Report:CLPXPR55 CLINICAL PATHOLOGY - HEMATOLOGY ALPHA RESULTS Run date:07/
Study (Ref) no.:B85-0460 Run time: 0
Period: 1 File no.:85

Grp d.	Animal Id.	Sex	Rbc/Plt Normal	Rbc Normal	Atypical Lymph	Lymph Reactive	Rouleaux	See separate repr
0003	2801	F					3+	
	2806						3+	
	2825						2+	
	2609	M					1+	
	2619						1+	
	2634						1+	
	2647						1+	

CLINICAL PATHOLOGY APPENDIX III

Report CLPXPRSS CLINICAL PATHOLOGY - HEMATOLOGY ALPHA RESULTS Run date:07
Study (Ref) no.:B85-0460 Run time: 0
Period: 1 File no.:85

Grp Id.	Animal Id.	Sex	Plasma Cells	HowellJolly Bodies	Monos,Vacuolated	Rbc agglutination	Toxic granulation	Target cells
0001	2770	F						RARE
	2787							OCC
	*2791							RARE
	2653	M						OCC
	2654							OCC
0002	2826	F						RARE
	2648	M						OCC
	2685							OCC
	2689							OCC
0003	*2725	F						FEW
	2738							OCC
	2754							OCC
	2768							RARE
	2771							OCC
	*2784							RARE
	*2813							RARE
	*2829							RARE
	2604	M						MOD
	2619							RARE
	2634							FEW
	2647							OCC
	2649							OCC
	2655							OCC
	2679							OCC
	2715							OCC
0004	2745	F		NOTED				
	2756			NOTED				
	2758			NOTED				TARGET
	2792							NOTED
	*2793							NOTED
	2811							NOTED
	2820			NOTED				NOTED
	2824			1+				NOTED
	2843			NOTED				NOTED

CCAL PATHOLOGY APPENDIX III

* These all are pregnant females

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

PROCTER & GAMBLE PATHOLOGY NUMBER B85-0460
(BYCR 0428)

TWO GENERATION REPRODUCTION AND TERATOLOGY

REVISED PATHOLOGY SUMMARY

EPL PROJECT NUMBER 101-141

Submitted to:

The Procter & Gamble Company
Cincinnati, Ohio

Submitted by:

Experimental Pathology Laboratories, Inc.
Ross, Ohio

JIM E. PROCTOR, D.V.M., Ph.D.
Veterinary Pathologist

May 7, 1976

SCIENTIFIC MERIT REVIEW
PATHOLOGIST
5 | 5/87

THE PROCTER & GAMBLE COMPANY

MIAMI VALLEY LABORATORIES

P. O. BOX 39175
CINCINNATI, OHIO 45

The following study was reviewed by the Quality Assurance Unit:

LABORATORY: Experimental Pathology Laboratories, Inc.
P. O. Box 487
Ross, OH 45061

STUDY NUMBER: B85-0460

EPL PROJECT NUMBER: 101-141

DIVISIONAL REQUEST DOCUMENT: BYCR 0428

TYPE OF STUDY: Two-Generation Reproduction and Teratology

PORTION OF STUDY REVIEWED:	REVIEWED BY:	REVIEW:	DATE FINDINGS REPORTED TO STUDY DIRECTOR AND PATHOLOGIST:
Precheck and Staining	M.P. Bauer	9/4/86	9/4/86

Significant audit findings (if any) were reported to the Study Director, the Pathologist and Facility Management immediately. All audit findings are reported to Management on a periodic basis.

The final Pathology report was reviewed for inaccuracies and procedural compliance. The results reflect the raw data of the study.

11/12/86
Quality Assurance Unit - Date

QAUfrm
4/85

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

PROCTER AND GAMBLE STUDY NUMBER B85-0460 (BYCR 0428)

TWO GENERATION REPRODUCTION AND TERATOLOGY

REVISED PATHOLOGY SUMMARY

CONCLUSIONS

The purpose of this study was to assess the reproductive and developmental toxicity of the test material administered continuously in the diet. One hundred males and one hundred females were divided into four equal groups and given G0539.02 in the diet at 0 (Group 1), 50 (Group 2), 100 (Group 3), or 300 (Group 4) mg/kg/day. Females were sacrificed on day 20 of gestation, and males were sacrificed at a scheduled sacrifice. Group 4 animals were sacrificed early due to the high death rate. At necropsy a full set of tissues was collected in neutral buffered formalin, and the necropsy weights were recorded for body, heart, liver, spleen, kidneys, testes, and ovaries. Hematoxylin an eosin stained histologic sections were prepared from formalin-fixed tissues, and an extra section of bone marrow was also stained for iron (Perls' stain).

No treatment-related gross or microscopic findings were present in Group 2 males and females when compared with controls. Microscopic changes were not present in the spleen of Group 2 males or in the liver o Group 2 females, but relative spleen weights of Group 2 males and relativ liver weights of Group 2 females were decreased.

Treatment-related findings were observed macroscopically and microscopically in Group 3 and Group 4 males and females. Twenty-three

males and twelve females in Group 4 died during the study, and pale tissues were noted in Group 4 animals indicating they were anemic. Heart enlargement was also seen in several animals. Splenic enlargement was seen in a few Group 4 animals. Tan feces caused by a decrease in urobilinoid pigments were also observed in several animals. Dystocia was diagnosed in the one Group 3 female which died.

Statistical analyses were not conducted on Group 4 organ and body weights because of the high death rate and the rescheduled early group terminal sacrifice. Group 4 average body weights were less than expected for rats of this age, and this decrease affected absolute and relative organ weights. Absolute and relative heart weights for Group 3 males were significantly increased ($P<.05$) when compared with controls, and linear regression suggested a dose-related trend. A similar increase for relative heart weights ($P<.05$) was evident for Group 3 females. Absolute ($P<.05$) and relative ($P<.01$) spleen and absolute ($P<.01$) and relative ($P<.001$) liver weights were decreased for Group 3 females. Biologically significant differences were not noted in other organ weights.

Treatment-related microscopic findings consisted of bone marrow hypercellularity, decreased hemosiderin in the spleen, hypercellular splenic red pulp, and inflammation of the stomach and intestinal tract of Group 3 and Group 4 animals. Histopathologically, changes were more severe in Group 4 than in Group 3. Immature erythropoietic cells produced the bone marrow hypercellularity. Insufficient iron was present in the marrow of controls for evaluation with Perls' stain. However, the amount of hemosiderin (iron-containing pigment) in the spleen was decreased in

Group 3 and Group 4 animals when compared with controls. Red pulp hypercellularity in the spleen was probably due to erythropoiesis, but the absence of metarubricytes in the areas of cellularity made this conclusion difficult to make. The amount of identifiable splenic erythropoiesis in control and treated animals was similar.

INTRODUCTION

Macroscopic examinations of tissues and organ and body weights were recorded for male and female Sprague-Dawley CD rats at necropsy. Hematoxylin and eosin stained tissues were examined microscopically. The purpose of this study was to assess the reproductive and developmental toxicity of the test substance administered continuously in the diet to two generations of rats.

MATERIALS AND METHODS

The rats evaluated for this study are outlined below under Animal Group Assignment.

Experimental Model

Type of Study:	Two Generation Reproduction and Teratology Study
Species:	Rats
Strain (Source):	Sprague-Dawley CD (Charles River)
Sex:	Males and females
Initial Age Range:	21-23 days when received and 28-30 days at study initiation
Test Substance:	G0539.02
Vehicle Control Substance:	Purina Laboratory Chow #5002
Route of Exposure:	Diet
Doses:	0, 50, 100, 300 mg/kg/day
Time of Sacrifice:	Day 20 of gestation for females

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Animal Group Assignment

Group	Males/Females	Treatment	Dose (mg/kg/day)
1	25/25	G0539.02	0
2	25/25	G0539.02	50
3	25/25	G0539.02	100
4	*25/25*	G0539.02	300

*One male was not necropsied, and tissues from one female were autolytic and not collected for histopathology.

Rats were anesthetized with ether, and blood was collected for hematology and clinical chemistry. Rats were sacrificed by exsanguination, and at necropsy each animal, heart, liver, spleen, kidneys, testes, and ovaries were weighed. After macroscopic examination and according to the protocol, the following tissues were preserved in 10% neutral buffered formalin by Experimental Pathology Laboratories, Inc.: lungs, heart, thoracic aorta, tongue, kidneys, trachea, esophagus, thyroid/parathyroid, submandibular lymph node, ileocecal lymph node, submandibular salivary gland, liver, duodenum, jejunum, ileum, cecum, colon, rectum, urinary bladder, testes (male), epididymides (male), prostate (male), seminal vesicles (male), ovaries (female), uterus (female), vagina (female), adrenals, thymus, psoas muscle, spleen, pancreas, bone/marrow (femur), skin/mammary gland, brain, thoracolumbar spinal cord, sciatic nerve, pituitary gland, eyes, stomach (forestomach, fundus, and pylorus), and any gross lesions. Two bone marrow smears were prepared from the femur of each animal at the terminal sacrifice.

Hematoxylin and eosin stained slides of portions of the above formalin-fixed tissues were prepared by Experimental Pathology

Laboratories, Inc., from all males and females in Groups 1-4. Sections were prepared from the left organ of paired organs. A section of bone marrow was also stained for iron with Perls' stain. Sections were evaluated microscopically. After the initial microscopic evaluation, sections of bone marrow and spleen were re-evaluated as target organs.

Weights of whole body, heart, liver, spleen, kidneys, testes, and ovaries were recorded at the scheduled terminal necropsy. These variables and organ/body weight ratios were statistically analyzed for males and pregnant females in Groups 1, 2, and 3 by R. D. Bruce and P. J. Sprong of Statistical Resources using P&G computer program B8944. Data from Group 4 were not analyzed due to the large number of deaths and the early rescheduled terminal sacrifice. Data were analyzed by analysis of variance. Provided the Bartlett's test for homogeneity of variance was not significant, treated groups were compared to the control group by the least significant difference test. If Bartlett's test was significant, the comparison was made by Wilcoxon's rank sum test. Non-parametric data was analyzed by Chi-square techniques. All statistical tests were conducted at a 5%, two-sided risk level. Results of these analyses were reviewed by J. E. Proctor of Experimental Pathology Laboratories, Inc.

RESULTS

Macroscopic Findings

Macroscopic lesions observed at necropsy are summarized in the Gross Pathology Incidence Summary Tables. Gross lesions for

individual animals are presented in the Correlation of Gross and Microscopic Findings Tables.

Group 1: Controls (0 mg/kg/day)

Terminal Sacrifice

Only a few incidental observations were made in controls at necropsy, and all animals in Group 1 were necropsied at the terminal sacrifice. The right submandibular lymph node of one male was slightly small. The right submandibular lymph node of one male and the left submandibular lymph node of one female were enlarged. Bilateral submandibular lymph node enlargement was observed in two males. Mucoid content was present in the jejunum and ileum of one male. Bilateral pelvic dilatation was noted in the kidneys of one male. The spleen was slightly enlarged with two 5 mm white nodules in one female. Bone marrow in the femur of one male was pale. Testes of one male were moderately small, and an erosion was seen on the left ear of one male.

Group 2: G0539.02, 50 mg/kg/day

Terminal Sacrifice

Treatment-related gross lesions were not evident in Group 2 males and females, and all animals were necropsied at the terminal sacrifice. Submandibular lymph nodes were bilaterally enlarged in two males and unilaterally enlarged in another two males. The right pelvis of one female kidney was enlarged, and a small cyst was present on the pancreas of one male. Crusty material was present around the eyes of

two males, and the testes were small in four males. The left seminal vesicle was small in one male. An erosion was observed above the left eye of one male, and the lower incisors were long in one female.

Group 3: G0539.02, 100 mg/kg/day

Moribund/Deaths

One female in Group 3 was found dead on study day 121. The stomach of this female was filled with nesting material, and multiple hemorrhages were noted in the mucosa of the stomach. Dark fluid was noted in the small intestine, and feces in the rectum were tan. A fetus which blocked one horn was present in the uterus, and a bloody discharge was present in the vagina. A necropsy diagnosis of dystocia was made.

Terminal Sacrifice

Twenty-five males and twenty-four females were necropsied at the terminal sacrifice. Pale tissues were noted in several animals, were considered to be treatment-related observations, and were a result of anemia. The liver of two males and one female was pale, and the bone marrow of one male was pale. Eyes of nine males were pale. Other findings observed at necropsy were considered incidental and are listed below: the submandibular lymph nodes of two males were enlarged; mucoid content was noted in the duodenum, jejunum, ileum, cecum, and colon of one male, in the jejunum and ileum of one female, and in the duodenum and jejunum of one female; unilateral pelvic dilatation was observed in the

kidneys of two males; slight splenic enlargement was present in one male, and cysts were noted on the spleen of another male; a 2 mm pale area was present on the right ovary of one female; dark thick content was present in the vagina of one female; a 5 mm nodule was present in the mesentery by or on the uterus of one female; and the lower teeth of one male were enlarged.

Group 4: G0539.02, 300 mg/kg/day

Moribund/Deaths

Twenty-three males and twelve females died and were necropsied during the study. One male died on each of the following study days: 35, 42, 64, 67, 68, 76, 77, 82, 84, 89, 90, 98, 105, and 117. Two males died on days 46, 93, and 97; and three males died on day 75. One female died on each of the following study days: 35, 84, 90, 101, 102, and 118. Two females died on days 106, 114, and 116. Autolysis was noted in several animals at necropsy.

