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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Research Triangle Park, NC 27709

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July 24, 2003

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Dear Document Control Office (7407):

In compliance with the National Toxicology Program's (NTP) mission to keep our colleagues informed of the current NTP findings during ongoing studies, a copy of the Pathology Working Group (PWG) report and the Summary Pathology Tables for the chronic Dosed Feed study on 2-METHYLIMIDAZOLE (693-98-1) are enclosed for your review.

The NTP assembles a Pathology Working Group to review every study and to resolve any differences between the study laboratory and quality assessment pathology evaluations. Please note that the PWG conclusion of the study results is based solely on the pathology for this study and may not reflect final NTP conclusions. In determining final conclusions, the NTP assesses a broad array of information that includes other results from this study and historical control data.

The Summary Pathology Tables contain the Incidence Rates of Neoplastic and Non-neoplastic Lesion data and the Statistical Analysis of Primary Tumors data pertaining to the laboratory animals. All study data are subject to an NTP retrospective audit and the interpretation may be modified based on the findings.

A wide variety of NTP information is also available in electronic format on the world-wide web, for example, the NTP Annual Plan, abstracts of NTP Reports, study data, and the status of all NTP studies. To view this information requires access to the internet and a Web browser such as Netscape Navigator or Internet Explorer. To access the NTP home page, use the URL <http://ntp-server.niehs.nih.gov/>. Comments on the usefulness of this site and suggestions for improvement are encouraged.

Please contact Central Data Management (CDM) at (919)541-3419 if you have any questions. You may also fax your requests for information to CDM at (919)541-3687 or send them via e-mail to cdm@niehs.nih.gov.



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Hard copies of documents such as NTP Technical Reports, short-term Toxicity Reports, and the Report on Carcinogens are available from the Environmental Health Information Service (EHIS). You can contact EHIS by phone at (919) 541-3841, by fax at (919)541-0273, or by e-mail at ehis@niehs.nih.gov.

Sincerely,

A handwritten signature in cursive script that reads "William Eastin".

William Eastin, Ph.D.
Head, Information Systems & Central Files
Environmental Toxicology Program

Encls: PWG Report and Pathology Summary Tables for Rats and Mice
cc: Central Data Management

NATIONAL TOXICOLOGY PROGRAM

TR-516 2-Methylimidazole

Pathology Tables - Rats Core Study

- * P03 - Incidence Rates of Non-Neoplastic Lesions
- * P05 - Incidence Rates of Neoplasms by Anatomic Site (systemic lesions abridged)
- * P08 - Statistical Analysis of Primary Tumors
- * P18 - Incidence Rates of Non-Neoplastic Lesions

Pathology Tables - Rats 27-Week Sac

- * P03 - Incidence Rates of Non-Neoplastic Lesions
- * P05 - Incidence Rates of Neoplasms by Anatomic Site (systemic lesions abridged)
- * P18 - Incidence Rates of Non-Neoplastic Lesions

Pathology Tables - Mice

- * P03 - Incidence Rates of Non-Neoplastic Lesions
- * P05 - Incidence Rates of Neoplasms by Anatomic Site (systemic lesions abridged)
- * P08 - Statistical Analysis of Primary Tumors
- * P18 - Incidence Rates of Non-Neoplastic Lesions

Pathology Tables - Mice 27-Week Sac

- * P03 - Incidence Rates of Non-Neoplastic Lesions
- * P05 - Incidence Rates of Neoplasms by Anatomic Site (systemic lesions abridged)
- * P18 - Incidence Rates of Non-Neoplastic Lesions

**PATHOLOGY WORKING GROUP
CHAIRPERSON'S REPORT**

**TWO YEAR CHRONIC STUDY OF 2-METHYLIMIDAZOLE (2-MI)
(C92012B92012-05) ADMINISTERED BY DOSED FEED IN MALE AND
FEMALE F344 RATS**

DATE OF PWG: October 22, 2002

LOCATION OF REVIEW: NIEHS, Research Triangle Park, NC

PARTICIPANTS:

Drs. Robert Sills (NIEHS – NTP Study Pathologist), Ronald Herbert (NIEHS), Gordon Flake (NIEHS), Gail Pearse (NIEHS), Georgette Hill (NIEHS), Darlene Dixon (NIEHS), John Peckham (EPL), Jim Maurer (PAI), Karen Cimon (EPL-QA Pathologist), Catherine Picut (ILS-PWG Chairperson), and Yoshiro Tani (NIEHS – observer).

SUMMARY OF FINDINGS FROM THE PWG:

The PWG convened to evaluate selected H&E slides from this two-year chronic study in F344 rats exposed to 2-Methylimidazole (2-MI) in food. The target organs are the thyroid gland in males and females, and the liver and spleen in females. The following is a summary of treatment-related lesions.

- **THYROID GLAND:** Chronic exposure of rats to 2-MI caused increased incidences and severities of follicular cell hyperplasia in both sexes; increased incidences of follicular cell adenomas and /or carcinomas in both sexes, and increased severities of mineralization of follicles in both sexes.
- **LIVER:** Treatment with 2-MI resulted in increased incidences and severities of granulomatous inflammation and bile duct hyperplasia in females.
- **SPLEEN:** Chronic exposure of rats to 2-MI caused increased incidences and severities of granulomatous inflammation in females.

INTRODUCTION:

2-Methylimidazole (2-MI) is an imidazole derivative used as an intermediate in the production of pharmaceuticals, photographic chemicals, dyes and pigments. 2-MI is also present in tobacco smoke, wine, soy sauce and other food products. It is formed when ammonia or molasses is added to livestock feed to enhance the nutritional value of food, and as a result, 2-MI is a contaminant of meat from livestock fed such enhanced feed.

STUDY DESIGN:

2-MI was administered to male rats at a dose level of 0 ppm (untreated), 300 ppm (low dose), 1000 ppm (mid dose), or 3000 ppm (high dose) for two years. In females, 2-MI was administered at dose levels of 0 ppm (untreated), 1000 ppm (low dose), 2500 ppm (mid dose), or 5000 ppm (high dose). There were 60 animals per dose group. Ten of these animals in each dose group were sacrificed at 27 weeks (interim sacrifice).

The study was conducted at Southern Research Institute, Birmingham, Alabama. The Study Pathologist (SP) was Dr. Daniel R. Farnell. The Quality Assessment Pathologist (QAP) was Dr. Karen Cimon of EPL.

CONDUCT OF THE PWG:

The PWG convened to review selected slides from F344 rats exposed to 2-MI in food for two years.

