

1. For animal number 5100 (200 mg/kg/day, female), the original findings in fundus consisted of a malignant chief cell adenocarcinoma and multiple malignant neuroendocrine (NE) cell tumors. The sponsor's reanalysis has reclassified the chief cell adenocarcinoma as a NE-cell tumor with areas of chief-cell-like differentiation. What percentage of cells stained positively with Grimelius stain and chromogranin? What percentage of cells stained positively with neuron-specific enolase? Were these staining procedures performed with freshly cut sections or previously stained slides, as this animal was not mentioned in GTR-31279? Analysis of this tumor by an independent group of pathologists is needed to confirm the diagnosis. The following materials are required: (1) original slides from _____ (2) subsequent slides prepared by Wyeth-Ayerst/Byk Gulden, and (3) original paraffin block of stomach.

2. For animal number 4908 (50 mg/kg/day, male), reanalysis has confirmed an adenocarcinoma; although, the original report listed the location of the tumor in the pyloric region at the gastroduodenal junction, while reanalysis suggested that the tumor originated from Brunner's glands in the duodenum with infiltration below the pyloric mucosa. The validity of the reanalysis is questionable since the only neoplastic finding listed for the small intestine in the original report was a malignant histiocytic sarcoma in the small intestine. Analysis of the duodenum and this tumor in the pyloric region by an independent group of pathologists is needed to confirm the diagnoses. The following materials are required: (1) original paraffin blocks of duodenum and stomach (includes pyloric region), (2) original slides from _____, and (3) subsequent slides prepared by Wyeth-Ayerst/Byk Gulden.

3. For animal number 4870 (50 mg/kg/day, male), malignant neuroendocrine cell tumors in the stomach and lymph node(s) adjacent to the pancreas listed in the original report were reclassified as acinar-cell carcinomas of the pancreas after reanalysis. The original study report listed no abnormalities for the pancreas. Analysis of the pancreas and tumors in the stomach and lymph node(s) adjacent to pancreas by an independent group of pathologists is needed to confirm these diagnoses. The following materials are required: (1) original paraffin blocks of pancreas and stomach, (2) original slides from _____ and (3) subsequent slides prepared by Wyeth-Ayerst/Byk Gulden.

4. For animal number 5070 (200 mg/kg/day, female), a malignant neuroendocrine cell tumor in a lymph node near the pancreas and multiple, malignant neuroendocrine cell tumors in the fundus in the original report were reclassified as acinar-cell carcinomas of the pancreas following reanalysis. Use of special stains and immunohistochemistry with tumors in the lymph node near the pancreas and fundus were inconclusive for either tumor type. Analysis of the pancreas and these tumors in the stomach and lymph node adjacent to pancreas by an independent group of pathologists is needed to confirm these diagnoses. The following materials are required: (1) original paraffin blocks of pancreas and stomach, (2) original slides from _____ and (3) subsequent slides prepared by Wyeth-Ayerst/Byk Gulden.

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Appendix 2: Macroscopic and microscopic findings for selected Sprague Dawley rats of the two-year carcinogenicity study with pantoprazole.

Animal number 4718 (5 mg/kg/day, male)
Animal number 4870 (50 mg/kg/day, male)
Animal number 4883 (50 mg/kg/day, male)
Animal number 4908 (50 mg/kg/day, male)
Animal number 4997 (200 mg/kg/day, male)
Animal number 5001 (200 mg/kg/day, male)
Animal number 5055 (200 mg/kg/day, male)
Animal number 5070 (200 mg/kg/day, female)
Animal number 5100 (200 mg/kg/day, female)
Animal number 5108 (200 mg/kg/day, female)
Animal number 5122, (200 mg/kg/day, female)

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Appendix 10 (Cont'd)

STUDY NUMBER: C88024 (Study Completed)
DOSE GROUP/SEX: Group III - 96022-E MALES
ANIMAL NUMBER: MICROSCOPIC & MACROSCOPIC FINDINGS

4718 Mode of Death: Moribund Kill
Day of Death: 422 Days

Macroscopic Findings:

BRAIN : Ventral brainstem indented by enlarged pituitary

LIVER : Raised, pale mass (10 mm diameter), left lateral lobe

Lesion 1: Raised, pale areas (up to 3 mm diameter), multiple,
median lobe

PITUITARY : Enlarged (11 X 11 mm) and multinodular

Macroscopic Findings:

BRAIN : Ventral brainstem indented (by enlarged pituitary)

HEART : Cardiomyopathy, minimal

KIDNEY : Nephropathy, minimal

LIVER : METROENDOCRINE CELL TUMOR (M), site of origin not determined,
Lesion 1 and routine sections

LUNG : Alveolitis, neutrophilic, multifocal, moderate

MAMMARY GLAND : Missing

PITUITARY : ADENOMA (B), part distalis

PROSTATE : Prostatitis, mixed
Hyperplasia, epithelial, reactive

STOMACH : Hyperplasia, squamous cell, nonneoplastic, focal, mild
Eosinophilic glandular, fundus, moderate
Eosinophilic coated cells, minimal
Increased mucosal height, fundus, mild

(B)=BENIGN, (M)=MALIGNANT

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Appendix 16 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group III 35022-1 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4718 (CONTINUED)

Microscopic Findings:

TESTIS/EPIDIDYMSIS : Degeneration, tubular, testicular, unilateral, mild

THYMUS : Missing

NO ABNORMALITIES DETECTED IN:

ADRENAL, AORTA, BONE MARROW, COLON, DUODENUM, ESOPHAGUS, EYE, ILEUM, JEJUNUM, LYMPH NODE - MESENTERIC, PANCREAS, PARATHYROID, SEMINAL VESICLE, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN, THYROID, TRACHEA, URINARY BLADDER, LYMPH NODE - MANDIBULAR, SALIVARY GLAND - MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY GLAND - SUBLINGUAL, STOMACH

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Appendix 10 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group IV 98822-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4870 Mode of Death: Found Dead
Day of Death: 722 Days

Macroscopic Findings:

ABDOMINAL CAVITY : Lesion 3: Soft mass (15 X 13 X 4 mm), adjacent to seminal vesicles

HEART : Pale area, scirrus - observed at tissue trimming

KIDNEY : Both pale

LYMPH NODE(S) : Lesion 1: Firm, nodular mass (12 X 6 X 4 mm), adjacent to pancreas
Lesion 2: Firm, nodular mass (6 X 5 X 3 mm), adjacent to pancreas

STOMACH : Fundic mucosa appears thickened and folded

Microscopic Findings:

ABDOMINAL CAVITY : SCROTUM (M) - Lesion 3

ADRENAL : Cortical hyperplasia, bilateral, multifocal, with vacuolation

HEART : Cardiomyopathy, mild
Thrombosis, arterial

ILEUM : Autolysis

JELIUM : Autolysis

KIDNEY : Nephropathy, severe

LIVER : Eosinophilic cell focus, multiple, with spongiosis hepatic and angiectasis

LUNG : Alveolar histiocytosis, diffuse, mild

(B)=BENIGN, (M)=MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group IV 96022-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4870 (CONTINUED)

Microscopic Findings:

LUNG : Alveolitis, mixed, focal, moderate

LYMPH NODE - MESENTERIC : Erythrophagocytosis

LYMPH NODE(S) : NEUROENDOCRINE CELL TUMOR (N); metastatic site, lymph node, - Lesion 1
Hemorrhage, acute, with sinus ectasia, lymph node, - Lesion 2

PANCREAS : Missing

PITUITARY : Hyperplasia, multifocal, pars distalis
Cholesterol clasts, cleft of Rathke's pouch

STOMACH : Ectasia, glandular, fundus, minimal
Eosinophilic chief cells, moderate
Increased mucosal height, tubous, mild
NEUROENDOCRINE CELL TUMOR (N), fundus, metastasizing

TESTIS/EPIDIDYMIS : Polyarteritis nodosa, testicular, bilateral, mild

THYMUS : Missing

NO ABNORMALITIES DETECTED IN:

AORTA, BONE MARROW, BRAIN, COLON, DUODENUM, ESOPHAGUS, EYE, PANCREAS, PARATHYROID, PROSTATE, SEMINAL VESICLE, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN, THYROID, TRACHEA, URINARY BLADDER, LYMPH NODE - MANDIBULAR, SALIVARY GLAND - MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY GLAND - SUBLINGUAL, UTERUS