Gross lesions considered to be treatment-related were enlarged heart, pale organs, tan feces, and edema in several locations; these changes were secondary to anemia which was the cause of death. Hearts were enlarged in nine males and ten females, and lesions were noted on the atria of two male and one female hearts. The eyes were pale orange or pale in 23 males and 11 females. An occasional tissue (liver in four males and three females) was noted as pale at necropsy. Feces were tan or pale, probably due to the absence of the breakdown products of hemoglobin, in the rectum of 22 males and 8 females (the

intestinal content in one of these animals was also tan). Soft feces, loose stool, or diarrhea was observed in the rectum of three males and one female; and fluid, diarrhea, or gas was noted in the intestines of eight males and four females. Gas was noted in the cecum of one male and one female and dark red material was noted in the cecum of one male. No formed stool was seen in the colon of one female. Fluid (edema) was observed in the pericardial sac of one male, the thoracic cavity of two males and one female, the peritoneal cavity of one male, the legs of two males, the head of one male (swollen), the neck of two males (one swollen and one fluid), and the eye of one male. Tail lesions were noted in three males and were probably due to anemia which produces poor oxygenation of tissue.

Scattered observations were noted in other tissues, but these observations were not directly related to treatment and included the following: hemorrhage, red areas, or reddish coloration in three male and one female lungs; slightly enlarged lungs in one male; yellowish material in the trachea and esophagus of one male; hemorrhage in the submandibular lymph nodes of five males; enlarged submandibular lymph nodes in one male; enlarged stomach which was distended with ingesta or gas and fluid in four males and one female; red foci or hemorrhage in the stomach of two males and one female; mucosal lacerations in the stomach of one female; hemorrhage in the liver of one female; grainy liver in one female; enlarged ileocecal lymph nodes in two males and one female; hemorrhagic (red) ileocecal lymph nodes in two males and one female; enlarged spleen in one female; yellowish areas in the spleen of one

female; yellowish skin in one male; enlarged, distended, and reddened urinary bladder in one male; reddish fluid in the urinary bladder of one male; fetuses in the uterus of one female; hemorrhage in the thymus of one female; dark red testes which contained red foci in one male; reddish testes in one male; crusted testes in one male; reddish material around the anus of one female; crusting around the nares or mouth of two males and three females and around the thorax of one male; and orange discoloration around the neck of one male.

Terminal Sacrifice

One male and thirteen females were necropsied at the terminal sacrifice. The heart was enlarged, and all tissues were pale in the one male and thirteen females necropsied. These changes were due to anemia. Slightly enlarged spleens were present in one male and twelve females. A few incidental lesions were also noted and included the following: a 3 mm red area in the median lobe of the liver of one female, nodular implantation sites in the uterus of one female, a pale nodule in the mesentery of two females, and a 3 mm pale area in the liver of one male.

Organ and Body Weights

The summary of group average body and relative and absolute organ weights and statistical analyses are presented in the Organ and Body

Weight Table 1. Organ and body weights for individual animals are presented in the Organ and Body Weight Appendix I.

Since animals in Group 4 died or were sacrificed prior to the scheduled terminal sacrifice for the other groups, statistical analyses were not conducted on Group 4 organ and body weights. Organ and body weights for nonpregnant females were not included in the statistical analyses but are summarized in the Organ and Body Weight Table 1 on page XV-3.

No significant differences were noted when male and female final necropsy body weights, male absolute and relative liver weights, male and female absolute and relative kidney weights, male absolute spleen weights, absolute and relative testicular weights, and absolute and relative ovarian weights of Groups 2 and 3 were compared with Group 1 males and pregnant females respectively. Significant differences were also not detected when female absolute heart weights were compared statistically.

The absolute and relative heart weights of Group 3 males were significantly greater ($P<.05$) than controls, and linear regression analyses ($P<.05$) suggested a dose-response was detected. Absolute heart weights of Group 3 females were slightly more than Group 1, but this was not a statistically significant difference. However, the relative heart weights of Group 3 females were significantly increased ($P<.05$) by the distribution-free method. Relative spleen weights of Group 2 males were significantly decreased ($P<.05$) when compared with controls. The spleen weights of Group 3 males were more than Group 1. The absolute ($P<.05$) and

relative (P<.01) spleen weights of Group 3 females were decreased, and linear regression analyses suggested a dose-related trend for decreased relative (P<.05) and absolute (P<.05) spleen weights in females. Absolute (P<.01) and relative (P<.001) liver weights for Group 3 females and relative liver weights (P<.001) for Group 2 females were decreased. Linear regression of female absolute (P<.01) and relative (P<.001) liver weights suggested a dose-related trend for decreased relative liver weights.

One male and one pregnant female were necropsied at the terminal early sacrifice for Group 4 animals. Organ and body weights for these two animals are presented in the Organ and Body Weight Table 1. No control data were available for comparison with these data, but the relative heart weights were increased for animals of this age and strain. It was not possible to evaluate other parameters with groups containing one animal.

Group average organ and body weights for nonpregnant females are presented in the Organ and Body Weight Table 1, but these data were not analyzed statistically. Group 4 females were sacrificed earlier than Group 1, Group 2, and Group 3 animals, and the final body weights were less than expected for rats of this age and strain. The decrease in final body weight affected absolute and relative organ weight parameters and made evaluation difficult; however, absolute and relative heart and spleen weights appeared to be increased in Group 4 nonpregnant females when compared with the two nonpregnant Group 1 females. In Group 3 nonpregnant females, the final body weight was also slightly less than controls.

Trends for changes were not noted in organ weights of Group 2 and Group 3 nonpregnant females when compared with controls.

Microscopic Findings

Microscopic changes and a detailed listing of all tissues evaluated are presented in the Individual Animal Cross Reference Tables. All lesions are summarized by treatment group and are presented in the Histopathology Incidence Summary Tables. A correlation of lesions observed at necropsy with the corresponding microscopic observation, where possible, is presented in the Correlation of Gross and Microscopic Findings Tables.

Inflammatory, degenerative, regenerative, or hyperplastic changes were graded on a scale of one to five depending upon severity. Nongradable changes, such as cyst, were designated as present (+) in the Individual Animal Cross Reference Tables. The number of animals for which a tissue was evaluated and the number of missing tissues are summarized in the Histopathology Incidence Summary Tables. The number of missing tissues was small and did not affect the final evaluation of the data or the integrity of the study. However, a few tissues were missing from the animals which died during the study, but these do not affect the target organ evaluation or study conclusions.

Group 1: Controls (0 mg/kg/day)

Terminal Sacrifice

Tissues were collected from all Group 1 animals at the terminal sacrifice. Incidental microscopic findings occasionally present in rats of this age and strain were seen in a few animals. A small cyst lined by ciliated cells was noted in the pituitary of one male and one female. A small focus of hyperplasia was noted in the pituitary of two males. An occasional small collection of mononuclear cells (myositis) was observed in the heart of six males and two females. The cause of the focal necrosis in one female spleen could not be determined. Acinar atrophy with a focal distribution was noted in the pancreas of two males and one female, and focal inflammation (pancreatitis) was noted in the pancreas of one male and one female. Focal pneumonia was found in one male lung. The following random incidental lesions were noted in the kidneys: tubular regeneration in eleven males and two females, pelvic mineralization in one male, chronic pyelitis in one male, and a tubular cyst in two males. Multifocal necrosis was noted in one male liver, biliary hyperplasia was noted in one male liver, and an eosinophilic focus was observed in one female liver. Reactive lymphadenitis was present in the submandibular lymph nodes of two males and three females (bilateral in males). Focal inflammation (mastitis) was present in the mammary gland of one female. Seminiferous tubules in the right and left testicles of one male were only lined by germinal epithelium and Sertoli's cells (hypospermatogenesis), and sperm were not present in the epididymis (hypospermia) of this animal. Chronic prostatitis was evident in one male

prostate. Focal deposits of hemosiderin (hemosiderosis) were noted in the uterine wall of two females. Implantation sites were observed in 17 uteri. Ulcerative dermatitis was seen in the ear skin of one male.

The spleen and bone marrow of all animals were read blindly as target organs. A Grade 1 hypercellularity of the bone marrow of a few controls (four males and twelve females) is within the range of normal for control rats of this age. All bone marrows were negative for iron with Perls' stain. Females had more cellular marrow, and this was due to pregnancy. Extramedullary hematopoiesis as noted in the male and female spleens is a normal finding in rats. A Grade 1 to Grade 4 hemosiderosis as observed in the spleens of males and females is also a normal finding in rat spleens.

Group 2: G0539.02, 50 mg/kg/day

Terminal Sacrifice

Treatment-related microscopic findings were not evident in Group 2 males and females. Spleen and bone marrows from Groups 1 and 2 could not be separated during a blind reading. Bone marrows were negative for iron with Perls' stain. The amount (grade) of hemosiderin (iron) and extramedullary hematopoiesis in the spleen of Group 1 and Group 2 males and females were similar. Bone marrow cellularity was also similar in Group 1 and Group 2 males and females. Decreased metarubricytes were noted in one male and two female during the blind reading.

The severity and number of incidental findings in Groups 1 and 2 were similar. Focal hyperplasia was seen in the pituitary of one male, and a cyst was seen in the pituitary of one male. The focal collections of inflammatory cells (mononuclear) in the heart (myositis) of seven males and two females were similar to findings in controls. Acinar atrophy in one female and focal pancreatitis in three males were noted in the pancreas. The following renal findings are not unusual findings for rats of this age and strain: tubular regeneration in seven males and two females, pelvic dilatation in one female, and a tubular cyst in one male. Multifocal necrosis noted in the liver of one female was similar to changes in a Group 1 male. Focal inflammation (hepatitis) was noted in the liver of the above female. Reactive lymphadenitis in the submandibular lymph node was present in three males. Ulcerative dermatitis was observed near the eye of one male. Hypospermatogenesis was noted bilaterally in two males and unilaterally in another two males, and this change was similar to the testicular change in a control male. A decreased number of sperm (hypospermia) were noted in the epididymis of these four males. Chronic prostatitis was seen in two males. Implantation sites were observed in the uteri of 13 females. Findings not noted in controls but considered incidental findings included: no corpora lutea in the ovary of one female, chronic glossitis (focal) on the tongue of one male, hemorrhage in the thymus of two males, focal pneumonia and alveolar macrophages in the lung of one male respectively, and a small embryonal cyst in the thyroid of two males.

Group 3: G0539.02, 100 mg/kg/day

Moribund/Deaths

Tissues were collected from one female which died. No hemosiderin was noted in the spleen of this female, and the splenic red pulp appeared hypercellular. A decreased number of metarubricytes were evident in the scattered foci of splenic erythropoiesis. Lymphocytic depletion was present in splenic germinal centers. The bone marrow was not more cellular than some controls, but a decreased number of metarubricytes were noted. Gastritis characterized by inflammatory cells in the lamina propria was noted in the forestomach of this female. The multifocal necrosis in the liver was similar to that observed in a control animal. Autolysis was present in several tissues.

Terminal Sacrifice

Treatment-related histopathologic findings were decreased hemosiderin in the spleen of males and females, hypercellularity of the splenic red marrow in females, and increased cellularity of the femur bone marrow with a decreased number of metarubricytes evident in the marrow of males and females. Bone marrows stained negative for iron with Perls' stain. The amount of hemosiderin (iron-containing pigment) in the spleen was decreased when compared with Group 1 and Group 2 animals as outlined in the Summary Table on pages 22 and 23. The red pulp of the spleen was hypercellular, and a decreased number of metarubricytes were noted in foci of erythropoiesis in females. Bone marrow of Group 3 males and females tended to contain more cells. These cells were immature forms

of erythrocytes, and a decreased number of metarubricytes were evident (see Summary Table on pages 22 and 23). An increased number of inflammatory cells were noted in the forestomach (gastritis) of eight males, in the cecum (enteritis) of two males and two females, in the colon (enteritis) of two males, and in the rectum (enteritis) of one male. These intestinal findings suggest the test material produced intestinal irritation.

Other microscopic changes noted did not have a treatment-related incidence or severity and were considered incidental findings. Focal hyperplasia and a cyst were observed in the pituitary of one and three males respectively. A small adenoma was seen in the pituitary of one female. Focal myositis was noted in one male heart. Acinar atrophy was seen in the pancreas of two males, and focal pancreatitis was seen in the pancreas of two males. Renal findings included tubular regeneration in eight males and two females, interstitial nephritis (focal) in two males, pelvic dilatation in one male, and chronic pyelitis in one female. Centrilobular vacuolization of hepatocytes was noted in two female livers, and reactive lymphadenitis was noted in the left submandibular lymph node of two females and in the right submandibular lymph node of two males. Inflammation (adenitis) was observed in the salivary gland of one male. Myositis was noted in the psoas muscle of one male, and chronic prostatitis was noted in one male. A focus of fat necrosis was present in a gross lesion found in the mesentery of one female. No corpora lutea were noted bilaterally in the

ovaries of one female and in the left ovary of one female. Implantation sites were observed in the uterine sections of 10 females.

Group 4: G0539.02, 300 mg/kg/day

Moribund/Deaths

Treatment-related changes were decreased hemosiderin in the spleen, hypercellular splenic red pulp, hypercellularity of the bone marrow, and decreased metarubricytes in the bone marrow. Bone marrows stained negative for iron with Perls' stain. No iron-staining pigment (hemosiderin) was present in most of the spleens examined. The splenic red pulp hypercellularity was probably due to increased erythropoiesis; however, late stages of erythropoiesis, i.e., metarubricytes, were not present to substantiate this hypothesis. In females few metarubricytes were evident in the small foci of erythropoiesis that were identifiable when compared with controls. Bone marrow hypercellularity was due to increased erythropoiesis; however, a decreased number of metarubricytes and later stages of erythropoiesis were evident in the marrow.

Gastrointestinal lesions suggested the test material was irritating. Hyperkeratosis in five males and gastritis (inflammatory cells in the submucosa) of one male and nine females were noted in the forestomach. Gastritis was evident in the fundic stomach of one male and in the pyloric stomach of one male and one female. Ulcers were also noted in the pyloric stomach of two females, and chronic peritonitis was noted on the serosal surface of the pyloric stomach of one

male. Enteritis was noted in the cecum of one male and one female and in the rectum of one female.