Before the PWG, the chairperson reviewed the laboratory reports and the SP's pathology narratives, the summary and individual animal pathology tables, the individual animal necropsy records, the pathology data review, the quality assessment reports, and microslides from the study. The PWG chairperson selected a set of slides for review by the PWG which included examples of treatment related lesions as well as slides for which there were differences of opinion in diagnoses among the SP, QAP or PWG chairperson. The PWG consensus opinion for each slide examined, including any additional diagnoses made by the PWG, was recorded on the PWG chairperson's worksheets attached to this report.

STUDY RESULTS:

Morbidity, Mortality, Clinical Signs, Organ Weights, Body Weight:

Treatment of rats with 2-MI caused a reduction in body weight gain in high dose male and high dose female rats. This reduction in body weight gain correlates to a decrease in food consumption in high dose males and females. The decrease in body weight gain was attributed to poor palatability of food rather than to a specific toxic effect of 2-MI.

The only clinical sign associated with 2-MI administration was a “thin” body condition in the high dose males and females.

Treatment of rats with 2-MI caused decreased survival in only the mid dose (2500 ppm) females. The following table shows the survival of animals per dose group.

Percent Survival Rate by Dose Group

Dose Group	Untreated	Low Dose	Mid Dose	High Dose
Males	68%	78%	70%	70%
Females	80%	78%	56%	82%

The following organ weight changes are attributable to the toxic effects of 2-MI administration. At study termination, there was a significant increase in absolute and relative thyroid gland weights in males and females; and an increase in *relative* liver weights in males and females. In addition, there was a statistically significant increase in the *relative* spleen weights in the females, but this increase was only seen at the 6 month time point and was not present at study termination.

Histopathology:

Thyroid Gland:

Follicular Cell Hyperplasia: There were increased incidences and severities of follicular cell hyperplasia in animals of both sexes from all groups of interim sacrifice and chronic sacrifice animals. There was good correlation between the SP and the QAP concerning this hyperplastic lesion in the thyroid gland. The PWG reviewed several examples of mild and moderate follicular cell hyperplasia in females and males, and the PWG unanimously confirmed the diagnosis. The PWG members discussed the possibility of separating the diagnoses of follicular cell hypertrophy from follicular cell hyperplasia, especially since hypertrophy and hyperplasia were made separate diagnoses in the related chronic mouse study. The PWG discussed how the non-neoplastic follicular cell lesion in rats was different from that seen in mice exposed to 2-MI. In mice, follicular cell hypertrophy occurred commonly as an isolated lesion without associated hyperplasia, especially in the interim sacrifice animals. In rats, epithelial cell hypertrophy did not occur as a solitary lesion without concomitant epithelial cell hyperplasia. The PWG decided by consensus it was appropriate to use one term (i.e., follicular cell hyperplasia) to classify the non-neoplastic lesion in the thyroid gland of rats.

Follicular cell hyperplasia was generally diffuse and characterized by a gland having an overall increased cellularity with an increase in the ratio of small follicles to large follicles. Typically the follicular epithelial cells were enlarged from low cuboidal to high cuboidal or tall columnar with increased amount of vacuolated cytoplasm. The

epithelial cells generally remained in a single layer. Commonly, colloid was rarified and less intensely stained. In a few cases, follicles were distended and had irregular, angular contours with invaginations and piling up of follicular epithelial cells.

Thyroid Gland Adenoma and Carcinoma: Chronic administration of 2-MI caused an increase in incidences of follicular cell adenomas or carcinomas in male and female rats. The histological appearance of these tumors was consistent with descriptions found in *Pathology of the Fischer Rat* (eds. Boorman, et al., 1990).

The PWG reviewed several examples of adenomas and carcinomas where there was no discrepancy in diagnoses between SP, QAP and PWG chairperson, and the PWG confirmed unanimously the diagnoses of the thyroid neoplasms. The PWG also reviewed any and all instances where there was a 2-way or 3-way disagreement between the SP, QAP and PWG chairperson in the diagnosis of a proliferative lesion in the thyroid gland. Each of these discrepancies was resolved by consensus opinion.

Follicular cell adenomas were unilateral or bilateral masses that were well-circumscribed, expansile, compressive, and generally non-encapsulated. The neoplastic follicular epithelium was single layered and consisted of complex papillary or follicular structures. The neoplastic epithelial cells exhibited atypia with an increase nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, and increased cytoplasmic basophilia. The adenomas in this study were commonly seen in association with diffuse follicular cell hyperplasia.

Follicular cell carcinomas were poorly circumscribed masses in one or both thyroid lobes and had a broad range of morphological patterns including papillary, follicular or solid variants. Significant cellular pleomorphism, atypia and invasion of the mass into the capsule or surrounding tissue were features that distinguished carcinomas from adenomas.

Follicle-Mineralization: Chronic administration of 2-MI was associated with a dose-related increase in mean severity of focal mineralization of thyroid follicles. There was excellent correlation between SP and QAP in the diagnosis and grading of follicle mineralization. The PWG examined several examples of follicle mineralization in the sections of thyroid gland and the panel confirmed unanimously the lesion.

Follicle mineralization was characterized by globular or ovoid-shaped bodies within the colloid of some follicles. These bodies stained intensely basophilic, and commonly had a concentric laminated appearance. They are a common background lesion; likely represent degenerative remnants of follicular epithelial cells; and may be referred to as corpora amylacea, calcospherules, or psammoma bodies. There was no mineralization of the intact follicular epithelial cells, the basement lamina or any part of the parenchyma of the thyroid gland. The toxic effect of 2-MI in this study exacerbated the incidence and severity of these mineralized bodies.

There was discussion that the term "follicle-mineralization" may be misleading since there is no mineralization of the thyroid gland parenchyma *per se*. In the absence of a better term available in TDMS, there was consensus agreement among panel members to maintain the terminology "follicle-mineralization" as a diagnosis for this lesion.

Liver:

Hepatocellular Adenomas and Carcinomas: There were differences in the diagnoses of hepatocellular adenoma or carcinoma between the SP, QAP, and PWG chairperson. Specifically, the PWG chairperson disagreed in many instances with the diagnosis of hepatocellular adenoma, and was of the opinion that many of the adenomas were hepatocellular foci. There was also some disagreement between the SP, QAP, and PWG chairperson regarding the diagnosis of hepatocellular carcinoma. The PWG reviewed several cases of hepatocellular adenomas and carcinomas with no discrepancy between the SP, QAP or PWG chairperson. The panel confirmed the diagnoses by consensus opinion. The PWG panel then reviewed all cases where there was disagreement in the diagnosis of adenoma vs. foci or adenoma vs. carcinoma. The PWG panel resolved each of these discrepancies by consensus opinion.

The criteria used by the PWG for classifying proliferative lesions as foci, adenomas or carcinomas were those outlined in the *Pathology of the F344 Rat (eds. Boorman, et al., 1990, pp. 77-83)*.