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(S)=SEEN, (I)=MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group IV 96022-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4083 Mode of Death: Found Dead
Day of Death: 735 Days

Macroscopic Findings:

LIVER : Lesion 1: Multinodular mass (6 X 6 X 4 cm) with red and
cream cut surfaces, median lobe
Lesion 2: Poorly circumscribed, tan area (4 X 2 X 2 cm),
substance of left lateral lobe

PANCREAS : Pale, raised area (10 mm diameter)

STOMACH : Pale, raised area (9 mm diameter), mucosa, nonglandular
stomach

Microscopic Findings:

ADRENAL : Cortical hyperplasia, unilateral, multifocal
haematopoiesis, extramedullary

HEART : Cardiomyopathy, mild

KIDNEY : Nephropathy, moderate

LIVER : NEUROENDOCRINE CELL TUMOR (N), site of origin not determined.
- Lesions 1 and 2
Necrosis, hepatocellular, centrilobular
Spongiosis hepatis, focal
Biliary hyperplasia, moderate
Hyperplasia, hepatocellular, regenerative, focal, left lateral
lobes

MAJORITY GLAND : Missing

PANCREAS : ACINAR CELL ADENOMA (B)
ISLET CELL ADENOMA (B)

VITUITARY : Cholesterol clefts, cleft of Rathke's pouch
(B)=BENIGN, (N)=MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: C89024 (Study Completed)
DOSE GROUP/SEX: Group IV 96023-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4883 (CONTINUED)

Microscopic Findings:

PROSTATE : Prostatitis, neutrophilic
Hyperplasia, epithelial, reactive

SEMINAL VESICLE : Vesiculitis, neutrophilic

SPLEEN : Hematopoiesis, extramedullary, moderate

STOMACH : SQUAMOUS CELL CARCINOMA (M)
Ectasia, glandular, foveas, moderate
Eosinophilic chief cells, moderate
Increased mucosal height, fundus, mild

TESTIS/EPIDIDYMI : Degeneration, tubular, testicular, unilateral,
moderate
Hyperplasia, interstitial cell, testicular, unilateral, focal

TESTES : Osteodystrophy, fibrous, mild

NO ABNORMALITIES DETECTED IN:

AORTA, BONE MARROW, BRAIN, COLON, DUODENUM, ESOPHAGUS, EYE,
ILEUM, JEJUNUM, LUNG, LYMPH NODE - MESENTERIC, PARATHYROID,
SKELETAL MUSCLE, SKIN, SPINAL CORD, THYMUS, THYROID, TRACHEA,
URINARY BLADDER, LYMPH NODE - MANDIBULAR, SALIVARY GLAND -
MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY GLAND - SUBLINGUAL

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(B)-BENIGN, (M)-MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: G89014 (Study Completed)
DOSE GROUP/SEX: Group IV 98022-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4908 Mode of Death: Moribund Kill
Day of Death: 678 Days

Macroscopic Findings:

LIVER : All lobes pale

PANCREAS : Serosa thickened, rough and yellow with adhesions to spleen

SKIN : Mass 1: Raised, ulcerated mass (2 X 2 X 1 cm), right dorsum

STOMACH : Fundic mucosa appears thickened

Microscopic Findings:

ADRENAL : Cortical hyperplasia, unilateral, focal

BRAIN : ASTROCYTOMA (M), forebrain

COLON : Missing

DUODENUM : HISTIOCYTIC SARCOMA (M)

KIDNEY : Nephropathy, minimal

LIVER : Hypertrophy, hepatocellular, centrilobular, moderate
Vacuolation, hepatocellular, multifocal, mild
HISTIOCYTIC SARCOMA (M)

LYMPH NODES - RESIDENTIAL : Erythrocytes in sinuses

PANCREAS GLAND : Missing

PANCREAS : HISTIOCYTIC SARCOMA (M)

PITUITARY : Cholesterol clefts, cleft of Rathke's pouch

PROSTATE : Prostatitis, neutrophilic

(B)-BENIGN, (M)-MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group IV 96022-5 MALES

ANIMAL NUMBER (MACROSCOPIC & MICROSCOPIC FINDINGS)

4908 (CONTINUED)