Centrilobular fibrosis was evident in the liver of 20 males and 11 females and was considered to be secondary to anemia which caused poor hepatic circulation. The poor circulation may have caused the focal tubular necrosis noted in the kidney of three males and one female, atrial thrombosis in three males and two females, cytoplasmic vacuolization in the adrenal of one male and seven females, necrosis in the lung of one male, tubular necrosis in the testis of one male, necrosis in the spleen of one female, and vascular thrombi in the lung of one male. Ulcerative glossitis on the tongue of two males and one female may also have been due to poor circulation. The lymphocytic depletion noted in the spleen of six males and one female, in the submandibular lymph node of three males, in the ileocecal lymph node of six males and two females, and in the thymus (involution) of four males was probably secondary to the severe stress of anemia.

Other incidental findings included: focal pneumonia in the lung of three males and three females, alveolar macrophages in the lung of four males, tubular regeneration in the kidney of one female, centrilobular vacuolization in the liver of two females, reactive lymphadenitis in the submandibular lymph node of one female, hemorrhage in the ileocecal lymph node of one male, no corpora lutea in the ovary of four females, hypospermatogenesis in the testis or absence of sperm in the epididymis (hypospermia) of six males, myositis in the heart

of one female, and chronic prostatitis in three males. Autolysis was noted in a few tissues.

Terminal Sacrifice

Treatment-related lesions were noted in the spleen and bone marrow. Iron-containing pigment (hemosiderin) was not present in most of the spleens. The splenic red pulp was hypercellular (due to immature or a blastic form of erythropoiesis), and fewer metarubricytes were evident in isolated identifiable foci of erythropoiesis. The marrow of all femurs was hypercellular, and a decreased number of metarubricytic cells were evident. Bone marrows stained negative for iron with Perls' stain.

Secondary changes were noted in the liver, adrenal, heart, and scattered other tissues which were attributed to anemia which produced poor circulation and stress. Centrilobular fibrosis was seen in the liver of all males (one) and females (thirteen). Atrial thrombosis was noted in the heart of one male and four females. Cortical cytoplasmic vacuolization was evident in the adrenal of ten females.

Gastrointestinal changes indicated the test material was irritating. Gastritis was seen in the forestomach of twelve females and in the pyloric stomach of one female. Ulcers were also noted in the pyloric stomach of two females. Enteritis was seen in the cecum of six females and in the colon of one female.

Incidental findings were noted in a few other tissues and included: focal pneumonia in the lung of two females, a cyst

in the ileocecal lymph node of two females, no corpora lutea in the ovary of seven females, implantation sites in the uterus of one female, and necrosis of mesenteric fat in two females.

Summary Table

Males	Groups 1	2	3(TS)	3(D)	4(TS)	4(D)
Spleen (No. Examined)	(25)	(24)	(24)	(0)	(1)	(22)
Extramedullary hematopoiesis						
Grade 0		2				16
Grade 1	25	21	10		1	4
Grade 2		1	14			
Grade 3						2
Hemosiderosis						
Grade 0			9		1	19
Grade 1	2	3	12			3
Grade 2	7	6	3			
Grade 3	9	12				
Grade 4	7	3				
Hypercellular red pulp						
Grade 0	25	24	24			5
Grade 1					1	12
Grade 2						5

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

Females	Groups 1	2	3(TS)	3(D)	4(TS)	4(D)
Spleen (No. Examined)	(25)	(25)	(24)	(1)	(13)	(11)
Extramedullary hematopoiesis						
Grade 0			4			4
Grade 1	12	9	17		8	7
Grade 2	13	16	3		4	
Grade 3				1	1	
Hemosiderosis						
Grade 0			13	1	13	10
Grade 1		1	7			1
Grade 2	1	5	3			
Grade 3	13	12	1			
Grade 4	11	7				
Hypercellular red pulp						
Grade 0	25	25	7			1
Grade 1			5			3
Grade 2			12	1	12	7
Grade 3					1	
Decreased metarubricytes			11	1	13	7

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

Males	Groups 1	2	3(TS)	3(D)	4(TS)	4(D)
Bone Marrow (Femur)						
(No. Examined)	(25)	(25)	(24)	(0)	(1)	(21)
Hypercellular						
Grade 0	21	18	5			1
Grade 1	4	6	4			3
Grade 2		1	8			6
Grade 3			7		1	11
Decreased metarubricytes		1	11			

Females	Groups 1	2	3(TS)	3(D)	4(TS)	4(D)
Bone Marrow (Femur)						
(No. Examined)	(25)	(25)	(24)	(1)	(13)	(9)
Hypercellular						
Grade 0	13	15	5			
Grade 1	12	9	10			1
Grade 2		1	9	1	4	2
Grade 3					9	6
Decreased metarubricytes		2	13	1	12	9

TS = Terminal Sacrifice
D = Deaths
Grade 0 = None Present

DISCUSSION

Treatment-related findings were noted in Group 3 and Group 4 males, and most of these lesions were due to anemia. Pale tissues were observed in a few Group 3 males and females at necropsy, i.e., eyes were pale in nine males. In Group 4 males and females, pale tissues were noted in most of the animals at necropsy, and most males and about half of the females in this group died. The remaining animals in Group 4 were necropsied at a scheduled early sacrifice. Secondary heart enlargement in

10 males and 23 females and edema in scattered tissues of a few animals were also observed in Group 4 males and females. Relative and absolute male heart weights in Group 3 were significantly increased when compared with controls, and linear regression analyses suggested a dose-related trend. Group 3 female relative heart weights were statistically significantly increased when compared with controls. Splenic weight changes were also secondary to anemia; splenic contraction which pushes stored erythrocytes in the blood stream would decrease the size of the spleen. Relative and absolute spleen weights were decreased in Group 3 females, and linear regression suggested a dose-related trend. Relative spleen weights were also decreased in Group 2 males. Tan feces observed in a few animals were due to a decreased amount of urobilinogin (hemoglobin breakdown product) in the feces.

Microscopic treatment-related findings were also due to anemia and were noted in tissues of Group 3 and Group 4 males and females. Bone marrow cellularity indicated the anemia was not an aplastic anemia. The marrow was hypercellular. Granulopoiesis was similar in the bone marrow of control and treated groups, but an increased number of immature erythropoietic cells were evident in the marrow of Group 3 and Group 4 animals. However, a decreased number in the latter stages of erythropoiesis, i.e., metarubricytes, were seen in sections of the bone marrow indicating that the final stages of erythrocytic maturation were inhibited by treatment. Bone marrows were stained for iron with Perls' stain, but insufficient iron was present in control (Group 1) marrow to determine whether or not treatment decreased bone marrow iron reserves.

The amount of iron-containing pigment (hemosiderin) was decreased in the spleen of Group 3 and Group 4 males and females. Hypercellular splenic red pulp was also noted in several animals. This was probably due to increased erythropoiesis, but few of the latter stages of erythrocytic maturation, i.e., metarubricytes, were noted in these spleens to confirm this hypothesis.

Centrilobular fibrosis was noted in the liver of Group 4 males and females. Anemia decreased the oxygen transporting capacity of the blood, and the hepatic centrilobular fibrosis observed microscopically was similar to that produced by hepatic hypoxia. Necrosis in a few other tissues was considered to be due to poor circulation (hypoxia). Significant microscopic changes were not noted in Group 2 and Group 3 female livers, although liver weights were decreased at necropsy.

Histologic findings in the stomach and intestinal tract of a few animals indicated the test material was irritating to the gastrointestinal tract in Groups 3 and 4. In Group 3 the only change observed was an increased number of inflammatory cells in the lamina propria and submucosa of the forestomach (eight males and one female) and in the lamina propria of the cecum, colon, or rectum of an occasional animal. Gastric lesions were more severe in Group 4 and consisted of hyperkeratosis and inflammation in the forestomach, inflammation in the fundic and pyloric areas of a few animals, ulcers in the pylorus of four females, and even peritonitis on the serosal surface in one male. Inflammation was also

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

observed in the wall of the cecum of six females and the colon of one female.

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Veterinary Pathologist

5/7/87
Date

JEP/vln

GROSS PATHOLOGY INCIDENCE SUMMARY TABLES (MALES, TERMINAL SACRIFICE)

Study: B85-0460
Compound: B0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Page: 1
Date: 20 Oct86
Time: 16:01
GPS002 V2.0

Format | First Dose | Director
None | | G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Lungs	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Heart	25	25	25	1
Not Remarkable	25	25	25	0
Slightly enlarged	0	0	0	1
Pale	0	0	0	1
Aorta	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Trachea	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Tongue	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Esophagus	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Thyroid	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Parathyroids	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Submandibular Lymph Node	25	25	25	1
Not Remarkable	21	21	23	0
Right, small, slightly	1	0	0	0
Enlarged slightly	2	1	2	0
Right, enlarged moderately	1	0	0	0
Left, enlarged	0	1	0	0
Enlarged moderately	0	1	0	0
Right, enlarged slightly	0	1	0	0
Pale	0	0	0	1

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 16 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format: None
First Dose:
Director: S. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Submandibular Salivary Gland	25	25	25	1
Not Remarkable	25	25	23	0
Pale	0	0	2	1
Stomach	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Duodenum	25	25	25	1
Not Remarkable	25	25	24	0
Mucoid content	0	0	1	0
Pale	0	0	0	1
Jejunum	25	25	25	1
Not Remarkable	24	25	24	0
Mucoid content	1	0	1	0
Pale	0	0	0	1
Ileum	25	25	25	1
Not Remarkable	24	25	24	0
Mucoid content	1	0	1	0
Pale	0	0	0	1
Cecum	25	25	25	1
Not Remarkable	25	25	24	0
Mucoid content	0	0	1	0
Pale	0	0	0	1
Colon	25	25	25	1
Not Remarkable	25	25	24	0
Mucoid content	0	0	1	0
Pale	0	0	0	1
Rectum	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Liver	25	25	25	1
Not Remarkable	25	25	23	0
Pale	0	0	2	1
Caudate lobe, 3 mm pale area	0	0	0	1
Kidneys	25	25	25	1
Not Remarkable	24	25	23	0
Bilateral, slight pelvic dilatation	1	0	0	0

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 - 16 Oct86

Forest	First Dose	Director
None		G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Right, pelvic dilatation, slight	0	0	1	0
Left, moderately dilated pelvis	0	0	1	0
Pale	0	0	0	1
Ileocecal Lymph Node	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Adrenals	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Psoas Muscle	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Spleen	25	25	25	1
Not Remarkable	25	25	23	0
Slightly enlarged	0	0	1	1
3-5 mm cysts on spleen	0	0	1	0
Pale	0	0	0	1
Pancreas	25	25	25	1
Not Remarkable	25	24	25	0
0.5 x 0.5 x 1.0 cm cyst with thick white content	0	1	0	0
Pale	0	0	0	1
Bone/Marrow (Femur)	25	25	25	1
Not Remarkable	25	25	24	0
Pale	0	0	1	1
Skin	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Brain	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Spinal Cord	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Sciatic Nerve	25	25	25	1
Not Remarkable	25	25	25	0

Removal Reasons Included:
Terminal Sac.
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 - 16 Oct86

Study: 885-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format: None
First Dose:
Director: G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Pale	0	0	0	1
Pituitary	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Eyes	25	25	25	1
Not Remarkable	25	23	16	0
Brown crusty material around eyes	0	1	0	0
Crusty material around eyes	0	1	0	0
Pale	0	0	9	1
Urinary Bladder	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Testes	25	25	25	1
Not Remarkable	24	21	25	0
Moderately small	1	2	0	0
Bilateral, moderately small	0	2	0	0
Pale	0	0	0	1
Epididymis	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Prostate	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Seminal Vesicle	25	25	25	1
Not Remarkable	25	24	25	0
Left, small, moderately	0	1	0	0
Pale	0	0	0	1
Thymus	25	25	25	1
Not Remarkable	25	25	25	0
Pale	0	0	0	1
Bone Marrow Smear	25	25	25	1
Not Remarkable	24	25	23	0
Pale	1	0	2	1
Skin/Ear	1	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Terminal Sac.
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 16 Oct86

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Erosion by left ear	1	0	0	0
Skin/Eye	0	1	0	0
Not Remarkable	0	0	0	0
2 mm erosion above left eye	0	1	0	0
Teeth	0	0	1	0
Not Remarkable	0	0	0	0
Long lower teeth	0	0	1	0
Small Intestinal Tract	0	0	0	0
Not Remarkable	0	0	0	0
Nares	0	0	0	0
Not Remarkable	0	0	0	0
Intestinal Tract	0	0	0	0
Not Remarkable	0	0	0	0
Thorax	0	0	0	0
Not Remarkable	0	0	0	0
Peritoneal Space	0	0	0	0
Not Remarkable	0	0	0	0
Intestines	0	0	0	0
Not Remarkable	0	0	0	0
Neck (Thorax)	0	0	0	0
Not Remarkable	0	0	0	0
Tail	0	0	0	0
Not Remarkable	0	0	0	0
Legs	0	0	0	0
Not Remarkable	0	0	0	0
Thoracic Cavity	0	0	0	0
Not Remarkable	0	0	0	0
Head	0	0	0	0
Not Remarkable	0	0	0	0
Neck	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 - 16 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format: None
First Dose:
Director: G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Mesentery	0	0	0	0
Not Remarkable	0	0	0	0
Oral Cavity	0	0	0	0
Not Remarkable	0	0	0	0
Anus	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reason Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May86 Data Collection Dates: 14 Oct86 - 16 Oct86

Study Comments

Animal #2681 (G1,M): Brown crusty material around right eye, not present. Animal #2699 (G1,M): Crusty material not around eyes. Animal #2751 (G3,F): Preimplantation sites were visible in the uterus with ammonium sulfide. Animal #2779 (G3,F): Right eye damaged during collection. Animal #2605 (G4,M): Coat ungroomed; tail, 6" piece of tail missing. Animal #2614 (G4,M): Coat ungroomed. Animal #2658 (G4,M): Coat ungroomed. Animal #2666 (G4,M): Anus, fecal staining around the anus and hair wet around anus; abdomen, hair matted on ventral aspect of abdomen; coat ungroomed; animal emaciated. Animal #2677 (G4,M): Coat ungroomed. Animal #2684 (G4,M): Blood appears watery; ---, reddish in color. Animal #2687 (G4,M): Coat ungroomed; animal emaciated. Animal #2700 (G4,M): Anus, mottling of area around the anus, no hair around area of anus, and hair wet around anus; penis, no hair around area of penis; coat ungroomed; animal emaciated. Animal #2704 (G4,M): Part of tail missing. Animal #2707 (G4,M): Coat ungroomed. Animal #2709 (G4,M): Coat ungroomed. Animal #2766 (G4,F): Severe post-mortem change that precluded any observations. Animal #2820 (G4,F): Femur in two pieces.