Mixed Cell Foci: There was fair agreement in the diagnoses of mixed cell foci between the SP and the QAP. In instances of disagreement, the QAP thought several of the lesions diagnosed by the SP as a mixed focus represented either a basophilic focus, focal vacuolization, or no lesion. All discrepancies in the diagnoses of mixed cell foci were presented to the PWG and these discrepancies were resolved by consensus opinion. Mixed cell foci appeared as well circumscribed areas composed mainly of a mixture of vacuolated hepatocytes and hepatocytes with abundant eosinophilic cytoplasm.

Due to the lack of summary tables with updated incidence profiles for mixed cell foci, the PWG was not in a position to confirm or comment on the biological significance of an increase in incidence of mixed cell foci in the high dose male and female rats.

Bile Duct Hyperplasia: There was excellent agreement between SP, QAP and PWG chairperson regarding the incidences and severities of bile duct hyperplasia in the chronic sacrifice females at dose levels 1000 ppm and 5000 ppm. Bile duct hyperplasia was regarded as a normal aging change in rats, which was accentuated by treatment with 2-MI. Bile duct hyperplasia consisted of increased numbers of small bile ducts in the portal areas with variable amounts of periductular fibrosis and mononuclear cell infiltrates. In general, the severity of the bile duct hyperplasia paralleled the severity of the granulomatous inflammation in the liver.

The PWG panel reviewed an example of the bile duct hyperplasia and confirmed unanimously the diagnosis of this lesion.

As part of a post-PWG action, the PWG chairperson determined whether the unusually low incidence of bile duct hyperplasia in mid dose females, as compared to the low and high dose females, may be due to the poor survival rate of animals in this group. Out of 22 early death animals in the mid dose females, 5/22 or 13% of the animals had bile duct hyperplasia. In contrast, out of the 28 animals in the mid dose females that survived until terminal sacrifice, 17/28 or 60% had bile duct hyperplasia. Further no female animal that survived less than 605 days on the study had a diagnosis of bile duct hyperplasia, except for one female animal (number 335) in the low dose group. This additional information suggests that the bile duct hyperplasia is a lesion that develops late in this study (generally after 600 days). Therefore, the high number of early deaths in the mid dose females may indeed account for the unusually low incidence of bile duct hyperplasia in this treatment group.

Liver and Spleen:

Granulomatous Inflammation in Liver: The PWG reviewed several examples of marked and moderate "histiocytic hyperplasia" in the livers of high dose female rats. These lesions were diagnosed by the SP as "liver, hyperplasia, histiocytic, focal". The QAP used the SP's terminology, and confirmed the findings of the SP. The QAP found additional animals having this lesion in the interim sacrifice female rats, and in the chronic sacrifice male rats at dose levels of 300 ppm and 1000 ppm.

The PWG was of unanimous decision that the lesion was more appropriately termed "granulomatous inflammation", and decided to globally change the diagnosis of "histiocytic hyperplasia" in the liver to "granulomatous inflammation".

There were dose-related increases in incidences and severities of granulomatous inflammation in the liver of female rats. Granulomatous inflammation was seen to some extent in all groups, and was considered a common focal background liver lesion. This lesion was seen near the portal areas, and consisted of aggregates of histiocytes and lymphocytes in varying proportions. The more advanced lesions consisted of clusters or whorls of histiocytes intermingled with or surrounded by a zone of lymphocytes. In some cases, the histiocytes contained finely granular pale golden brown pigment.

Granulomatous Inflammation in Spleen: There were dose-related increases in the incidences and severities of granulomatous inflammation in the spleens of females, and to a lesser extent, males. As in the liver, granulomatous inflammation of the spleen is considered a normal background lesion in aged rats. 2-MI apparently accentuates this otherwise normal background lesion. The lesion was observed in controls and in all treatment groups in females, and was observed in only the mid and high dose groups of males. As in the liver, this lesion was originally diagnosed as "histiocytic hyperplasia" by the SP and QAP. However, the PWG agreed unanimously that granulomatous inflammation was the more appropriate terminology for this lesion. The lesion was

similar histologically to that of granulomatous inflammation in the liver, in that it consisted of clusters of histiocytes surrounded by lymphocytes. In the spleen the lesion generally occupied a focal to locally extensive area. The pathogenesis of the granulomatous inflammation is not known, however, the PWG was of the opinion that 2-MI exaggerated the common background lesion.

The occurrence and severity of granulomatous inflammation in the spleen generally correlated with the occurrence and severity of this lesion in the liver. The lesion further correlates with the leukocytosis, seen in the high dose females.

There was excellent correlation between SP and QAP regarding the diagnosis of granulomatous inflammation in the spleen, and there were no discrepancies. The PWG reviewed an example of marked granulomatous inflammation, and unanimously agreed with the lesion as described by the SP and QAP.

Pituitary:

Mitotic Alteration: The SP reported "mitotic alteration" of the pars distalis of the pituitary in interim sacrifice female rats. This lesion consisted of an increase in the number of mitotic figures in the pars distalis; however, there is no increase in incidence in treated groups.

The PWG reviewed several photomicrographs of the pars distalis of animals with mitotic alteration and confirmed unanimously the lesion and the terminology, thereof.

Miscellaneous:

Clitoral Gland Adenomas or Carcinomas: The incidence of clitoral gland carcinomas was 5/50 in untreated female rats, and this incidence was out of the historical control range. The PWG reviewed two cases where there was discrepancy between the QAP and the PWG chairperson in the diagnosis of carcinoma of the clitoral gland. In both cases, the PWG agreed by consensus that one lesion represented an adenoma, and the other represented a squamous papilloma. The criteria for diagnosing the proliferative lesions of the clitoral gland were those described in the *Pathology of the F344 Rat*, p. 292.

C cell Adenomas: There was considerable discrepancy between the SP and QAP regarding the classification of proliferative C cell lesions in rats. The SP diagnosed C cell adenomas apparently when there was a discrete mass of C cells. The SP provided no criteria for the diagnosis of C cell adenoma in the narrative. The QAP on the other hand down graded many of these C cell adenomas to C cell hyperplasia. The QAP's criterium was that C cell adenomas are masses with a diameter of at least 5 contiguous follicles, in accordance with the *Pathology of the F344 Rat*, p. 531, and this criterium was agreed upon by the PWG. The PWG by unanimous decision agreed to globally accept the QAP's diagnoses of C cell proliferative lesions (i.e., hyperplasia and adenomas), which were

each verified by the PWG chairperson. The PWG did not review any slides of these discrepancies.