Microscopic Findings:

PROSTATE : Hyperplasia, epithelial, reactive

SKIN : KERATOCYSTITIS (S). - Mass 1

STOMACH : ADENOCARCINOMA (M), pyloric region, at gastroduodenal junction
HISTIOCYTIC SARCOMA (M)
Ectasia, glandular, fundus, moderate
Eosinophilic chief cells, moderate
Increased mucosal height, fundus, mild

TESTIS/EPIDIDYME : HISTIOCYTIC SARCOMA (M)
Degeneration, tubular, testicular, bilateral, mild

URINARY BLADDER : HISTIOCYTIC SARCOMA (M)
Cystitis, neutrophilic, moderate
Hyperplasia, epithelial, reactive, severe

NO ABNORMALITIES DETECTED IN:

ADRENAL, BONE MARROW, ESOPHAGUS, EYE, HEART, ILEUM, JEJUNUM, LUNG,
PARATHYROID, SEMINAL VESICLE, SKELETAL MUSCLE, SPINAL CORD,
SPLEEN, THYMUS, THYROID, TRACHEA, LYMPH NODE - MANDIBULAR,
SALIVARY GLAND - MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY
GLAND - SUBLINGUAL, TESTIS/EPIDIDYME

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(S) = SEVERE, (M) = MALIGNANT

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PLACES VS.204

Appendix 10 (Cont'd)

STUDY NUMBER: 088024 (Study Completed)
DOSE GROUP/SEX: Group V 96022-3 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

4997 Mode of Death: FOUND DEAD
Day of Death: 619 Days

Macroscopic Findings:

KIDNEY : Both enlarged with pitted surfaces
LIVER : All lobes enlarged and mottled
Lesion 1: White area (3 mm diameter), subcapsular, medial lobe
PITUITARY : Slightly enlarged (6 X 5 mm)
STOMACH : Fundic mucosa appears thickened
THYROID : Both lobes slightly enlarged
THORACIC CAVITY : Contains 5 ml clear fluid

Microscopic Findings:

ADRENAL : Cortical hyperplasia, bilateral, multifocal, with
vacuolation
Medullary hyperplasia, bilateral, focal
Accessory adrenocortical tissue, capsular, unilateral, focal
HEART : Cardiomyopathy, moderate
KIDNEY : Nephropathy, severe
LIVER : Necrosis, hepatocellular, centrilobular
Vacuolation, hepatocellular, multifocal, mild
Eosinophilic cell focus, large, multiple, with apoptosis
hepatitis
NEUROENDOCRINE CELL TUMOR (N), site of origin not determined.
Lesion 1 and routine sections
LUNG : Alveolar histiocytosis, diffuse, moderate
PANCREAS GLAND : Missing
(B)-BENIGN, (M)-MALIGNANT

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PLACES VS.204

Appendix 10 (Cont'd)

STUDY NUMBER: 089034 (Study Completed)
DOSE GROUP/SEX: Group V 96023-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

(997) (CONTINUED)

Microscopic Findings:

PITUITARY : ADENOMA (B), pars distalis

PROSTATE : Prostatitis, mixed
Hyperplasia, epithelial, reactive

STOMACH : Gastritis, eosinophilic, fundus, focal
Ectasia, glandular, fundus, moderate
Eosinophilic chief cells, moderate
Increased mucosal height, fundus, moderate

THYRUS : Atrophy

THYROID : Hypertrophy, follicular cell, mild

THORACIC CAVITY : No microscopic evidence of macroscopic finding

NO ABNORMALITIES DETECTED IN:
AORTA, BONE MARROW, BRAIN, COLON, DUODENUM, ESOPHAGUS, EYE,
ILEUM, JEJUNUM, LYMPH NODE - MESENTERIC, PANCREAS, PARATHYROID,
SEMINAL VESICLE, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN,
TESTIS/EPIDIDYMIS, TRACHEA, URINARY BLADDER, LYMPH NODE -
MANDIBULAR, SALIVARY GLAND - MANDIBULAR, SALIVARY GLAND -
PAROTID, SALIVARY GLAND - SUBLINGUAL, TESTES

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(B)-BENIGN. (M)-MALIGNANT

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PLACES VS.304

Appendix 10 (Cont'd)