GROSS PATHOLOGY INCIDENCE SUMMARY TABLES (MALES, MORIBUND/DEATHS)

Study: R85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format	First Dose	Director
None		G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Lungs	0	0	0	23
Not Remarkable	0	0	0	15
Autolysis	0	0	0	5
Focal areas of hemorrhage	0	0	0	1
Slightly enlarged	0	0	0	1
Focal hemorrhage	0	0	0	1
2 x 5 mm red area on the lobe	0	0	0	1
Reddish in color	0	0	0	1
Heart	0	0	0	23
Not Remarkable	0	0	0	8
Autolysis	0	0	0	5
Enlarged	0	0	0	9
Multifocal lesion on the heart, atrium area	0	0	0	1
White substance in the heart at atrium	0	0	0	1
Serous fluid in pericardial sac	0	0	0	1
Aorta	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Trachea	0	0	0	23
Not Remarkable	0	0	0	17
Autolysis	0	0	0	5
Yellowish --- material	0	0	0	1
Tongue	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Esophagus	0	0	0	23
Not Remarkable	0	0	0	17
Autolysis	0	0	0	5
Yellowish --- material	0	0	0	1
Thyroid	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Parathyroids	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 17 Oct86

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Submandibular Lymph Node	0	0	0	23
Not Remarkable	0	0	0	13
Autolysis	0	0	0	5
Focal hemorrhage	0	0	0	1
Hemorrhage	0	0	0	2
Left, hemorrhage	0	0	0	1
Hemorrhagic	0	0	0	1
Enlarged	0	0	0	1
Submandibular Salivary Gland	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Stomach	0	0	0	23
Not Remarkable	0	0	0	12
Autolysis	0	0	0	5
Distended with ingesta	0	0	0	1
Appears large	0	0	0	1
Filled with gas and fluid	0	0	0	1
Multiple red foci	0	0	0	1
Petechial hemorrhage	0	0	0	1
Enlarged	0	0	0	1
Duodenum	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Jejunum	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Ileum	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Cecum	0	0	0	23
Not Remarkable	0	0	0	16
Autolysis	0	0	0	5
Gas in cecal contents	0	0	0	1
Dark reddened material	0	0	0	1
Colon	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 - 17 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format__ First Dose Director_____
None G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Rectum	0	0	0	23
Not Remarkable	0	0	0	1
Autolysis	0	0	0	5
Feces tan in color	0	0	0	21
Soft feces	0	0	0	2
Feces tan, soft	0	0	0	1
Diarrhea	0	0	0	1
Liver	0	0	0	23
Not Remarkable	0	0	0	14
Autolysis	0	0	0	5
Pale	0	0	0	3
Appears pale	0	0	0	1
Kidneys	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Ileocecal Lymph Node	0	0	0	23
Not Remarkable	0	0	0	14
Autolysis	0	0	0	5
Enlarged	0	0	0	1
Hemorrhage	0	0	0	2
Enlarged and congested	0	0	0	1
Adrenals	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Psoas Muscle	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Spleen	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Pancreas	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Bone/Marrow (Femur)	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 - 17 Oct86

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format: None
First Dose:
Director: G. Nolen

	1 M	2 M	3 M	4 N
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Skin	0	0	0	23
Not Remarkable	0	0	0	17
Autolysis.	0	0	0	5
Yellowish in color	0	0	0	1
Brain	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis.	0	0	0	5
Spinal Cord	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis.	0	0	0	5
Sciatic Nerve	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis.	0	0	0	5
Pituitary	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis.	0	0	0	5
Eyes	0	0	0	23
Not Remarkable	0	0	0	0
Autolysis.	0	0	0	5
Pale orange in color	0	0	0	19
Pale orange	0	0	0	4
Right, swollen, edema	0	0	0	1
Urinary Bladder	0	0	0	23
Not Remarkable	0	0	0	16
Autolysis.	0	0	0	5
Enlarged	0	0	0	1
Reddened in color	0	0	0	1
Distended	0	0	0	1
Contained reddish-pink colored fluid	0	0	0	1
Testes	0	0	0	23
Not Remarkable	0	0	0	15
Autolysis.	0	0	0	5
Orange-brown crusting	0	0	0	1
Dark red in color	0	0	0	1
Bilateral multi-red foci on surface area	0	0	0	1
Appear reddish	0	0	0	1
Epididymis	0	0	0	23

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 17 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Format	First Dose	Director
None		G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Prostate	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Seminal Vesicle	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Thymus	0	0	0	23
Not Remarkable	0	0	0	18
Autolysis	0	0	0	5
Bone Marrow Smear	0	0	0	23
Not Remarkable	0	0	0	0
Missing	0	0	0	23
Skin/Ear	0	0	0	0
Not Remarkable	0	0	0	0
Skin/Eye	0	0	0	0
Not Remarkable	0	0	0	0
Teeth	0	0	0	0
Not Remarkable	0	0	0	0
Small Intestinal Tract	0	0	0	0
Not Remarkable	0	0	0	0
Nares	0	0	0	2
Not Remarkable	0	0	0	0
Orange-brown crusing around the nares	0	0	0	1
Brown crusting around the nares	0	0	0	1
Intestinal Tract	0	0	0	4
Not Remarkable	0	0	0	0
Filled with fluid and gas	0	0	0	2
Diarrhea	0	0	0	1
Filled with orange material and gas	0	0	0	1
Fluid and air in intestinal tract	0	0	0	1
Thorax	0	0	0	1
Not Remarkable	0	0	0	0

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 17 Oct86

Format: None | First Dose: | Director: G. Nolen

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Serous fluid in thorax	0	0	0	1
Peritoneal Space	0	0	0	1
Not Remarkable	0	0	0	0
Serous fluid in peritoneal space	0	0	0	1
Intestines	0	0	0	3
Not Remarkable	0	0	0	0
Yellowish fluid	0	0	0	1
Filled with yellow-colored gases and fluid	0	0	0	1
Intestinal contents tannish and contain gas	0	0	0	1
Neck (Thorax)	0	0	0	1
Not Remarkable	0	0	0	0
Orange discoloration around neck	0	0	0	1
Tail	0	0	0	3
Not Remarkable	0	0	0	0
Tip of tail dry and necrotic	0	0	0	1
Necrotic, part of tail missing	0	0	0	1
Half the tail purple in color	0	0	0	1
Legs	0	0	0	2
Not Remarkable	0	0	0	0
Edema on both front legs	0	0	0	1
Left, edema	0	0	0	1
Thoracic Cavity	0	0	0	2
Not Remarkable	0	0	0	0
Brown crusty material around the thoracic cavity	0	0	0	1
Dark colored fluid	0	0	0	1
Head	0	0	0	1
Not Remarkable	0	0	0	0
Swollen	0	0	0	1
Neck	0	0	0	1
Not Remarkable	0	0	0	0
Swollen	0	0	0	1
Yellowish fluid in neck area	0	0	0	1
Mesentery	0	0	0	0
Not Remarkable	0	0	0	0
Oral Cavity	0	0	0	0

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 15 Oct86 - 17 Oct86

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Not Remarkable	0	0	0	0
Anus	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 10 Feb86 Data Collection Dates: 15 Oct86 17 Oct86

Study Comments

Animal #2681 (G1,M): Brown crusty material around right eye, not present. Animal #2699 (G1,M): Crusty material not around eyes. Animal #2751 (G3,F): Freimplantation sites were visible in the uterus with ammonium sulfide. Animal #2779 (G3,F): Right eye damaged during collection. Animal #2605 (G4,M): Coat ungroomed; tail, 6" piece of tail missing. Animal #2614 (G4,M): Coat ungroomed. Animal #2658 (G4,M): Coat ungroomed. Animal #2666 (G4,M): Anus, fecal staining around the anus and hair wet around anus; abdomen, hair matted on ventral aspect of abdomen; coat ungroomed; animal emaciated. Animal #2677 (G4,M): Coat ungroomed. Animal #2684 (G4,M): Blood appears watery; ---, reddish in color. Animal #2687 (G4,M): Coat ungroomed; animal emaciated. Animal #2700 (G4,M): Anus, mottling of area around the anus, no hair around area of anus, and hair wet around anus; penis, no hair around area of penis; coat ungroomed; animal emaciated. Animal #2704 (G4,M): Part of tail missing. Animal #2707 (G4,M): Coat ungroomed. Animal #2709 (G4,M): Coat ungroomed. Animal #2766 (G4,F): Severe post-mortem change that precluded any observations. Animal #2820 (G4,F): Femur in two pieces.

GROSS PATHOLOGY INCIDENCE SUMMARY TABLES (FEMALES, TERMINAL SACRIFICE)

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Page: 1
Date: 20 Oct86
Time: 15:07
GPS002 V3.0

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	25	25	24	13
Lungs	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Heart	25	25	24	13
Not Remarkable	25	25	24	0
Slightly enlarged	0	0	0	13
Pale	0	0	0	13
Aorta	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Trachea	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Tongue	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Esophagus	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Thyroid	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Parathyroids	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Submandibular Lymph Node	25	25	24	13
Not Remarkable	24	25	24	0
Left, enlarged slightly	1	0	0	0
Pale	0	0	0	13
Submandibular Salivary Gland	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Stomach	25	25	24	13

Removal Reasons Included:
Terminal Sac.
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 14 Oct86 20 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Format__ First Dose Director_____
None G. Nolen

	1	2	3	4
	F	F	F	L
Animals on Study:	25	25	25	25
Animals Logged:	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Duodenum	25	25	24	13
Not Remarkable	25	25	23	0
Mucoid content	0	0	1	0
Pale	0	0	0	13
Jejunum	25	25	24	13
Not Remarkable	25	25	22	0
Mucoid content	0	0	2	0
Pale	0	0	0	13
Ileum	25	25	24	13
Not Remarkable	25	25	23	0
Mucoid content	0	0	1	0
Pale	0	0	0	13
Cecum	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Colon	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Rectum	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Liver	25	25	24	13
Not Remarkable	25	25	23	0
Pale	0	0	0	13
Pale, slightly	0	0	1	0
Median lobe, 3 mm red area	0	0	0	1
Kidneys	25	25	24	13
Not Remarkable	25	24	24	0
Right, pelvis dilated, mild	0	1	0	0
Pale	0	0	0	13
Ileocecal Lymph Node	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13

Removal Reasons Included:
Terminal Sac.
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 14 Oct86 - 20 Oct86

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	25	25	24	13
Adrenals	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Psoas Muscle	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Spleen	25	25	24	13
Not Remarkable	24	25	24	0
Slightly enlarged	1	0	0	12
Two 5 mm white nodules	1	0	0	0
Pale	0	0	0	13
Pancreas	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Bone/Marrow (Femur)	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Skin	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Brain	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Spinal Cord	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Sciatic Nerve	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Pituitary	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Eyes	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 14 Oct86 - 20 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Format__ First Dose Director_____
None G. Nolen

	1_____	2_____	3_____	4_____
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	25	25	24	13
Urinary Bladder	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Ovaries	25	25	24	13
Not Remarkable	25	25	23	0
Right, 2 mm pale area	0	0	1	0
Pale	0	0	0	13
Uterus (Horns)	25	25	24	13
Not Remarkable	25	25	23	0
5 mm nodule in mesentery by or on uterus	0	0	1	0
Right, 5 nodules (similar to implantation sites)	0	0	0	1
Left, 3 nodules (similar to implantation sites)	0	0	0	1
Pale	0	0	0	13
Vagina	25	25	24	13
Not Remarkable	25	25	23	0
Dark thick content	0	0	1	0
Pale	0	0	0	13
Thymus	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Bone Marrow Smear	25	25	24	13
Not Remarkable	25	25	24	0
Pale	0	0	0	13
Skin/Ear	0	0	0	0
Not Remarkable	0	0	0	0
Skin/Eye	0	0	0	0
Not Remarkable	0	0	0	0
Teeth	0	1	0	0
Not Remarkable	0	0	0	0
Elongated lower incisors	0	1	0	0
Small Intestinal Tract	0	0	0	0
Not Remarkable	0	0	0	0
Nares	0	0	0	0
Not Remarkable	0	0	0	0

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Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 14 Oct86 - 20 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	E	E	E	E
Animals on Study:	25	25	25	25
Animals Logged:	25	25	24	13
Intestinal Tract	0	0	0	0
Not Remarkable	0	0	0	0
Thorax	0	0	0	0
Not Remarkable	0	0	0	0
Peritoneal Space	0	0	0	0
Not Remarkable	0	0	0	0
Intestines	0	0	0	0
Not Remarkable	0	0	0	0
Neck (Thorax)	0	0	0	0
Not Remarkable	0	0	0	0
Tail	0	0	0	0
Not Remarkable	0	0	0	0
Legs	0	0	0	0
Not Remarkable	0	0	0	0
Thoracic Cavity	0	0	0	0
Not Remarkable	0	0	0	0
Head	0	0	0	0
Not Remarkable	0	0	0	0
Neck	0	0	0	0
Not Remarkable	0	0	0	0
Mesentery	0	0	0	2
Not Remarkable	0	0	0	0
10 x 4 mm pale nodule	0	0	0	2
Oral Cavity	0	0	0	0
Not Remarkable	0	0	0	0
Anus	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 14 Oct86 - 20 Oct86

Study Comments

Animal #2681 (G1,M): Brown crusty material around right eye, not present. Animal #2699 (G1,M): Crusty material not around eyes. Animal #2751 (G3,F): Preimplantation sites were visible in the uterus with ammonium sulfide. Animal #2779 (G3,F): Right eye damaged during collection. Animal #2605 (G4,M): Coat ungroomed; tail, 6" piece of tail missing. Animal #2614 (G4,M): Coat ungroomed. Animal #2658 (G4,M): Coat ungroomed. Animal #2666 (G4,M): Anus, fecal staining around the anus and hair wet around anus; abdomen, hair matted on ventral aspect of abdomen; coat ungroomed; animal emaciated Animal #2677 (G4,M): Coat ungroomed. Animal #2684 (G4,M): Blood appears watery; ---, reddish in color. Animal #2687 (G4,M): Coat ungroomed; animal emaciated. Animal #2700 (G4,M): Anus, mottling of area around the anus, no hair around area of anus, and hair wet around anus; penis, no hair around area of penis; coat ungroomed; animal emaciated. Animal #2704 (G4,M): Part of tail missing. Animal #2707 (G4,M): Coat ungroomed. Animal #2709 (G4,M): Coat ungroomed. Animal #2766 (G4,F): Severe post-mortem change that precluded any observations. Animal #2820 (G4,F): Femur in two pieces.