Basal Cell Carcinomas: There was a statistically significant increase in the incidence of basal cell carcinomas of the skin in high dose male rats. The PWG reviewed one such neoplasm involving a discrepancy in diagnosis between the SP, QAP or PWG chairperson. The panel unanimously decided the lesion represented a trichoepithelioma rather than a basal cell carcinoma. The PWG did not consider basal cell carcinomas to be related to 2-MI administration.

Other: Several additional discrepancies in diagnoses were presented to the PWG panel. These discrepancies included two preputial gland neoplasms, one metastatic lung neoplasm, one animal with a discrepancy in the diagnosis of cholangiofibrosis or cholangiocarcinoma in the liver, and one case involving a discrepancy in the diagnosis of bile duct hyperplasia or cholangiofibrosis in the liver. In all instances, the PWG resolved the discrepancies by consensus opinion.

HISTOTECHNIQUE QUALITY:

The histotechnique quality assessment indicated that the overall histological processing and slide preparation was good, with no artifacts that would interfere with the interpretation of tissue sections.



Catherine A. Picut, VMD, JD
Diplomate, ACVP
PWG Chairperson

12/9/02
Date

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLMIDAZOLE

Report: PEIRPT03
Date: 02/24/03
Time: 14:19:18

FINAL #1/RATS

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25019 Moribund Sacrifice 25020 Natural Death
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
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Report: PEIRPT03
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FINAL #1/RAFS

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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS FEMALE OPPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Disposition	0 PPM	1000 PPM	2500 PPM	5000 PPM
Animals Initially In Study	60	60	60	60
Early Deaths				
Natural Death	4	3	10	1
Moribund Sacrifice	6	8	12	7
Survivors				
Terminal Sacrifice	40	39	28	41
Natural Death				1
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(48)	(47)	(44)	(50)
Edema				1 (2%)
Intestine Small, Jejunum	(47)	(46)	(44)	(49)
Necrosis, Focal				1 (2%)
Liver				(50)
Angiectasis, Focal	(50)	(49)	(50)	
Basophilic Focus	2 (4%)	1 (2%)	2 (4%)	39 (78%)
Cholangiofibrosis	42 (84%)	44 (90%)	43 (86%)	1 (2%)
Congestion				1 (2%)
Congestion, Focal		1 (2%)		
Degeneration, Cystic, Focal				2 (4%)
Eosinophilic Focus		2 (4%)		
Fatty Change			1 (2%)	
Hemorrhage	2 (4%)		1 (2%)	
Hepatodiaphragmatic Nodule	6 (12%)		1 (2%)	
Hyperplasia, Focal, Lymphoid		11 (22%)	14 (28%)	2 (4%)
Infarct				13 (26%)
Infiltration Cellular, Mixed Cell	42 (84%)	44 (90%)	34 (68%)	2 (4%)
Inflammation, Granulomatous	18 (36%)	23 (47%)	22 (44%)	38 (76%)
Mixed Cell Focus	15 (30%)	14 (29%)	11 (22%)	42 (84%)
Necrosis, Focal		1 (2%)		26 (52%)
Bile Duct, Cholangiofibrosis, Focal			1 (2%)	
Bile Duct, Cyst	2 (4%)			1 (2%)
Bile Duct, Cyst, Multiple				40 (80%)
Bile Duct, Hyperplasia	20 (40%)	29 (59%)	20 (40%)	2 (4%)
Hepatocyte, Necrosis, Focal				1 (2%)
Hepatocyte, Vacuolization Cytoplasmic, Focal	9 (18%)	10 (20%)	11 (22%)	9 (18%)
Hepatocyte, Periportal, Vacuolization Cytoplasmic				1 (2%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
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Report: PEIRPT03
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FISCHER 344 RATS FEMALE	0PPM	1000 PPM	2500 PPM	5000 PPM
ALIMENTARY SYSTEM - CONT				
Hepatocyte, Centrilobular, Necrosis			1 (2%)	1 (2%)
Hepatocyte, Centrilobular, Vacuolization			4 (8%)	1 (2%)
Cytoplasmic	1 (2%)	(10)	(12)	(9)
Mesentery	(8)	1 (10%)		
Fibrosis				1 (11%)
Hemorrhage, Focal			1 (8%)	
Infiltration Cellular, Mixed Cell		1 (10%)		
Inflammation, Chronic		1 (10%)		1 (11%)
Artery, Inflammation, Chronic, Focal		7 (70%)		
Fat, Necrosis			2 (17%)	
Fat, Necrosis, Focal	5 (63%)	1 (10%)	6 (50%)	3 (33%)
Pancreas	(50)	(49)	(49)	(50)
Infiltration Cellular, Diffuse, Mixed Cell		1 (2%)		1 (2%)
Acinus, Atrophy, Diffuse	1 (2%)	1 (2%)		11 (22%)
Acinus, Atrophy, Focal	13 (26%)	14 (29%)		1 (2%)
Duct, Cyst, Focal	1 (2%)			5 (10%)
Duct, Cyst, Focal, Multiple	9 (18%)	12 (24%)		(50)
Salivary Glands	(50)	(49)	4 (8%)	(50)
Duct, Mineralization, Focal				2 (4%)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Diverticulum	1 (2%)	1 (2%)		2 (4%)
Edema				1 (2%)
Erosion				1 (2%)
Inflammation, Chronic		1 (2%)		1 (2%)
Inflammation, Focal				1 (2%)
Ulcer		2 (4%)		1 (2%)
Epithelium, Hyperplasia	3 (6%)	1 (2%)	4 (8%)	1 (2%)
Stomach, Glandular	(49)	(49)	(48)	(50)
Erosion		1 (2%)		1 (2%)
Inflammation, Chronic			1 (2%)	
Necrosis, Focal			1 (2%)	
Ulcer				1 (2%)
Epithelium, Hyperplasia, Focal	1 (2%)			
Glands, Degeneration, Cystic, Focal	1 (2%)		1 (2%)	
Glands, Ectasia, Focal				
Glands, Hyperplasia, Focal	1 (2%)			
Tongue				2 (4%)
Epithelium, Hyperplasia, Focal	(3)		(1)	
Tooth	1 (33%)			
Peridental Tissue, Inflammation, Chronic	(1)			
	1 (100%)			

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLIMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS FEMALE

0PPM

1000 PPM

2500 PPM

5000 PPM

CARDIOVASCULAR SYSTEM

Heart	(50)	(49)	(50)	(50)
Cardiomyopathy	5 (10%)	8 (16%)	7 (14%)	6 (12%)
Infiltration Cellular, Mixed Cell		4 (8%)	3 (6%)	2 (4%)