STUDY NUMBER: 089024 (Study Completed)
DOSE GROUP/SEX: Group V 96022-8 MALES
ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

5001 Mode of Death: Found Dead
Day of Death 703 Days

Macroscopic Findings:

BRAIN : Ventral brainstem indented by enlarged pituitary
LIVER : All lobes enlarged and mottled
LYMPH NODES - MESAENTERIC : Mass 1: Firm, pale, multilobular mass (8 X 6 X 4 cm)
PITUITARY : Enlarged (7 X 5 mm)
STOMACH : Fundic mucosa appears thickened and folded
Pale, raised nodule (3 mm diameter), mucosa, fundus
THORACIC CAVITY : Contains 7 ml red fluid

Microscopic Findings:

BRAIN : Ventral brainstem indented (by enlarged pituitary)
HEART : Cardiomyopathy, mild
KIDNEY : Nephropathy, severe
LIVER : Necrosis, hepatocellular, centrilobular
Eosinophilic cell focus, with spongiosis hepatis
LUNG : Alveolar histiocytosis, diffuse, mild
LYMPH NODE - MESAENTERIC - SCIRRHOMA (M), - Mass 1
THYROID GLAND : Missing
PANCREAS : Atrophic, lobular
Islet cell hyperplasia, multifocal
(B)-BENIGN, (M)-MALIGNANT

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PLACES V8.204

Appendix 10 (cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group V --- 96022-2 MALES
ANIMAL NUMBER: MICROSCOPIC & MICROSCOPIC FINDINGS
5001 (CONTINUED)

Microscopic Findings:

PARATHYROID : One missing

PITUITARY : ADENOMA (B), pars distalis

PROSTATE : Prostatitis, neutrophilic
Hyperplasia, epithelial, reactive

STOMACH : ADENOMATOUS POLYP (B), fundus
SQUAMOUS CELL PAPILLOMA (B)
Ectasia, glandular, fundus, moderate
Eosinophilic chief cells, moderate
Increased mucosal height, fundus, mild

TESTIS/EPIDIDYMIS : Polyarteritis nodosa, testicular, bilateral, mild
Degeneration, tubular, testicular, bilateral, mild

THYROID : Hypertrophy, follicular cell, mild

THORACIC CAVITY : No microscopic evidence of macroscopic finding

NO ABNORMALITIES DETECTED IN:
ADRENAL, AORTA, BONE MARROW, COLON, DUODENUM, ESOPHAGUS, EYE,
ILEUM, JEJUNUM, PARATHYROID, PERINEAL VESICLE, SKELETAL MUSCLE,
SKIN, SPINAL CORD, SPLEEN, THYMUS, TRACHEA, URINARY BLADDER,
UTERUS BOWEL - MANDIBULAR, SALIVARY GLAND - MANDIBULAR, SALIVARY
GLAND - PAROTID, SALIVARY GLAND - SUBLINGUAL, STOMACH

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(B) = BENIGN, (IN) = INCIDENTAL

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Appendix 10 (Cont'd)

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PLACES 48,204

STUDY NUMBER: G99024 (Study Completed)
DOSE GROUP/SEX: Group V --- 96032-2 MALE

ANGL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

5055 Mode of Death: Found Dead
Day of Death: 470 Days

Macroscopic Findings:

LIVER : All lobes pale
SKIN : Mass 1: Soft, raised mass with green caseous cut surfaces
(1.5 cm diameter), dorsal tail
STOMACH : Fundic mucosa appears thickened and folded
Lesion 2: Raised, dark area (10 mm diameter), mucosa, fundus

Microscopic Findings:

ADRENAL : Cortical hyperplasia, unilateral, focal
Medullary hyperplasia, bilateral, focal
HEART : Cardiomyopathy, mild
ILEUM : Autolysis
KIDNEY : Nephropathy, minimal
LIVER : Necrosis, hepatocellular, centrilobular
LUNG : Thrombosis, arterial
PANCREAS : Atrophy, lobular
PARATHYROID : One missing
PITUITARY : Hyperplasia, multifocal, pars distalis
Cyst, NOS, pars intermedia, Multiple
SKIN : Epidermal cyst, abscessated, - Mass 1
STOMACH : ADENOMATOUS POLYP (B), fundus, - Lesion 2
Dilation, glandular, fundus
IM-BENIGN. (M)-NEG/IGENT