GROSS PATHOLOGY INCIDENCE SUMMARY TABLES (FEMALES, MORIBUND/DEATHS)

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Formal__ First Dose Director_____
None G. Nolen

	1 F	2 F	3 F	4 F
Animals on Study:	25	25	25	25
Animals Logged:	0	0	1	12
Lungs	0	0	1	11
Not Remarkable	0	0	1	10
Red area on the lung (2-3 mm)	0	0	0	1
Heart	0	0	1	11
Not Remarkable	0	0	1	1
Enlarged	0	0	0	5
Slightly enlarged	0	0	0	4
Yellow lesion on auricle	0	0	0	1
Enlarged (animal pregnant)	0	0	0	1
Aorta	0	0	1	11
Not Remarkable	0	0	1	11
Trachea	0	0	1	11
Not Remarkable	0	0	1	11
Tongue	0	0	1	11
Not Remarkable	0	0	1	11
Esophagus	0	0	1	11
Not Remarkable	0	0	1	11
Thyroid	0	0	1	11
Not Remarkable	0	0	1	11
Parathyroids	0	0	1	11
Not Remarkable	0	0	1	11
Submandibular Lymph Node	0	0	1	11
Not Remarkable	0	0	1	11
Submandibular Salivary Gland	0	0	1	11
Not Remarkable	0	0	1	11
Stomach	0	0	1	11
Not Remarkable	0	0	0	8
Filled with rat's nesting material	0	0	1	0
Multifocal hemorrhage	0	0	1	1
Multiple lacerations of the mucosal layer	0	0	0	1
Enlarged, full of food	0	0	0	1
Duodenum	0	0	1	11

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 21 Feb86 Data Collection Dates: 15 Oct86 20 Oct86

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format	First Dose	Director
None		G. Nolen

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	0	0	1	12
Not Remarkable	0	0	1	11
Jejunum	0	0	1	11
Not Remarkable	0	0	1	11
Ileum	0	0	1	11
Not Remarkable	0	0	1	11
Cecum	0	0	1	11
Not Remarkable	0	0	1	10
Filled with gas	0	0	0	1
Colon	0	0	1	11
Not Remarkable	0	0	1	10
No formed stool	0	0	0	1
Rectum	0	0	1	11
Not Remarkable	0	0	0	3
Feces tan in color	0	0	1	7
Pale feces, loose stool	0	0	0	1
Liver	0	0	1	11
Not Remarkable	0	0	1	7
Pale	0	0	0	1
Very pale and grainy	0	0	0	1
Areas of hemorrhage	0	0	0	1
Pale in color	0	0	0	1
Kidneys	0	0	1	11
Not Remarkable	0	0	1	11
Ileocecal Lymph Node	0	0	1	11
Not Remarkable	0	0	1	10
Enlarged and hemorrhagic	0	0	0	1
Adrenals	0	0	1	11
Not Remarkable	0	0	1	11
Psoas Muscle	0	0	1	11
Not Remarkable	0	0	1	11
Spleen	0	0	1	11
Not Remarkable	0	0	1	10
Enlarged	0	0	0	1
Multiple focal yellowish-brown areas on surface	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 21 Feb86 Data Collection Dates: 15 Oct86 - 20 Oct86

Study: 885-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Format__ First Dose Director_____
None G. Nolen

	1 F	2 F	3 F	4 F
Animals on Study:	25	25	25	25
Animals Logged:	0	0	1	12
Pancreas	0	0	1	11
Not Remarkable	0	0	1	11
Bone/Marrow (Femur)	0	0	1	11
Not Remarkable	0	0	1	11
Skin	0	0	1	11
Not Remarkable	0	0	1	11
Brain	0	0	1	11
Not Remarkable	0	0	1	11
Spinal Cord	0	0	1	11
Not Remarkable	0	0	1	11
Sciatic Nerve	0	0	1	11
Not Remarkable	0	0	1	11
Pituitary	0	0	1	11
Not Remarkable	0	0	1	11
Eyes	0	0	1	11
Not Remarkable	0	0	1	0
Pale	0	0	0	2
Pale orange in color	0	0	0	7
Pale in color	0	0	0	2
Urinary Bladder	0	0	1	11
Not Remarkable	0	0	1	11
Ovaries	0	0	1	11
Not Remarkable	0	0	1	11
Uterus (Horns)	0	0	1	11
Not Remarkable	0	0	0	10
Fetus blocking the uterine horn preventing normal delivery	0	0	1	0
Two fetuses in left uterine horn	0	0	0	1
Vagina	0	0	1	11
Not Remarkable	0	0	0	11
Pinkish-red, bloody discharge from vaginal area	0	0	1	0
Thymus	0	0	1	11

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 21 Feb86 Data Collection Dates: 15 Oct86 - 20 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Page: 4
Date: 20 Oct86
Time: 15:02
GPS002 V3.0

Format__ First_Dose Director_____
None G. Nolen

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	0	0	1	12
Not Remarkable	0	0	1	10
Hemorrhage	0	0	0	1
Bone Marrow Smear	0	0	1	11
Not Remarkable	0	0	1	0
Missing.	0	0	0	11
Skin/Ear	0	0	0	0
Not Remarkable	0	0	0	0
Skin/Eye	0	0	0	0
Not Remarkable	0	0	0	0
Teeth	0	0	0	0
Not Remarkable	0	0	0	0
Small Intestinal Tract	0	0	1	0
Not Remarkable	0	0	0	0
Filled with dark fluid	0	0	1	0
Nares	0	0	0	2
Not Remarkable	0	0	0	0
Crusty around nares	0	0	0	1
Crusty area around nares	0	0	0	1
Intestinal Tract	0	0	0	2
Not Remarkable	0	0	0	0
Filled with fluid	0	0	0	1
Filled with gas	0	0	0	1
Thorax	0	0	0	0
Not Remarkable	0	0	0	0
Peritoneal Space	0	0	0	0
Not Remarkable	0	0	0	0
Intestines	0	0	0	2
Not Remarkable	0	0	0	0
Filled with fluid and gases	0	0	0	1
Filled with yellowish gases	0	0	0	1
Neck (Thorax)	0	0	0	0
Not Remarkable	0	0	0	0
Tail	0	0	0	0

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 21 Feb86 Data Collection Dates: 15 Oct86 20 Oct86

Study: 885-0460
Compound: G0539.02
Start Date:

Two-Generation Reproduction and Teratology

Gross Pathology Incidence Summary

Page: 5
Date: 20 Oct86
Time: 15:02
GPS002 V3.0

Format: None
First Dose:
Director: G. Nolen

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	25
Animals Logged:	0	0	1	12
Not Remarkable	0	0	0	0
Legs	0	0	0	0
Not Remarkable	0	0	0	0
Thoracic Cavity	0	0	0	1
Not Remarkable	0	0	0	0
Fluid	0	0	0	1
Head	0	0	0	0
Not Remarkable	0	0	0	0
Neck	0	0	0	0
Not Remarkable	0	0	0	0
Mesentery	0	0	0	0
Not Remarkable	0	0	0	0
Oral Cavity	0	0	0	1
Not Remarkable	0	0	0	0
Brown crusty material around oral cavity	0	0	0	1
Anus	0	0	0	1
Not Remarkable	0	0	0	0
Reddish substance around anus	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 21 Feb86 Data Collection Dates: 15 Oct86 - 20 Oct86

Study Comments

Animal #2681 (G1,M): Brown crusty material around right eye, not present. Animal #2699 (G1,M): Crusty material not around eyes. Animal #2751 (G3,F): Preimplantation sites were visible in the uterus with ammonium sulfide. Animal #2779 (G3,F): Right eye damaged during collection. Animal #2605 (G4,M): Coat ungroomed; tail, 6" piece of tail missing. Animal #2614 (G4,M): Coat ungroomed. Animal #2658 (G4,M): Coat ungroomed. Animal #2666 (G4,M): Anus, fecal staining around the anus and hair wet around anus; abdomen, hair matted on ventral aspect of abdomen; coat ungroomed; animal emaciated. Animal #2677 (G4,M): Coat ungroomed. Animal #2684 (G4,M): Blood appears watery; ---, reddish in color. Animal #2687 (G4,M): Coat ungroomed; animal emaciated. Animal #2700 (G4,M): Anus, mottling of area around the anus, no hair around area of anus, and hair wet around anus; penis, no hair around area of penis; coat ungroomed; animal emaciated. Animal #2704 (G4,M): Part of tail missing. Animal #2707 (G4,M): Coat ungroomed. Animal #2709 (G4,M): Coat ungroomed. Animal #2766 (G4,F): Severe post-mortem change that precluded any observations. Animal #2820 (G4,F): Femur in two pieces.

HISTOPATHOLOGY INCIDENCE SUMMARY TABLES (MALES, TERMINAL SACRIFICE)

Study: D85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Page: 1
Date: 10 Oct86
Time: 10:41
DMS002 V3.0

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Brain	25	25	25	1
Not Remarkable	25	25	25	1
Spinal Cord	25	25	25	1
Not Remarkable	23	25	25	1
Missing.	2	0	0	0
Thyroid/Parathyroid	25	25	25	1
Not Remarkable	25	23	25	1
Cyst	0	2	0	0
Trachea	25	25	25	1
Not Remarkable	25	25	25	1
Esophagus	25	25	25	1
Not Remarkable	24	25	25	1
Missing.	1	0	0	0
Pituitary	25	25	25	1
Not Remarkable	22	22	20	1
Missing.	1	1	1	0
Focal hyperplasia	2	1	1	0
Cyst	1	1	3	0
Adrenal	25	25	25	1
Not Remarkable	25	25	25	1
Sciatic Nerve	25	25	25	1
Not Remarkable	24	25	23	0
Missing.	1	0	2	1
Heart	25	25	25	1
Not Remarkable	19	18	24	0
Myositis	6	7	1	0
Atrial thrombosis	0	0	0	1
Aorta	25	25	25	1
Not Remarkable	24	23	25	1
Missing.	1	2	0	0
Thymus	25	25	25	1
Not Remarkable	24	23	25	1
Missing.	1	0	0	0

Removal Reasons Included:
Terminal Sac.,
Removal Dates: 19 Feb86 - 9 May88 Date Collection Dates: 9 Oct86 - 9 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Hemorrhage	0	2	0	0
Spleen	25	25	25	1
Not Remarkable	0	0	0	0
Missing.	0	1	1	0
Extramedullary hematopoiesis	25	22	24	1
Hemosiderosis	25	24	15	0
Cyst	0	0	1	0
Hypercellular red pulp	0	0	0	1
Pancreas	25	25	25	1
Not Remarkable	22	22	22	1
Acinar atrophy	2	0	2	0
Focal pancreatitis	1	3	2	0
Lung	25	25	25	1
Not Remarkable	24	23	25	1
Focal pneumonia	1	1	0	0
Alveolar macrophages	0	1	0	0
Kidney	25	25	25	1
Not Remarkable	11	18	15	1
Tubular regeneration	11	7	8	0
Pelvic mineralization	1	0	0	0
Chronic pyelitis	1	0	0	0
Tubular cyst	2	1	0	0
Interstitial nephritis	0	0	2	0
Pelvic dilatation	0	0	1	0
Liver	25	25	25	1
Not Remarkable	23	25	25	0
Multifocal necrosis	1	0	0	0
Biliary hyperplasia	1	0	0	0
Centrilobular fibrosis	0	0	0	1
Submandibular Lymph Node	25	25	25	1
Not Remarkable	23	23	24	1
Missing.	0	0	1	0
Reactive lymphadenitis	2	2	0	0
Submandibular Salivary Gland	25	25	25	1
Not Remarkable	25	25	24	1
Adenitis	0	0	1	0
Tongue	25	25	25	1

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May88 Data Collection Dates: 9 Oct86 - 9 Oct86