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(49)	(50)	(50)
Accessory Adrenal Cortical Nodule	2 (4%)	2 (4%)	5 (10%)	5 (10%)
Angiectasis	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Cytoplasmic Alteration, Focal	3 (6%)		1 (2%)	5 (10%)
Hematopoietic Cell Proliferation		1 (2%)		
Hemorrhage		1 (2%)		
Hemorrhage, Focal		1 (2%)		
Vacuolization Cytoplasmic, Focal	8 (16%)	3 (6%)	7 (14%)	12 (24%)
Adrenal Medulla	(49)	(49)	(50)	(50)
Hyperplasia, Focal	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Pituitary Gland	(50)	(48)	(50)	(50)
Angiectasis	5 (10%)	9 (19%)	7 (14%)	2 (4%)
Cyst		1 (2%)		
Hemorrhage		1 (2%)		
Metaplasia, Focal, Lipocyte		1 (2%)	1 (2%)	1 (2%)
Pars Distalis, Angiectasis		3 (6%)	2 (4%)	1 (2%)
Pars Distalis, Cyst	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Pars Distalis, Cyst, Multiple		4 (8%)	1 (2%)	3 (6%)
Pars Distalis, Cytoplasmic Alteration, Focal	4 (8%)			
Pars Distalis, Degeneration, Cystic	1 (2%)			
Pars Distalis, Degeneration, Cystic, Focal	9 (18%)	14 (29%)	8 (16%)	5 (10%)
Pars Distalis, Hemorrhage, Focal	1 (2%)	3 (6%)	4 (8%)	6 (12%)
Pars Distalis, Hyperplasia, Focal		1 (2%)	1 (2%)	1 (2%)
Pars Distalis, Pigmentation, Focal			1 (2%)	
Pars Intermedia, Cyst			1 (2%)	3 (6%)
Pars Intermedia, Degeneration, Cystic, Focal				1 (2%)
Pars Intermedia, Hemorrhage				1 (2%)
Pars Intermedia, Pars Nervosa, Atypia				1 (2%)
Cellular, Focal		1 (2%)		
Rathke's Cleft, Cyst	1 (2%)		1 (2%)	
Rathke's Cleft, Hemorrhage				2 (4%)
Thyroid Gland	(49)	(48)	(42)	(48)
Vacuolization Cytoplasmic, Focal	48 (98%)	46 (96%)	40 (95%)	25 (52%)
C-Cell, Hyperplasia		2 (4%)	1 (2%)	
Follicle, Cyst				

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS FEMALE

0PPM

1000 PPM

2500 PPM

5000 PPM

ENDOCRINE SYSTEM - CONT

Follicle, Mineralization, Focal
 Follicular Cell, Hyperplasia

42 (86%)

47 (98%)
 41 (85%)

41 (98%)
 34 (81%)

48 (100%)
 46 (96%)

GENERAL BODY SYSTEM

Tissue NOS
 Mediastinum, Infiltration Cellular, Mixed
 Cell
 Pelvic, Hemorrhage, Focal
 Thoracic, Infiltration Cellular, Focal,
 Mixed Cell

(3)

(4)

(2)

1 (25%)
 1 (50%)

1 (25%)

GENITAL SYSTEM

Clitoral Gland
 Degeneration, Cystic
 Fibrosis, Focal
 Hyperplasia, Cystic
 Inflammation, Chronic
 Ovary
 Angiectasis
 Atrophy
 Congestion
 Cyst
 Bilateral, Cyst, Multiple
 Periovarian Tissue, Cyst
 Periovarian Tissue, Cyst, Multiple
 Uterus
 Cyst
 Hemorrhage
 Inflammation, Chronic
 Cervix, Hyperplasia
 Endometrium, Hyperplasia, Cystic
 Vagina
 Inflammation, Chronic
 Epithelium, Cyst

(50)

6 (12%)

1 (2%)

2 (4%)

(50)

1 (2%)

1 (2%)

5 (10%)

4 (8%)

1 (2%)

(50)

3 (6%)

5 (10%)

4 (8%)

1 (2%)

(50)

10 (20%)

(2)

1 (50%)

(49)

4 (8%)

1 (2%)

4 (8%)

5 (10%)

(49)

1 (2%)

1 (2%)

5 (10%)

5 (10%)

5 (10%)

5 (10%)

(50)

1 (2%)

2 (4%)

1 (2%)

15 (30%)

(2)

1 (50%)

(50)

1 (2%)

1 (2%)

1 (2%)

(50)

6 (12%)

(50)

1 (2%)

1 (2%)

1 (2%)

15 (30%)

(2)

1 (50%)

HEMATOPOIETIC SYSTEM

Bone Marrow

(49)

(50)

(50)

(50)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

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HEMATOPOIETIC SYSTEM - CONT	FISCHER 344 RATS FEMALE			
	0PPM	1000 PPM	2500 PPM	5000 PPM
Atrophy	1 (2%)			
Fibrosis		1 (2%)		1 (2%)
Hyperplasia, Focal, Histiocytic				4 (8%)
Myelofibrosis				1 (2%)
Necrosis				1 (2%)
Myeloid Cell, Hyperplasia	2 (4%)	3 (6%)	5 (10%)	2 (4%)
Myeloid Cell, Erythroid Cell, Hyperplasia	(32)	2 (4%)	1 (2%)	
Lymph Node		(31)	(34)	(41)
Deep Cervical, Hemorrhage	1 (3%)			2 (5%)
Mediastinal, Angiectasis				
Mediastinal, Congestion				
Mediastinal, Ectasia	5 (16%)	3 (10%)	1 (3%)	7 (17%)
Mediastinal, Hemorrhage	2 (6%)	3 (10%)	2 (6%)	8 (20%)
Mediastinal, Hyperplasia		1 (3%)	2 (6%)	
Mediastinal, Hyperplasia, Histiocytic	8 (25%)	8 (26%)	5 (15%)	12 (29%)
Mediastinal, Hyperplasia, Lymphoid		1 (3%)	1 (3%)	1 (2%)
Mediastinal, Pigmentation	1 (3%)		2 (6%)	
Pancreatic, Atrophy		1 (3%)		
Pancreatic, Ectasia	2 (6%)	2 (6%)		11 (27%)
Pancreatic, Hemorrhage	5 (16%)	3 (10%)	2 (6%)	9 (22%)
Pancreatic, Hyperplasia, Histiocytic	16 (50%)	24 (77%)	17 (50%)	18 (44%)
Pancreatic, Hyperplasia, Plasma Cell	1 (3%)			
Pancreatic, Infiltration Cellular, Mixed Cell	4 (13%)	2 (6%)		1 (2%)
Pancreatic, Pigmentation	(5)	(4)	(5)	1 (2%)
Lymph Node, Mandibular	1 (20%)			(1)
Ectasia	(49)	(49)	(49)	(50)
Lymph Node, Mesenteric				
Angiectasis				
Ectasia	1 (2%)			5 (10%)
Hemorrhage	1 (2%)			2 (4%)
Hyperplasia, Histiocytic	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Hyperplasia, Lymphoid				
Pigmentation	2 (4%)	1 (2%)		
Spleen	(50)	(49)	(48)	(50)
Accessory Spleen		1 (2%)		
Angiectasis, Focal		1 (2%)		
Congestion		1 (2%)		
Fibrosis, Focal		1 (2%)		
Hematopoietic Cell Proliferation	6 (12%)	8 (16%)	1 (2%)	4 (8%)
Hemorrhage				
Infarct				
Inflammation, Granulomatous	3 (6%)	2 (4%)	4 (8%)	1 (2%)
Pigmentation		1 (2%)		27 (54%)

