued)

NDA 20,987
Page 463

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143
DAYS: ALL

FATES: ALL
SEX: FEMALE

PAGE 69

GROUP: -- mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
thoracic cavity	# Ex 0	0	0	0	2
pleuritis	0	0	0	0	2
hemorrhage	0	0	0	0	1
foreign material	0	0	0	0	1
thymus	# Ex 45	48	45	46	49
involution	35	37	28	32	30
branchiogenic cyst	0	0	1	0	1
epithelial hyperplasia	5	1	0	4	2
hyperemia / congestion	11	24	27	19	26
agonal bleeding	4	10	13	12	11
edema	0	1	0	0	2
thyroid 1	# Ex 46	50	49	49	49
follicular cell activation	3	1	9	3	3
hyperemia / congestion	4	6	5	4	9
C-cell hyperplasia, diffuse	4	1	7	11	4
follicular cell hyperplasia	1	2	1	3	2
branchiogenic cyst	1	2	2	1	1
lympho-histiocytic infiltr.	0	0	0	1	0
leukocytostasis	0	0	0	0	1
parenchymal atrophy	0	0	1	0	0
C-cell hyperplasia	11	13	6	6	11
thyroid 2	# Ex 46	49	46	48	48
follicular cell activation	3	1	8	3	3
hyperemia / congestion	4	6	5	4	9
C-cell hyperplasia, diffuse	5	1	7	11	4
follicular cell hyperplasia	1	1	1	2	1
branchiogenic cyst	1	0	0	0	0
lympho-histiocytic infiltr.	0	0	0	1	0
leukocytostasis	0	0	0	0	1
C-cell hyperplasia	12	8	5	3	6
tibia	# Ex 50	50	50	50	49
hemorrhage	1	0	0	0	0
necrosis	0	0	0	0	1

(Report Continued)

NDA 20987
Page 464

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings.

PROJECT ID. NO: KR0143 FATES: ALL PAGE 70
DAYS : ALL SEX: FEMALE

GROUP: ++ mg/kg 0 mg/kg 5 mg/kg 15 mg/kg 50 mg/kg
NUMBER OF ANIMALS: 50 50 50 50 50

	#	#	#	#	#
	Ex	50	50	50	50
tibia	49	50	50	50	49
hemosiderosis	1	2	1	0	0
osteomyelofibrosis	0	0	1	0	0
granulomatous inflammation	2	8	11	9	3
bone marrow atrophy	0	1	0	0	2
bone marrow depletion	0	0	0	0	1
reactive hyperplasia	2	1	1	3	0
tongue	49	50	50	50	50
inflammation	1	0	0	0	0
peri- / vasculitis	2	1	3	1	0
hyperemia / congestion	0	0	1	0	0
vascular calcification	37	27	23	29	24
lympho-histiocytic infiltr.	1	1	2	1	0
squamous cell hyperplasia	1	0	0	0	0
leukocytostasis	0	0	0	0	1
trachea	49	50	50	50	50
intraluminal blood	0	1	0	0	0
lympho-histiocytic infiltr.	0	1	0	0	1
squamous metaplasia	0	1	0	0	0
ureter	0	0	0	0	0
urinary bladder	50	50	45	45	48
lympho-histiocytic infiltr.	3	1	0	2	2
edema	6	7	4	4	2
dilatation	0	0	1	0	0
residuals of sediment	0	0	1	0	0
leukocytostasis	0	0	0	0	1
uterus / ut.-cervix / vagina	49	50	50	50	50
hyperemia / congestion	4	2	8	2	5
mucosal cell degeneration	0	1	0	0	0
eosinophilic infiltration	1	0	0	0	1
lympho-histiocytic infiltr.	3	1	0	1	1

(Report Continued)

NDA 20,987
Page 465

B8610-023
220/94 Rat, Carcinogenicity study p.o.

Project Summary Table

SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: KR0143
DAYS : ALL

FATES: ALL
SEX: FEMALE

PAGE 71

GROUP:	-- mg/kg	0 mg/kg	5 mg/kg	15 mg/kg	50 mg/kg
NUMBER OF ANIMALS:	50	50	50	50	50

	#	#	#	#	#
uterus / ut.-cervix / vagina # Ex	49	50	50	50	50
luminal dilatation (muconetra)	12	6	11	12	9
endometrial hyperplasia	1	2	2	2	0
pyo- / hemometra	2	2	2	2	2
submucosal hemosiderosis	1	0	0	1	0
stromal fibrosis	3	1	0	0	1
cystic dilatation of glands	1	0	0	0	0
peri- / vasculitis	0	1	0	0	0
stromal hyperplasia	0	0	1	0	0
cervical squamous hyperplasia	4	5	6	5	3
mucoid epithelium (diestrus)	14	6	6	18	13
necrosis	0	0	0	0	1

(End of Report)

APPEARS THIS WAY
ON ORIGINAL