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PLACES V8.204

Appendix 10 (Cont'd)

STUDY NUMBER: 089024 (Study Completed)
DOSE GROUP/SEX: Group V 96022-2 MALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

5055 (CONTINUED)

Microscopic Findings:

STOMACH : Ectasia, glandular, fundus, minimal
Eosinophilic chief cells, submucosa
Increased mucosal height, fundus, mild

THYROID : FOLLICULAR CELL ADENOMA (B)

NO ABNORMALITIES DETECTED IN:
AORTA, BONE MARROW, BRAIN, COLON, DUODENUM, EUPHRASUS, EYE,
JEJUNUM, LYMPH NODE - MESENTERIC, MAMMARY GLAND, PARATYROID,
PROSTATE, SEMINAL VESICLE, SKELETAL MUSCLE, SPINAL CORD, SPLEEN,
TESTIS/EPIDIDYMUS, THYROID, TRACHEA, URINARY BLADDER, LYMPH NODE
- MANDIBULAR, SALIVARY GLAND - MANDIBULAR,
SALIVARY GLAND - PAROTID, SALIVARY GLAND - SUBLINGUAL, STERNUM

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(B)=BENIGN, (M)=MALIGNANT

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Appendix 10 (Cont'd)

STUDY NUMBER: G89024 (Study Completed)
DOSE GROUP/SEX: Group V 96022-2 FEMALES
ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

8070 Mode of Death: Terminal Kill
Day of Death: 735 Days

Macroscopic Findings:

BRAIN : Ventral brainstem indented by enlarged pituitary
LIVER : Dark, raised area (2.5 X 2 X 1.5 cm), left lateral lobe
Lesion 1: Median lobe enlarged (3 X 3 X 2 cm) and nodular
Pale nodule (3 mm diameter), right lateral lobe
PANCREAS : Firm nodule (4 mm diameter)
PARATHYROID : Not found at microscopy
PITUITARY : Enlarged (9 X 6 mm)
STOMACH : Fundic mucosa appears thickened
Pink, raised area (2.3 X 6 mm), mucosa, fundus
Multiple raised areas (up to 10 mm diameter), mucosa,
nonplandular stomach

Microscopic Findings:

ADRENAL : Angiectasis, cortical, bilateral, multifocal
Cortical hyperplasia, unilateral, focal
BRAIN : Ventral brainstem indented (by enlarged pituitary)
KIDNEY : Nephropathy, minimal
LIVER : Eosinophilic cell focus, multiple, with spongiosis hepatis
HEPATOCELLULAR ADENOMA (B), left lateral lobe
HEPATOCELLULAR ADENOMA (B), - Lesion 1
LUNG : Alveolar macrocytosis, focal, minimal
PANCREAS : NEUROENDOCRINE CELL TUMOR (M), metastatic site, lymph node
(B)=BENIGN, (M)=MALIGNANT

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- C1534 -

PAGE 4216
DATE 15-DEC-92
TIME 17:53:13
PLACES 08.304

Appendix 10 (Cont'd)

STUDY NUMBER: C89034 (Study Completed)
DOSE GROUP/SEX: Group V 6025-2 FEMALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

5070 (CONTINUED)

Microscopic Findings:

PANCREAS: MISSING

PITUITARY: ADENOMA (B), pars distalis

STOMACH: Ectasia, glandular, fundus, moderate
Eosinophilic chief cells, moderate
Increased mucosal height, fundus, mild
NEUROENDOCRINE CELL TUMOR (M), fundus, multiple, metastasizing,
with submucosal and vascular invasion
SQUAMOUS CELL CARCINOMA (M)

TESTES: Proliferative epithelial cords

THYROID: C-CELL ADENOMA (B)

NO ABNORMALITIES DETECTED IN:

ADRENAL, BONE MARROW, COLON, DUODENUM, ESOPHAGUS, EYE, HEART,
LIVER, SUTURUM, LYMPH NODE - MESENTERIC, PANCREAS, SPLEEN, UTERUS,
VAGINA, VULVA, SKIN, SPINAL CORD, TRACHEA, URINARY
BLADDER, UTERUS, LYMPH NODE - MANDIBULAR, SALIVARY GLAND -
MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY GLAND -
SUBLINGUAL, STERNUM