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NTP Experiment-Test: 92012-05
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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

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FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

HEMATOPOIETIC SYSTEM - CONT	0PPM	1000 PPM	2500 PPM	5000 PPM
Pigmentation, Focal	1 (2%)	1 (2%)	1 (2%)	(49)
Thymus	(48)	(45)	(49)	
Angiectasis			2 (4%)	
Hyperplasia, Lymphoid	1 (2%)	1 (2%)		2 (4%)

INTEGUMENTARY SYSTEM

Mammary Gland	(50)	(50)	(50)	(50)
Dilatation	33 (66%)	35 (70%)	22 (44%)	19 (38%)
Ectasia	2 (4%)	3 (6%)	7 (14%)	
Fibrosis		1 (2%)		
Hyperplasia		5 (10%)	4 (8%)	3 (6%)
Hyperplasia, Cystic	3 (6%)		2 (4%)	
Inflammation, Focal	1 (2%)			
Skin		1 (2%)		
Necrosis, Focal	(50)	(50)	(50)	(50)
Ulcer				4 (8%)
Subcutaneous Tissue, Angiectasis, Focal			1 (2%)	1 (2%)
Subcutaneous Tissue, Hemorrhage, Focal				1 (2%)
Subcutaneous Tissue, Inflammation, Focal, Suppurative				1 (2%)

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

Brain	(50)	(49)	(50)	(50)
Compression, Focal	10 (20%)	8 (16%)	12 (24%)	4 (8%)
Hemorrhage, Focal	2 (4%)	1 (2%)	2 (4%)	
Necrosis, Focal			1 (2%)	
Pigmentation, Focal			1 (2%)	
Cerebellum, Developmental Malformation			1 (2%)	
Spinal Cord	(3)	(1)	(4)	
Hemorrhage, Focal	1 (33%)			
Necrosis, Focal	1 (33%)			

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NTP Experiment--Test: 92012-05
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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLLIMIDAZOLE

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FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

RESPIRATORY SYSTEM

	0PPM	1000 PPM	2500 PPM	5000 PPM
Lung	(50)	(49)	(50)	(50)
Congestion	2 (4%)	4 (8%)	2 (4%)	2 (4%)
Emphysema			1 (2%)	
Hemorrhage	1 (2%)			2 (4%)
Hemorrhage, Focal	1 (2%)			1 (2%)
Hyperplasia, Focal, Histiocytic		6 (12%)	1 (2%)	1 (2%)
Hyperplasia, Focal, Histiocytic	6 (12%)		7 (14%)	1 (2%)
Infiltration Cellular, Focal, Mixed Cell		3 (6%)	1 (2%)	6 (12%)
Infiltration Cellular, Mixed Cell	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Inflammation, Chronic, Focal	1 (2%)			1 (2%)
Inflammation, Focal, Granulomatous	1 (2%)			1 (2%)
Pigmentation, Focal	7 (14%)	5 (10%)	3 (6%)	3 (6%)
Alveolar Epithelium, Hyperplasia, Focal			1 (2%)	1 (2%)
Alveolus, Inflammation, Focal, Granulomatous				
Interstitialium, Edema	(50)	(49)	(50)	(50)
Nose				
Foreign Body	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Inflammation, Suppurative	4 (8%)	2 (4%)	4 (8%)	2 (4%)
Nasolacrimal Duct, Inflammation				

SPECIAL SENSES SYSTEM

Eye	(50)	(49)	(49)	(50)
Atrophy	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Cataract	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Iris, Synechia		2 (4%)	1 (2%)	1 (2%)
Retina, Degeneration	(50)	(49)	(50)	(50)
Harderian Gland	1 (2%)		1 (2%)	1 (2%)
Hyperplasia, Cystic, Focal	2 (4%)	2 (4%)	1 (2%)	4 (8%)
Hyperplasia, Focal	1 (2%)		3 (6%)	1 (2%)
Hyperplasia, Focal, Histiocytic			1 (2%)	
Inflammation, Chronic, Focal			1 (2%)	
Inflammation, Focal, Granulomatous		2 (4%)	2 (4%)	1 (2%)
Epithelium, Hyperplasia, Focal				

URINARY SYSTEM

Kidney	(50)	(48)	(47)	(50)
Atrophy, Focal		2 (4%)	1 (2%)	
Congestion			2 (4%)	

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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
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FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

URINARY SYSTEM - CONT	0PPM	1000 PPM	2500 PPM	5000 PPM
Cyst			1 (2%)	1 (2%)
Infarct				40 (80%)
Nephropathy			38 (81%)	1 (2%)
Glomerulus, Amyloid Deposition, Diffuse	38 (76%)	40 (83%)		
Pelvis, Inflammation			1 (2%)	
Renal Tubule, Accumulation, Hyaline Droplet	11 (22%)	7 (15%)	3 (6%)	4 (8%)
Renal Tubule, Pigmentation	8 (16%)	4 (8%)	5 (11%)	
Urethra				(2)
Transitional Epithelium, Hyperplasia, Diffuse	(50)	(49)	(49)	1 (50%)
Urinary Bladder				(50)
Transitional Epithelium, Hyperplasia				2 (4%)

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FISCHER 344 RATS MALE

OPPM

300 PPM

1000 PPM

3000 PPM

DISPOSITION SUMMARY

Animals Initially In Study 60
 Early Deaths 60
 Moribund Sacrifice 13
 Natural Death 2
 Survivors 34
 Terminal Sacrifice 1
 Moribund Sacrifice 39
 Natural Death 1