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Not Remarkable	25	24	25	1
Chronic glossitis	0	1	0	0
Stomach (Forestomach)	25	25	25	1
Not Remarkable	25	25	17	1
Gastritis	0	0	8	0
Stomach (Fundic)	25	25	25	1
Not Remarkable	25	25	25	1
Stomach (Pyloric)	25	25	25	1
Not Remarkable	25	25	25	1
Ileocecal Lymph Node	25	25	25	1
Not Remarkable	25	24	25	1
Missing.	0	1	0	0
Duodenum	25	25	25	1
Not Remarkable	25	25	25	1
Jejunum	25	25	25	1
Not Remarkable	25	25	25	1
Ileum	25	25	25	1
Not Remarkable	25	25	25	1
Cecum	25	25	25	1
Not Remarkable	25	25	23	1
Enteritis	0	0	2	0
Colon	25	25	25	1
Not Remarkable	25	25	23	1
Enteritis	0	0	2	0
Rectum	25	25	25	1
Not Remarkable	24	25	24	1
Missing.	1	0	0	0
Enteritis	0	0	1	0
Skin/Mammary Gland	25	25	25	1
Not Remarkable	25	24	25	1
Missing.	0	1	0	0
Psoas Muscle	25	25	25	1
Not Remarkable	25	25	25	1

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 FebBb - 9 MayBB Data Collection Dates: 9 OctBb 9 OctBb

ANATOMIC PATHOLOGY
APPENDIX I

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Missing	0	0	1	0
Myositis	0	0	1	0
Eye	25	25	25	1
Not Remarkable	25	25	25	1
Urinary Bladder	25	25	25	1
Not Remarkable	25	25	25	1
Testis	25	25	25	1
Not Remarkable	24	21	25	1
Hypospermatogenesis	1	4	0	0
Prostate	25	25	25	1
Not Remarkable	24	23	24	1
Chronic prostatitis	1	2	1	0
Epididymis	25	25	25	1
Not Remarkable	24	21	25	1
Hypospermia	1	4	0	0
Seminal Vesicle	25	25	25	1
Not Remarkable	25	25	25	1
Bone (Femur)	25	25	25	1
Not Remarkable	25	25	24	1
Missing	0	0	1	0
Marrow (Femur)	25	25	25	1
Not Remarkable	21	18	5	0
Missing	0	0	1	0
Hypercellular	4	7	19	1
Decreased metarubricytes	0	1	11	0
Marrow (Femur, Special Stain)	25	25	25	1
Not Remarkable	0	0	0	0
Missing	0	0	1	0
Negative	25	25	24	1
Skin, Ear	1	0	0	0
Not Remarkable	0	0	0	0
Ulcerative dermatitis	1	0	0	0
Eye, Right	0	2	9	0
Not Remarkable	0	2	7	0

Removal Reasons Included:
Terminal Sac.
Removal Dates: 12 Feb86 - 9 May88 Data Collection Dates: 9 Oct86 - 9 Oct86

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Forest	First Dose	Director	Metastatic Sites
None		B. Nolen	Included

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	25	25	25	1
Missing.	0	0	2	0
Submandibular Lymph Node, Right	4	3	2	0
Not Remarkable	2	2	0	0
Reactive lymphadenitis	2	1	2	0
Skin, Eye	0	1	0	0
Not Remarkable	0	0	0	0
Ulcerative dermatitis	0	1	0	0
Testis, Right	1	4	0	0
Not Remarkable	0	1	0	0
Missing.	0	1	0	0
Hypospermatogenesis	1	2	0	0
Mesenteric Fat	0	0	0	0
Not Remarkable	0	0	0	0
Penis	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 9 May88 Data Collection Dates: 9 Oct86 9 Oct86

HISTOPATHOLOGY INCIDENCE SUMMARY TABLES (MALES, MORIBUND/DEATHS)

Study: BBG-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Brain	0	0	0	23
Not Remarkable	0	0	0	23
Spinal Cord	0	0	0	23
Not Remarkable	0	0	0	19
Missing	0	0	0	4
Thyroid/Parathyroid	0	0	0	23
Not Remarkable	0	0	0	8
Missing	0	0	0	15
Trachea	0	0	0	23
Not Remarkable	0	0	0	23
Esophagus	0	0	0	23
Not Remarkable	0	0	0	22
Missing	0	0	0	1
Pituitary	0	0	0	23
Not Remarkable	0	0	0	9
Missing	0	0	0	14
Adrenal	0	0	0	23
Not Remarkable	0	0	0	21
Autolysis	0	0	0	1
Cortical cytoplasmic vacuolization	0	0	0	1
Sciatic Nerve	0	0	0	23
Not Remarkable	0	0	0	18
Missing	0	0	0	5
Heart	0	0	0	23
Not Remarkable	0	0	0	19
Missing	0	0	0	1
Atrial thrombosis	0	0	0	3
Aorta	0	0	0	23
Not Remarkable	0	0	0	22
Missing	0	0	0	1
Thymus	0	0	0	23
Not Remarkable	0	0	0	7
Missing	0	0	0	16

Removal Reason: Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Involution	0	0	0	4
Spleen	0	0	0	23
Not Remarkable	0	0	0	0
Missing.	0	0	0	1
Autolysis.	0	0	0	2
Extramedullary hematopoiesis	0	0	0	6
Hemosiderosis	0	0	0	3
Lymphocytic depletion	0	0	0	6
Hypercellular red pulp	0	0	0	17
Pancreas	0	0	0	23
Not Remarkable	0	0	0	21
Missing.	0	0	0	1
Autolysis.	0	0	0	1
Lung	0	0	0	23
Not Remarkable	0	0	0	15
Focal pneumonia	0	0	0	3
Alveolar macrophages	0	0	0	4
Focal necrosis	0	0	0	1
Vascular thrombi	0	0	0	1
Kidney	0	0	0	23
Not Remarkable	0	0	0	10
Autolysis.	0	0	0	10
Focal tubular necrosis	0	0	0	3
Liver	0	0	0	23
Not Remarkable	0	0	0	2
Autolysis.	0	0	0	1
Centrilobular fibrosis	0	0	0	20
Submandibular Lymph Node	0	0	0	23
Not Remarkable	0	0	0	19
Missing.	0	0	0	1
Lymphocytic depletion	0	0	0	3
Submandibular Salivary Gland	0	0	0	23
Not Remarkable	0	0	0	22
Tongue	0	0	0	23
Not Remarkable	0	0	0	20
Missing.	0	0	0	1
Ulcerative glossitis	0	0	0	2

Removal Reasons Included:
Found Dead.
Removal Dates: 17 Nov85 - 18 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Stomach (Forestomach)	0	0	0	23
Not Remarkable	0	0	0	15
Missing.	0	0	0	2
Hyperkeratosis	0	0	0	5
Gastritis	0	0	0	1
Stomach (Fundic)	0	0	0	23
Not Remarkable	0	0	0	16
Missing.	0	0	0	2
Autolysis.	0	0	0	4
Gastritis	0	0	0	1
Stomach (Pyloric)	0	0	0	23
Not Remarkable	0	0	0	15
Missing.	0	0	0	1
Autolysis.	0	0	0	5
Chronic peritonitis	0	0	0	1
Gastritis	0	0	0	1
Ileocecal Lymph Node	0	0	0	23
Not Remarkable	0	0	0	9
Missing.	0	0	0	7
Lymphocytic depletion	0	0	0	6
Hemorrhage	0	0	0	1
Duodenum	0	0	0	23
Not Remarkable	0	0	0	7
Missing.	0	0	0	2
Autolysis.	0	0	0	14
Jejunum	0	0	0	23
Not Remarkable	0	0	0	4
Autolysis.	0	0	0	19
Ileum	0	0	0	23
Not Remarkable	0	0	0	5
Missing.	0	0	0	1
Autolysis.	0	0	0	17
Cecum	0	0	0	23
Not Remarkable	0	0	0	2
Autolysis.	0	0	0	20
Enteritis	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

Study: 885-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolan	Included

	1	2	3	4
	M	M	M	M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Colon	0	0	0	23
Not Remarkable	0	0	0	3
Autolysis.	0	0	0	20
Rectum	0	0	0	23
Not Remarkable	0	0	0	4
Autolysis.	0	0	0	19
Skin/Mammary Gland	0	0	0	23
Not Remarkable	0	0	0	23
Psoas Muscle	0	0	0	23
Not Remarkable	0	0	0	16
Missing.	0	0	0	7
Eye	0	0	0	23
Not Remarkable	0	0	0	23
Urinary Bladder	0	0	0	23
Not Remarkable	0	0	0	11
Missing.	0	0	0	11
Autolysis.	0	0	0	1
Testis	0	0	0	23
Not Remarkable	0	0	0	17
Hypospermatogenesis	0	0	0	6
Prostate	0	0	0	23
Not Remarkable	0	0	0	8
Missing.	0	0	0	12
Chronic prostatitis	0	0	0	3
Epididymis	0	0	0	23
Not Remarkable	0	0	0	16
Missing.	0	0	0	1
Hypospermia	0	0	0	6
Seminal Vesicle	0	0	0	23
Not Remarkable	0	0	0	10
Missing.	0	0	0	13
Bone (Femur)	0	0	0	23
Not Remarkable	0	0	0	20
Missing.	0	0	0	3

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov85 - 18 Feb86 Data Collection Dates: 9 Oct86 9 Oct86

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1 M	2 M	3 M	4 M
Animals on Study:	25	25	25	24
Animals Logged:	0	0	0	23
Marrow (Femur)	0	0	0	23
Not Remarkable	0	0	0	1
Missing.	0	0	0	2
Hypercellular	0	0	0	20
Marrow (Femur, Special Stain)	0	0	0	23
Not Remarkable	0	0	0	0
Missing.	0	0	0	3
Negative	0	0	0	20
Skin, Ear	0	0	0	0
Not Remarkable	0	0	0	0
Eye, Right	0	0	0	19
Not Remarkable	0	0	0	12
Missing.	0	0	0	7
Submandibular Lymph Node, Right	0	0	0	0
Not Remarkable	0	0	0	0
Skin, Eye	0	0	0	0
Not Remarkable	0	0	0	0
Testis, Right	0	0	0	3
Not Remarkable	0	0	0	1
Autolysis.	0	0	0	1
Hypospermatogenesis	0	0	0	1
Focal tubular necrosis	0	0	0	1
Mesenteric Fat	0	0	0	0
Not Romarkable	0	0	0	0
Penis	0	0	0	1
Not Remarkable	0	0	0	0
Missing.	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 27 Nov86 - 18 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

HISTOPATHOLOGY INCIDENCE SUMMARY TABLES (FEMALES, TERMINAL SACRIFICE)

Study: BBS-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Date: 10 Oct86
Time: 10:05
DMS002 V3.0

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	24
Animals Logged:	25	25	24	13
Brain	25	25	24	13
Not Remarkable	25	25	24	13
Spinal Cord	25	25	24	13
Not Remarkable	24	25	23	13
Missing	1	0	1	0
Thyroid/Parathyroid	25	25	24	13
Not Remarkable	25	25	24	13
Trachea	25	25	24	13
Not Remarkable	25	25	24	13
Esophagus	25	25	24	13
Not Remarkable	25	25	24	13
Pituitary	25	25	24	13
Not Remarkable	23	23	23	12
Missing	1	2	0	1
Cyst	1	0	0	0
Adenoma	0	0	1	0
Adrenal	25	25	24	13
Not Remarkable	24	25	24	3
Missing	1	0	0	0
Cortical cytoplasmic vacuolization	0	0	0	10
Sciatic Nerve	25	25	24	13
Not Remarkable	24	24	24	13
Missing	1	1	0	0
Heart	25	25	24	13
Not Remarkable	23	23	24	9
Myositis	2	2	0	0
Atrial thrombosis	0	0	0	4
Aorta	25	25	24	13
Not Remarkable	25	25	23	13
Missing	0	0	1	0
Thymus	25	25	24	13
Not Remarkable	25	25	24	8
Missing	0	0	0	0

Removal Reason Included:
Terminal Sac.
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 9 Oct86 - 9 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	E	E	E	E
Animals on Study:	25	25	25	24
Animals Logged:	25	25	24	13
Involution	0	0	0	5
Spleen	25	25	24	13
Not Remarkable	0	0	0	0
Extramedullary hematopoiesis	25	25	20	13
Hemosiderosis	25	25	11	0
Focal necrosis	1	0	0	0
Hypercellular red pulp	0	0	17	13
Decreased metarubricytes	0	0	11	13
Pancreas	25	25	24	13
Not Remarkable	23	24	23	12
Missing.	0	0	1	1
Acinar atrophy	1	1	0	0
Focal pancreatitis	1	0	0	0
Lung	25	25	24	13
Not Remarkable	25	25	24	11
Focal pneumonia	0	0	0	2
Kidney	25	25	24	13
Not Remarkable	23	22	21	13
Tubular regeneration	2	2	2	0
Chronic pyelitis	0	0	1	0
Pelvic dilatation	0	1	0	0
Liver	25	25	24	13
Not Remarkable	24	24	22	0
Multifocal necrosis	0	1	0	0
Centrilobular fibrosis	0	0	0	13
Eosinophilic focus	1	0	0	0
Centrilobular vacuolization	0	0	2	0
Hepatitis	0	1	0	0
Submandibular Lymph Node	25	25	24	13
Not Remarkable	19	25	22	13
Missing.	3	0	0	0
Reactive lymphadenitis	3	0	2	0
Submandibular Salivary Gland	25	25	24	13
Not Remarkable	25	25	24	13
Tongue	25	25	24	13
Not Remarkable	25	25	24	13

Removal Reasons Included:
Terminal Sac.
Removal Dates: 12 Feb86 - 8 May06 Data Collection Dates: 9 Oct86 - 9 Oct86