CS/SL
16 Dec. 1992

(B)=BENIGN, (M)=MALIGNANT

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PLACES VS.204

Appendix 10 (Cont'd)

STUDY NUMBER: C89024 (Study Completed)
TREATMENT GROUP/SEX: Group V - 81022-E FEMALES
ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

8100 Mode of Death: Found Dead
Day of Death: 837 Days

Macroscopic Findings:

LIVER : All lobes enlarged and pale
MAMMARY GLAND : Mass 1: Soft, nodular mass (6 X 4 X 2 cm), subcutis, left inguinal area
STOMACH : Fungic mucosa appears thickened and folded
Firm, raised area (6 mm diameter), mucosa, fundus

Microscopic Findings:

ADRENAL : Cortical hyperplasia, unilateral, focal
DUODENUM : Autolysis
HEART : Cardiomyopathy, mild
KIDNEY : Nephropathy, mild
LIVER : Necrosis, hepatocellular, centrilobular
Vasculitis, hepatocellular, centrilobular, mild
Eosinophilic cell focus
MAMMARY GLAND : FIBROADENOMA (B), - Mass 1
OVARY : Hyperplasia, lutealiform, minimal
PITUITARY : ADENOMA (B), pars distalis
STOMACH : ADENOCARCINOMA (M), chief cell, fundus, with vascular invasion
NEUROENDOCRINE CELL TUMOR (M), fundus, multiple, with mucosal and vascular invasion
THYROID : Missing
(B)=BENIGN, (M)=MALIGNANT

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PLANNER V8.204

Appendix 10 (Cont'd)

STUDY NUMBER: 089024 (Study Completed)
DOSE GROUP/SEX: Group V 96022-2 FEMALES
ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS
S100 (CONTINUED)

Microscopic Findings:

NO ABNORMALITIES DETECTED IN:
AORTA, BONE MARROW, BRAIN, COLON, ESOPHAGUS, EYE, ILEUM, JEJUNUM,
LUNG, LYMPH NODE - MESENTERIC, PANCREAS, PARATHYROID, SKELETAL
MUSCLE, SKIN, SPINAL CORD, SPLEEN, THYROID, TRACHEA, URINARY
BLADDER, UTERUS, LYMPH NODE - MANDIBULAR, SALIVARY GLAND -
MANDIBULAR, SALIVARY GLAND - PAROTID, SALIVARY GLAND -
SUBLINGUAL, TESTIS/ERRA

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PLACER V8.204

Appendix 10 (Cont'd)

STUDY NUMBER: C89024 (Study Completed)
DOSE GROUP/SEX: Group V — 86022-3 FEMALES

ANIMAL NUMBER: MACROSCOPIC & MICROSCOPIC FINDINGS

S100 Mode of Death: Found Dead
Day of Death: 723 Days

Macroscopic Findings:

LIVER : All lobes mottled
Pale focus (2 mm diameter), left lateral lobe
Pale, spherical mass (2 cm diameter), hilus of right lateral lobe
Lesion 3: Pale nodule (9 X 8 mm), substance of accessory caudate lobe
Lesion 4: Multiple pale foci (up to 5 mm diameter), median lobe

MAMMARY GLAND : Mass 2: Firm, multinodular mass (3 X 3 X 2 cm), subcutis, right inguinal area

PANCREAS : Enlarged (6 X 4 X 3 cm), pale and multinodular

PITUITARY : Red, raised focus (2 mm diameter)

STOMACH : Fundic mucosa appears thickened and folded

THYROID : Right lobe enlarged (10 X 6 mm)

THORACIC CAVITY : Contains 2 ml red fluid

Microscopic Findings:

ADRENAL : Adiectasis, cortical, bilateral, multifocal, with thrombosis
Cortical hyperplasia, bilateral, multifocal, with cystic degeneration

DUODENUM : NEUROENDOCRINE CELL TUMOR (N), metastatic site

ETE : Autolysis

HEART : Cardiomyopathy, moderate
Thrombosis, atrial

(B)-BENIGN, (N)-MALIGNANT

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