Animals Examined Microscopically 50 50 50 50 50

ALIMENTARY SYSTEM

Intestine Large, Rectum	(49)	(48)	(48)	(50)
Angiectasis, Focal			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Angiectasis, Focal	23 (46%)	23 (46%)	8 (16%)	2 (4%)
Basophilic Focus	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Cholangiofibrosis			2 (4%)	1 (2%)
Congestion			2 (4%)	7 (14%)
Degeneration, Cystic, Focal	4 (8%)	3 (6%)	6 (12%)	1 (2%)
Eosinophilic Focus	3 (6%)		1 (2%)	
Fibrosis, Focal			4 (8%)	2 (4%)
Hematopoietic Cell Proliferation	6 (12%)	5 (10%)	4 (8%)	9 (18%)
Hepatodiaphragmatic Nodule	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Hyperplasia, Focal, Lymphoid	25 (50%)	30 (60%)	27 (54%)	36 (72%)
Infiltration Cellular, Mixed Cell	12 (24%)	11 (22%)	4 (8%)	11 (22%)
Inflammation, Granulomatous	14 (28%)	16 (32%)	23 (46%)	26 (52%)
Mixed Cell Focus			2 (4%)	1 (2%)
Necrosis, Focal	2 (4%)		2 (4%)	
Pigmentation, Focal			2 (4%)	
Bile Duct, Cyst			47 (94%)	49 (98%)
Bile Duct, Hyperplasia	49 (98%)	49 (98%)	1 (2%)	
Centrilobular, Congestion	1 (2%)	1 (2%)	3 (6%)	2 (4%)
Hepatocyte, Necrosis, Focal			1 (2%)	1 (2%)
Hepatocyte, Vacuolization Cytoplasmic, Diffuse	23 (46%)	30 (60%)	26 (52%)	23 (46%)
Hepatocyte, Vacuolization Cytoplasmic, Focal		2 (4%)		
Hepatocyte, Centrilobular, Necrosis			2 (4%)	
Hepatocyte, Centrilobular, Vacuolization Cytoplasmic	5 (10%)	4 (8%)		3 (6%)

a Number of animals examined microscopically at site and number of animals with lesion

ALIMENTARY SYSTEM - CONT	FISCHER 344 RATS MALE				
	0PPM	300 PPM	1000 PPM	3000 PPM	
Hepatocyte, Midzonal, Vacuolization					
Cytoplasmic	1 (2%)	1 (2%)	2 (4%)	1 (2%)	
Oval Cell, Hyperplasia					
Serosa, Fibrosis, Focal		2 (4%)			
Mesentery	(26)	(46)	(35)	(20)	
Fibrosis, Focal				1 (5%)	
Hemorrhage				2 (10%)	
Necrosis, Focal				1 (5%)	
Artery, Inflammation, Chronic				1 (5%)	
Fat, Necrosis	1 (4%)	1 (2%)	2 (6%)		
Fat, Necrosis, Focal	8 (31%)	10 (22%)	16 (46%)	10 (50%)	
Pancreas	(49)	(49)	(50)	(50)	
Atrophy, Diffuse					
Atrophy, Focal					
Fibrosis, Focal					
Acinus, Atrophy, Diffuse					
Acinus, Atrophy, Focal					
Acinus, Hyperplasia, Focal	22 (45%)	1 (2%)	20 (40%)	36 (72%)	
Duct, Cyst	1 (2%)		1 (2%)		
Duct, Cyst, Focal					
Duct, Cyst, Multiple		1 (2%)	5 (10%)	12 (24%)	
Duct, Hyperplasia, Cystic	6 (12%)	2 (4%)	1 (2%)		
Duct, Hyperplasia, Cystic, Focal					
Duct, Hyperplasia, Focal		2 (4%)	3 (6%)		
Salivary Glands	(50)	(50)	(50)	(50)	
Atrophy, Focal					
Inflammation, Chronic					
Stomach, Fore stomach					
Diverticulum	(50)	(50)	(50)	(50)	
Edema	1 (2%)	1 (2%)	2 (4%)		
Erosion	1 (2%)				
Inflammation, Focal					
Ulcer					
Epithelium, Hyperplasia	1 (2%)	1 (2%)	1 (2%)		
Epithelium, Hyperplasia, Focal	2 (4%)	3 (6%)			
Serosa, Foreign Body					
Serosa, Inflammation, Chronic, Focal					
Stomach, Glandular					
Erosion	(50)	(50)	(50)	(50)	
Erosion, Focal	4 (8%)	1 (2%)	1 (2%)		
Inflammation, Focal	1 (2%)				
Ulcer	1 (2%)				
Epithelium, Necrosis, Focal	2 (4%)			1 (2%)	

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PETRPT03
 Date: 02/24/03
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FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

ALIMENTARY SYSTEM - CONT

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Glands, Hyperplasia, Cystic, Focal	1 (2%)	1 (2%)		
Glands, Hyperplasia, Focal	1 (1)	2		1 (1)
Tongue				1 (100%)
Epithelium, Hyperplasia, Focal	1 (1)	1 (1)	1 (1)	2 (2)
Tooth				
Malformation				
Periodontal Tissue, Inflammation	1 (100%)			1 (50%)
Periodontal Tissue, Inflammation, Chronic				
Periodontal Tissue, Inflammation, Focal, Suppurative			1 (100%)	

CARDIOVASCULAR SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Heart				
Cardiomyopathy	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Cardiomyopathy, Focal	3 (6%)	5 (10%)	10 (20%)	5 (10%)
Congestion			2 (4%)	1 (2%)
Fibrosis			1 (2%)	1 (2%)
Infiltration Cellular, Mixed Cell		1 (2%)		
Thrombosis	1 (2%)	1 (2%)		
Endocardium, Myocardium, Fibrosis, Focal	1 (2%)			

ENDOCRINE SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Adrenal Cortex	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Accessory Adrenal Cortical Nodule	1 (2%)	4 (8%)	9 (18%)	5 (10%)
Cytoplasmic Alteration, Focal	2 (4%)	1 (2%)	1 (2%)	3 (6%)
Degeneration, Cystic, Focal			1 (2%)	
Hemorrhage	2 (4%)			
Vacuolization Cytoplasmic, Focal	6 (12%)	9 (18%)	10 (20%)	10 (20%)
Adrenal Medulla	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Angiectasis		1 (2%)		
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Hyperplasia, Focal	7 (14%)	5 (10%)	3 (6%)	7 (14%)
Infiltration Cellular, Lymphoid		1 (2%)		
Vacuolization Cytoplasmic, Focal		1 (2%)		
Islets, Pancreatic	1 (50%)	1 (49)	1 (50)	1 (50)
Atrophy		1 (2%)		
Hyperplasia, Focal		2 (4%)	1 (2%)	1 (2%)
Parathyroid Gland	1 (47)	1 (49)	1 (48)	1 (49)
Cyst		1 (2%)		

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FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