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	E	E	E	E
Animals on Study:	25	25	25	24
Animals Logged:	25	25	24	13
Stomach (Forestomach)	25	25	24	13
Not Remarkable	25	25	24	1
Gastritis	0	0	0	12
Stomach (Fundic)	25	25	24	13
Not Remarkable	25	25	24	13
Stomach (Pyloric)	25	25	24	13
Not Remarkable	25	25	24	10
Gastritis	0	0	0	1
Ulcer	0	0	0	2
Ileocecal Lymph Node	25	25	24	13
Not Remarkable	25	24	24	11
Missing	0	1	0	0
Cyst	0	0	0	2
Duodenum	25	25	24	13
Not Remarkable	25	25	24	13
Jejunum	25	25	24	13
Not Remarkable	25	24	24	13
Missing	0	1	0	0
Ileum	25	25	24	13
Not Remarkable	25	25	24	13
Cecum	25	25	24	13
Not Remarkable	25	25	22	7
Enteritis	0	0	2	6
Colon	25	25	24	13
Not Remarkable	25	25	24	12
Enteritis	0	0	0	1
Rectum	25	25	24	13
Not Remarkable	25	25	24	13
Skin/Mammary Gland	25	25	24	13
Not Remarkable	24	25	24	13
Missing	0	0	0	0
Focal mastitis	1	0	0	0
Psoas Muscle	25	25	24	13
Not Remarkable	24	25	24	13

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 9 Oct86 - 9 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Page: 4
Date: 10 Oct86
Time: 16:05
DMS002 V3.0

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	24
Animals Logged:	25	25	24	13
Missing	1	0	0	0
Eye	25	25	24	13
Not Remarkable	25	25	24	12
Missing	0	0	0	1
Urinary Bladder	25	25	24	13
Not Remarkable	25	25	23	13
Missing	0	0	1	0
Ovary	25	25	24	13
Not Remarkable	25	24	21	5
Missing	0	0	1	1
No corpora lutea	0	1	2	7
Uterus	25	25	24	13
Not Remarkable	7	12	14	12
Implantation sites	17	13	10	1
Hemosiderosis	2	0	0	0
Vagina	25	25	24	13
Not Remarkable	25	25	24	13
Bone (Femur)	25	25	24	13
Not Remarkable	25	25	24	13
Marrow (Femur)	25	25	24	13
Not Remarkable	13	15	5	0
Hypercellular	12	10	19	13
Decreased metarubricytes	0	2	13	12
Marrow (Femur, Special Stain)	25	25	24	13
Not Remarkable	0	0	0	0
Negative	25	25	24	13
Skin, Ear	0	0	0	0
Not Remarkable	0	0	0	0
Eye, Right	0	0	0	0
Not Remarkable	0	0	0	0
Submandibular Lymph Node, Right	0	0	0	0
Not Remarkable	0	0	0	0
Skin, Eye	0	0	0	0

Removal Reasons Included:
Terminal Sac..
Removal Dates: 19 Feb86 - 8 May86 Data Collection Dates: 9 Oct86 - 9 Oct86

	1	2	3	4
	E	E	E	E
Animals on Study:	25	25	25	24
Animals Logged:	25	25	24	13
Not Remarkable	0	0	0	0
Mesenteric Fat	0	0	1	2
Not Remarkable	0	0	0	0
Necrosis	0	0	1	2
Ovary, Right	0	0	1	0
Not Remarkable	0	0	0	0
No corpora lutea	0	0	1	0

HISTOPATHOLOGY INCIDENCE SUMMARY TABLES (FEMALES, MORIBUND/DEATHS)

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	E	E	E	E
Animals on Study:	25	25	25	24
Animals Logged:	0	0	1	11
Brain	0	0	1	11
Not Remarkable	0	0	1	11
Spinal Cord	0	0	1	11
Not Remarkable	0	0	0	10
Missing.	0	0	1	1
Thyroid/Parathyroid	0	0	1	11
Not Remarkable	0	0	1	8
Missing.	0	0	0	2
Autolysis.	0	0	0	1
Trachea	0	0	1	11
Not Remarkable	0	0	1	11
Esophagus	0	0	1	11
Not Remarkable	0	0	1	11
Pituitary	0	0	1	11
Not Remarkable	0	0	1	7
Missing.	0	0	0	4
Adrenal	0	0	1	11
Not Remarkable	0	0	1	3
Autolysis.	0	0	0	1
Cortical cytoplasmic vacuolization	0	0	0	7
Sciatic Nerve	0	0	1	11
Not Remarkable	0	0	1	10
Missing.	0	0	0	1
Heart	0	0	1	11
Not Remarkable	0	0	1	8
Myositis	0	0	0	1
Atrial thrombosis	0	0	0	2
Aorta	0	0	1	11
Not Remarkable	0	0	1	11
Thymus	0	0	1	11
Not Remarkable	0	0	0	7
Missing.	0	0	0	4
Autolysis.	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 16 Jan86 - 21 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	24
Animals Logged:	0	0	1	11
Involution	0	0	1	3
Spleen	0	0	1	11
Not Remarkable	0	0	0	0
Autolysis.	0	0	0	1
Extramedullary hematopoiesis	0	0	1	7
Hemosiderosis	0	0	0	1
Lymphocytic depletion	0	0	1	1
Focal necrosis	0	0	0	1
Hypercellular red pulp	0	0	1	10
Decreased metarubricytes	0	0	1	7
Pancreas	0	0	1	11
Not Remarkable	0	0	1	10
Autolysis.	0	0	0	1
Lung	0	0	1	11
Not Remarkable	0	0	1	7
Autolysis.	0	0	0	1
Focal pneumonia	0	0	0	3
Kidney	0	0	1	11
Not Remarkable	0	0	1	6
Autolysis.	0	0	0	4
Focal tubular necrosis	0	0	0	1
Tubular regeneration	0	0	0	1
Liver	0	0	1	11
Not Remarkable	0	0	0	0
Multifocal necrosis	0	0	1	0
Centrilobular fibrosis	0	0	0	11
Centrilobular vacuolization	0	0	0	2
Submandibular Lymph Node	0	0	1	11
Not Remarkable	0	0	1	9
Missing.	0	0	0	1
Reactive lymphadenitis	0	0	0	1
Submandibular Salivary Gland	0	0	1	11
Not Remarkable	0	0	1	11
Tongue	0	0	1	11
Not Remarkable	0	0	0	10
Missing.	0	0	1	0
Chronic glossitis	0	0	0	1

Removal Reasons Included:
Found Dead.
Removal Dates: 16 Jan86 - 21 Feb86 Data Collection Dates: 9 Oct86 9 Oct86

Study: B85-0460
Compound: B0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format: None | First Dose | Director: G. Nolen | Metastatic Sites: Included

	1 E	2 C	3 E	4 E
Animals on Study:	25	25	25	24
Animals Logged:	0	0	1	11
Stomach (Forestomach)	0	0	1	11
Not Remarkable	0	0	0	1
Autolysis	0	0	0	1
Gastritis	0	0	1	9
Stomach (Fundic)	0	0	1	11
Not Remarkable	0	0	1	10
Autolysis	0	0	0	1
Stomach (Pyloric)	0	0	1	11
Not Remarkable	0	0	0	7
Autolysis	0	0	1	2
Gastritis	0	0	0	1
Ulcer	0	0	0	2
Ileocecal Lymph Node	0	0	1	11
Not Remarkable	0	0	1	7
Missing	0	0	0	2
Lymphocytic depletion	0	0	0	2
Duodenum	0	0	1	11
Not Remarkable	0	0	0	4
Autolysis	0	0	1	7
Jejunum	0	0	1	11
Not Remarkable	0	0	0	3
Missing	0	0	0	1
Autolysis	0	0	1	7
Ileum	0	0	1	11
Not Remarkable	0	0	0	3
Autolysis	0	0	1	8
Cecum	0	0	1	11
Not Remarkable	0	0	0	1
Autolysis	0	0	1	9
Enteritis	0	0	0	1
Colon	0	0	1	11
Not Remarkable	0	0	0	3
Autolysis	0	0	1	8
Rectum	0	0	1	11
Not Remarkable	0	0	0	4

Removal Reasons Included:
Found Dead.
Removal Dates: 16 Jan86 - 21 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

ANATOMIC PATHOLOGY
APPENDIX I

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format: None | First Dose | Director: G. Nolen | Metastatic Sites: Included

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	24
Animals Logged:	0	0	1	11
Autolysis	0	0	1	6
Enteritis	0	0	0	1
Skin/Mammary Gland	0	0	1	11
Not Remarkable	0	0	1	11
Psoas Muscle	0	0	1	11
Not Remarkable	0	0	1	8
Missing	0	0	0	3
Eye	0	0	1	11
Not Remarkable	0	0	1	11
Urinary Bladder	0	0	1	11
Not Remarkable	0	0	0	10
Missing	0	0	1	0
Autolysis	0	0	0	1
Ovary	0	0	1	11
Not Remarkable	0	0	1	3
Missing	0	0	0	4
No corpora lutea	0	0	0	4
Uterus	0	0	1	11
Not Remarkable	0	0	1	10
Missing	0	0	0	1
Vagina	0	0	1	11
Not Remarkable	0	0	0	8
Missing	0	0	1	2
Autolysis	0	0	0	1
Bone (Femur)	0	0	1	11
Not Remarkable	0	0	1	9
Missing	0	0	0	2
Marrow (Femur)	0	0	1	11
Not Remarkable	0	0	0	0
Missing	0	0	0	2
Hypercellular	0	0	1	9
Decreased metarubricytes	0	0	1	9
Marrow (Femur, Special Stain)	0	0	1	11
Not Remarkable	0	0	0	0
Missing	0	0	0	2

Removal Reasons Included:
Found Dead.
Removal Dates: 16 Jan86 - 21 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

Two Generation Reproduction and Teratology

Histopathology Incidence Summary

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	1	2	3	4
	F	F	F	F
Animals on Study:	25	25	25	24
Animals Logged:	0	0	1	11
Negative	0	0	1	9
Skin, Ear	0	0	0	0
Not Remarkable	0	0	0	0
Eye, Right	0	0	0	11
Not Remarkable	0	0	0	8
Missing.	0	0	0	3
Submandibular Lymph Node, Right	0	0	0	0
Not Remarkable	0	0	0	0
Skin, Eye	0	0	0	0
Not Remarkable	0	0	0	0
Mesenteric Fat	0	0	0	0
Not Remarkable	0	0	0	0
Ovary, Right	0	0	0	0
Not Remarkable	0	0	0	0

Removal Reasons Included:
Found Dead.
Removal Dates: 16 Jan86 - 21 Feb86 Data Collection Dates: 9 Oct86 - 9 Oct86

INDIVIDUAL ANIMAL CROSS REFERENCE TABLES (MALES, TERMINAL SACRIFICE)

Study: 885-0460
Compound: 80539.02
Start Date:

Two Generation Reproduction and Teratology

Individual Animal Cross Reference

Page: 1
Date: 10 Oct86
Time: 10:45
DMS006 V3.0

Format: None | First Dose | Director: G. Nolen | Metastatic Sites: Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6	6	6
	9	0	0	1	1	2	2	2	3	3	3	4	5	5	6	7	8	8	8	9	9	0	1	1	1	9	0	0	1	1	1	3	3	3	4
	6	3	8	1	5	0	3	5	1	5	7	6	3	4	0	5	0	1	2	0	9	1	0	1	8	7	2	6	3	7	8	2	6	8	8
Group:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brain	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spinal Cord	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-
Thyroid/Parathyroid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Cyst	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	.	.	.	.	.	.	.
Trachea	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Esophagus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	+	?	+	-	-	-	-
Focal hyperplasia	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	3	.	.	1	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.
Cyst	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	.	.	.	.	.	.	.	.	.	+	.	.	.	.
Adrenal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sciatic Nerve	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	-	-		-	-	-	-	+	+	-	-	-	-	+	+	+	-	+	-	-	-	+	-	+	-	-	-	-	-	+
Myositis	.	.	.	.	.	.	.	.	.	.	.	.	3	2	.	.	.	.	1	1	1	.	1	.	.	.	1	.	1	.	.	.	.	.	1
Aorta	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-
Thymus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	+	-	-	-	-	-	-
Hemorrhage	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	+
Extramedullary hematopoiesis	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	.	1	2	1	1	1	1	1	1	1	1
Hemosiderosis	4	2	3	2	4	3	2	2	3	2	3	3	4	3	3	4	4	2	3	4	1	1	4	2	3	.	1	2	3	3	3	3	2	2	2
Pancreas	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	+
Acinar atrophy	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.
Focal pancreatitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	2

Note: . = not recorded.
- = not remarkable.
? = animal or tissue missing.
n = specified tissue note.
+ = morphology present.
* = probable cause of death.

Tissue Autolysis
1 = Autolysis

Morphology Severity
1 = Minimal
2 = Slight
3 = Moderate
4 = Mod.Sev./High
5 = Severe/High

Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Individual Animal Cross Reference

Format__ None | First Dose | Director G. Nolen | Metastatic Sites Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6
	9	0	0	1	1	2	2	2	3	3	3	4	5	5	6	7	8	8	8	9	9	0	1	1	1	0	0	1	1	1	3	3	3	4
	6	3	9	1	5	9	3	5	1	9	7	6	3	4	9	5	9	1	2	0	9	1	0	1	8	7	2	6	3	7	8	2	6	8	9
Group:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lung	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Focal pneumonia	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Alveolar macrophages	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.
Kidney	-	-	-	-	-	-	-	+	+	+	+	+	+	-	-	-	+	+	+	+	+	+	+	-	-	+	-	-	-	-	-	-	+	-
Tubular regeneration	.	.	.	.	.	.	.	1	.	.	1	1	1	1	.	.	.	1	2	.	1	1	1	1	.	.	2	.	.	.	.	.	.	3	.
Pelvic mineralization	.	.	.	.	.	.	.	.	3	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Chronic pyelitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Tubular cyst	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	+	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-
Multifocal necrosis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Biliary hyperplasia	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Submandibular Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+
Reactive lymphadenitis	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	3	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	2
Submandibular Salivary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tongue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Chronic glossitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.
Stomach (Forestomach)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach (Fundic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach (Pyloric)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ileocecal Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-
Duodenum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Jejunum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ileum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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Note: . = not recorded.
- = not remarkable.
' = animal or tissue missing.
n = specified tissue note.
+ = morphology present.
* = probable cause of death.

Tissue Autolysis
1 = autolysis

Morphology Severity
1 = Minimal
2 = Slight
3 = Moderate
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Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

Format: None | First Dose | Director: G. Nolen | Metastatic Sites: Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6	4
	9	0	0	1	1	2	2	2	3	3	3	4	5	5	6	7	8	8	8	9	9	0	1	1	1	9	0	0	1	1	1	3	3	3	4
	6	3	8	1	5	0	3	5	1	5	7	6	3	4	0	5	0	1	2	0	9	1	0	1	8	7	2	6	3	7	8	2	6	8	8
Group:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cecum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Colon	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rectum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin/Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-
Psoas Muscle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eye	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Testis	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Hypospermatogenesis	.	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	5	.	.	.	.	.	.	.	.
Prostate	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-
Chronic prostatitis	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.
Epididymis	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Hypospermia	.	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	5	.	.	.	.	.	.	.	.
Seminal Vesicle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone (Femur)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Marrow (Femur)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	+	+	+	+	-	-	-	-	+	+	-	-	-
Hypercellular	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	1	.	.	1	1	2	1	.	.	.	.	1	1	.	.	.
Decreased metarubricytes	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	.	.	.	.	.	.	.	.	.
Marrow (Femur, Special Stain)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Negative	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin, Ear	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Note: . = not recorded.
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Tissue Autolysis
1 = Autolysis

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2 = Slight
3 = Moderate
4 = Mod.Sev./High
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Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

Study: B85-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Individual Animal Cross Reference

Page: 4
Date: 10 Oct86
Time: 10:45
DMS006 V3.0

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6
	9	0	0	1	1	2	2	2	3	3	3	4	5	5	6	7	8	8	8	9	9	0	1	1	9	0	0	1	1	1	3	3	3
	6	3	8	1	5	0	3	5	1	5	7	6	3	4	0	5	0	1	2	0	9	1	0	1	8	7	2	6	3	7	8	2	6	8	8
Group:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ulcerative dermatitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
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Ulcerative dermatitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	.
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Hypospermatogenesis	.	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Mesenteric Fat	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
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Note: . = not recorded.
= not remarkable.
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+ = morphology present.
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Tissue Autolysis
1 = Autolysis

Morphology Severity
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Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
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4 = Premature Sac.
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Format__ None | First Done | Director_____ B. Nolen | Metastatic Sites Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	6	7	7	7	8	8	9	9	0	0	0	1	9	0	0	1	1	2	3	4	4	4	4	4	5	5	6	6	7	7	7	8
	0	2	7	2	4	6	8	5	9	5	6	3	6	8	4	8	4	9	2	9	1	4	0	1	5	7	9	5	6	1	5	1	2	9	3
Group:	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brain	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spinal Cord	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroid/Parathyroid	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cyst	.	.	.	+	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Trachea	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Esophagus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	+	-	+	+	-	-	-	-	-	-	-	-	+
Focal hyperplasia	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2
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Adrenal	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sciatic Nerve	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-
Heart	-	-	-	-	-	+	+	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Myositis	.	.	.	.	.	1	1	.	1	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Aorta	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hemorrhage	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Extramedullary hematopoiesis	1	1	.	1	1	1	1	1	.	1	1	1	1	1	1	2	.	2	1	2	1	2	1	2	1	1	2	2	2	2	1	1	1	2	1
Hemosiderosis	3	3	1	3	4	3	3	2	1	3	4	2	4	3	2	.	.	1	.	.	1	.	1	.	.	2	1	2	1	.	1	1	1	1	1
Cyst	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	.	.
Pancreas	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-
Acinar atrophy	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.

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Removal Reason
0 = Terminal Sac.
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Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	6	7	7	7	8	8	9	9	0	0	0	1	9	0	0	1	1	2	3	4	4	4	4	4	5	5	6	6	7	7	7	8
	9	2	7	2	4	6	8	5	7	5	6	3	6	8	4	8	4	7	2	9	1	4	0	1	5	7	9	5	6	1	5	1	2	9	3
Group:	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Focal pancreatitis	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	1	.	.	.	.	.	.
Lung	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
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Kidney	-	-	-	+	-	+	-	+	-	+	-	-	-	+	-	+	-	+	-	-	-	-	+	+	-	+	+	-	-	+	-	-	-	+	-
Tubular regeneration	.	.	.	1	.	1	.	1	.	3	.	.	.	1	.	1	.	.	.	.	.	.	.	1	.	1	1	.	.	1	.	.	.	1	.
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Liver	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Submandibular Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-
Submandibular Salivary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-
Adenitis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.
Tongue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach (Forestomach)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	-	-	-	-	+	-	-	-	-	-	-	+	+	-
Gastritis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	3	3	.	.	.	.	3	.	.	.	.	.	.	1	2	.
Stomach (Fundic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stomach (Pyloric)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ileocecal Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Duodenum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Jejunum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ileum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cecum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-

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n = specified tissue note.
+ = morphology present.
* = probable cause of death.

Tissue Autolysis
1 = autolysis

Morphology Severity
1 = Minimal
2 = Slight
3 = Moderate
4 = Mod.Sev./High
5 = Severe/High

Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

Study: B85-0460 | Two Generation Reproduction and Teratology | Page: 7
Compound: B0539.02 | | Date: 10 Oct86
Start Date: | Individual Animal Cross Reference | Time: 10:46
| | DMS006 V3.0

Format None | **First Dose** | **Director** G. Nolen | **Metastatic Sites** Included

Animal	2650	2652	2657	2662	2674	2676	2678	2685	2689	2695	2696	2703	2706	2708	2714	2518	2694	2609	2602	2619	2621	2634	2640	2641	2645	2647	2649	2655	2656	2661	2665	2671	2672	2679	2683
Group:	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Enteritis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	3	.	.	.	.	.	.	.	.
Colon	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Enteritis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	3	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.
Rectum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
Enteritis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	.	.
Skin/Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Psoas Muscle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-
Myositis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.
Eye	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary Bladder	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Testis	-	-	-	-	-	+	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypospermatogenesis	.	.	.	.	.	5	.	.	3	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Prostate	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-
Chronic prostatitis	.	.	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.
Epididymis	-	-	-	-	-	+	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypospermia	.	.	.	.	.	5	.	.	5	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Seminal Vesicle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone (Femur)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-
Marrow (Femur)	-	-	-	-	-	-	-	-	-	-	-	+	+	-	+	+	-	+	+	+	+	+	+	?	+	+	+	+	+	-	+	-	+	+	+
Hypercellular	.	.	.	.	.	.	.	.	.	.	.	1	1	.	1	3	.	3	2	2	2	2	1	.	1	1	3	2	3	.	2	.	2	3	1
Decreased metarubricytes	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	+	.	+	+	+	+	.	+	.	.	+	+	.	.	.	+	.	.	+	.
Marrow (Femur, Special Stain)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	+	+
Negative	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	+	+

Note: . = not recorded.
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+ = morphology present.
* = probable cause of death.

Tissue Autolysis
1 = Autolysis

Morphology Severity
1 Minimal
2 Slight
3 Moderate
4 Mod./Sev./High
5 Severe/High

Removal Reason
0 = Terminal Sac.
1 = Serial Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

ANATOMIC PATHOLOGY
APPENDIX I

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	6	7	7	7	8	8	9	9	0	0	0	1	9	0	0	1	1	2	3	4	4	4	4	4	5	5	6	6	7	7	7	8
	0	3	7	2	4	6	8	5	2	5	6	3	6	8	4	8	4	9	2	9	1	4	0	1	5	7	9	5	6	1	5	1	2	9	3
Group:	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Animal Sex (M or F):	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin, Ear	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Eye, Right	.	.	.	.	.	.	.	-	.	.	.	.	.	-	.	.	.	.	.	.	.	.	.	.	-	.	-	.	-	.	?	.	-	-	.
Submandibular Lymph Node, Right	.	.	.	.	.	.	.	+	.	.	.	-	.	.	.	.	.	+	.	.	.	.	.	.	.	+	.	.	.	.	.	.	.	.	.
Reactive lymphadenitis	.	.	.	.	.	.	.	2	.	.	.	.	.	.	.	.	.	3	.	.	.	.	.	.	.	3	.	.	.	.	.	.	.	.	.
Skin, Eye	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Testis, Right	.	.	.	.	.	+	.	.	-	+	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Hypospermatogenesis	.	.	.	.	.	5	.	.	.	5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Mesenteric Fat	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Penis	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

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Tissue Autolysis
1 = autolysis

Morphology Severity
1 = Minimal
2 = Slight
3 = Moderate
4 = Mod.Sev./High
5 = Severe/High

Removal Reason
0 = Terminal Sac.
1 = Sacrif. Sac.
2 = Moribund
3 = Found Dead
4 = Premature Sac.
5 = Accident

Study: BB5-0460
Compound: G0539.02
Start Date:

Two Generation Reproduction and Teratology

Individual Animal Cross Reference

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	2	2	2	2	2	2
	6	6	6	7	7	6
	8	9	9	0	1	5
	6	4	7	5	5	9
Group:	3	3	3	3	3	4
Animal Sex (M or F):	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0
Brain	-	-	-	-	-	-
Spinal Cord	-	-	-	-	-	-
Thyroid/Parathyroid	-	-	-	-	-	-
Trachea	-	-	-	-	-	-
Esophagus	-	-	-	-	-	-
Pituitary	-	-	-	-	-	-
Adrenal	-	-	-	-	-	-
Sciatic Nerve	-	-	-	-	-	-
Heart	-	+	-	-	-	+
Myositis	.	1	.	.	.	.
Atrial thrombosis	.	.	.	.	.	+
Aorta	-	-	-	-	-	-
Thymus	-	-	-	-	-	-
Spleen	+	+	+	+	+	+
Extramedullary hematopoiesis	2	2	1	2	2	1
Hemosiderosis	1	1	.	2	.	.
Hypercellular red pulp	.	.	.	.	.	1
Pancreas	-	-	-	+	-	-
Acinar atrophy	.	.	.	3	.	.
Lung	-	-	-	-		-

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Individual Animal Cross Reference

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

		2	2	2	2	2	2
		6	6	6	7	7	6
		8	9	9	0	1	5
		6	4	7	5	5	9
Group:		3	3	3	3	3	4
Animal Sex (M or F):		M	M	M	M	M	M
Animal Removal Code (0-7,?):		0	0	0	0	0	0
Kidney		-	-	+	-	+	-
Tubular regeneration		.	.	2	.	2	.
Liver		-	-	-	-	-	+
Centrilobular fibrosis		.	.	.	.	.	2
Submandibular Lymph Node		-	-	-	-	-	-
Submandibular Salivary Gland		-	-	-	-	-	-
Tongue		-	-	-	-	-	-
Stomach (Forestomach)		+	-	-	-	+	-
Gastritis		3	.	.	.	2	.
Stomach (Fundic)		-	-	-	-	-	-
Stomach (Pyloric)		-	-	-	-	-	-
Ileocecal Lymph Node		-	-	-	-	-	-
Duodenum		-	-	-	-	-	-
Jejunum		-	-	-	-	-	-
Ileum		-	-	-	-	-	-
Cecum		-	-	-	-	-	-
Colon		-	-	-	-	-	-
Rectum		-	-	-	-	-	-
Skin/Mammary Gland		-	-	-	-	-	-
Psoas Muscle		-	-	-	-	-	?

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Tissue Autolysis:
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Removal Reason
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4 = Premature Sac.
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Study: B85-0460
Compound: 60539.02
Start Date:

Two Generation Reproduction and Teratology

Individual Animal Cross Reference

Format	First Dose	Director	Metastatic Sites
None		G. Nolen	Included

	2	2	2	2	2	2
	6	6	6	7	7	6
	8	9	9	0	1	5
	6	4	7	5	5	9
Group:	3	3	3	3	3	4
Animal Sex (M or F):	M	M	M	M	M	M
Animal Removal Code (0-7,?):	0	0	0	0	0	0
Eye	-	-	-	-	-	-
Urinary Bladder	-	-	-	-	-	-
Testis	-	-	-	-	-	-
Prostate	-	-	-	-	-	-
Epididymis	-	-	-	-	-	-
Seminal Vesicle	-	-	-	-	-	-
Bone (Femur)	-	-	-	-	-	-
Marrow (Femur)	+	-	-	+	+	+
Hypercellular	3	.	.	3	2	3
Decreased metarubricytes	.	.	.	+	.	.
Marrow (Femur, Special Stain)	+	+	+	+	+	+
Negative	+	+	+	+	+	+
Skin, Ear	.	.	.	.	.	.
Eye, Right	-	.	.	?	-	.
Submandibular Lymph Node, Right	.	.	.	.	.	.
Skin, Eye	.	.	.	.	.	.
Testis, Right	.	.	.	.	.	.
Mesenteric Fat	.	.	.	.	.	.
Penis	.	.	.	.	.	.

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Removal Reason
0 = Terminal Sac.
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4 = Premature Sac.
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INDIVIDUAL ANIMAL CROSS REFERENCE TABLES (MALES, MORIBUND/DEATHS)

ANATOMIC PATHOLOGY
APPENDIX I