ENDOCRINE SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Hyperplasia	1 (2%)		1 (2%)	1 (2%)
Hyperplasia, Focal	1 (2%)			
Bilateral, Hyperplasia, Focal	(50)	(50)	(50)	(50)
Pituitary Gland	2 (4%)	2 (4%)	3 (6%)	1 (2%)
Angiectasis	3 (6%)	4 (8%)	2 (4%)	3 (6%)
Pars Distalis, Angiectasis	1 (2%)	4 (8%)	2 (4%)	5 (10%)
Pars Distalis, Cyst	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Pars Distalis, Cytoplastic Alteration, Focal	1 (2%)	1 (2%)		2 (4%)
Pars Distalis, Degeneration, Cystic, Focal	2 (4%)	1 (2%)		
Pars Distalis, Hyperplasia, Focal			1 (2%)	
Pars Distalis, Inflammation, Chronic, Focal, Granulomatous		1 (2%)	1 (2%)	
Pars Distalis, Pars Intermedia, Angiectasis		2 (4%)		1 (2%)
Pars Intermedia, Cyst		1 (2%)		
Pars Intermedia, Hemorrhage				
Pars Intermedia, Hyperplasia, Focal		1 (2%)		
Pars Nervosa, Infiltration Cellular, Focal, Mixed Cell	(48)	(46)	1 (2%)	(50)
Thyroid Gland		1 (2%)	(43)	
Cyst	41 (85%)	43 (93%)	38 (88%)	34 (68%)
C-Cell, Hyperplasia	1 (2%)			1 (2%)
Follicle, Cyst	48 (100%)	45 (98%)	43 (100%)	49 (98%)
Follicle, Mineralization, Focal	1 (2%)	17 (37%)	37 (86%)	42 (84%)
Follicular Cell, Atrophy, Focal				1 (2%)
Follicular Cell, Hyperplasia				1 (2%)
Follicular Cell, Hyperplasia, Cystic, Focal	1 (2%)			
Follicular Cell, Hyperplasia, Focal				

GENERAL BODY SYSTEM

Tissue NOS	(7)	(2)	(6)	(4)
Mediastinum, Hemorrhage				1 (25%)
Thoracic, Hemorrhage				1 (25%)

GENITAL SYSTEM

Epididymis	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		1 (2%)
Granuloma Sperm		1 (2%)		1 (2%)
Inflammation, Chronic		1 (2%)		1 (2%)
Preputial Gland	(50)	(50)	(50)	(50)

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FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

GENITAL SYSTEM - CONT

Cyst	1 (2%)				2 (4%)
Degeneration, Cystic					
Hyperplasia				1 (2%)	1 (2%)
Hyperplasia, Cystic	2 (4%)			2 (4%)	1 (2%)
Hyperplasia, Focal	1 (2%)				
Inflammation, Chronic	4 (8%)		10 (20%)	10 (20%)	11 (22%)
Inflammation, Chronic, Focal			1 (2%)	1 (2%)	2 (4%)
Inflammation, Suppurative			1 (2%)	1 (2%)	2 (4%)
Prostate	(50)	(50)	(50)	(50)	(50)
Atrophy	1 (2%)				
Hyperplasia, Focal		1 (2%)			
Inflammation, Chronic	15 (30%)	10 (20%)		17 (34%)	19 (38%)
Epithelium, Degeneration, Focal, Mucoid	1 (2%)				
Epithelium, Hyperplasia, Focal	4 (8%)	2 (4%)		(50)	5 (10%)
Testes	(50)	(50)	(50)	(50)	(50)
Atrophy	5 (10%)	4 (8%)		13 (26%)	13 (26%)
Mineralization, Focal	1 (2%)				
Bilateral, Atrophy	2 (4%)				
Bilateral, Interstitial Cell, Hyperplasia, Focal		3 (6%)		2 (4%)	
Germinal Epithelium, Atrophy	2 (4%)	3 (6%)		1 (2%)	2 (4%)
Interstitial Cell, Hyperplasia		2 (4%)		1 (2%)	1 (2%)
Interstitial Cell, Hyperplasia, Focal	1 (2%)	4 (8%)		4 (8%)	9 (18%)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(47)	(50)
Fibrosis			1 (2%)	
Hyperplasia		1 (2%)		
Hyperplasia, Focal, Histiocytic		1 (2%)		
Myeloid Cell, Hyperplasia	(39)	1 (2%)	1 (2%)	5 (10%)
Lymph Node		(49)	(42)	(38)
Hemorrhage				1 (3%)
Hyperplasia, Lymphoid			1 (2%)	
Mediastinal, Angiectasis			1 (2%)	
Mediastinal, Congestion			1 (2%)	
Mediastinal, Ectasia	1 (3%)			1 (3%)
Mediastinal, Hemorrhage	1 (3%)	1 (2%)		1 (3%)
Mediastinal, Hyperplasia, Histiocytic	2 (5%)	1 (2%)		4 (11%)
Mediastinal, Hyperplasia, Lymphoid	1 (3%)	1 (2%)		1 (3%)
Mediastinal, Pigmentation		1 (2%)		1 (3%)
Pancreatic, Angiectasis	1 (3%)			1 (3%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

HEMATOPOIETIC SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Pancreatic, Ectasia	1 (3%)	3 (6%)	3 (7%)	2 (5%)
Pancreatic, Hemorrhage	1 (3%)		1 (2%)	4 (11%)
Pancreatic, Hyperplasia, Focal, Histiocytic	1 (3%)			
Pancreatic, Hyperplasia, Histiocytic	13 (33%)	12 (24%)	15 (36%)	19 (50%)
Pancreatic, Hyperplasia, Lymphoid			1 (2%)	1 (3%)
Pancreatic, Pigmentation	1 (3%)			1 (3%)
Lymph Node, Mandibular	(2)	(1)	(2)	(2)
Hyperplasia, Plasma Cell			1 (50%)	
Lymph Node, Mesenteric	(47)	(50)	(50)	(50)
Ectasia		2 (4%)		2 (4%)
Hemorrhage			1 (2%)	1 (2%)
Hyperplasia, Histiocytic	1 (2%)	2 (4%)	1 (2%)	4 (8%)
Hyperplasia, Lymphoid	2 (4%)	1 (2%)	1 (2%)	
Spleen	(49)	(49)	(50)	(50)
Angiectasis, Focal	1 (2%)		1 (2%)	1 (2%)
Congestion				
Cyst		1 (2%)		
Fibrosis, Focal	2 (4%)		2 (4%)	1 (2%)
Hematopoietic Cell Proliferation	4 (8%)	4 (8%)	1 (2%)	6 (12%)
Hemorrhage			1 (2%)	
Hemorrhage, Focal			2 (4%)	1 (2%)
Hyperplasia, Lymphoid				
Infarct	1 (2%)	1 (2%)		
Inflammation, Granulomatous			2 (4%)	3 (6%)
Necrosis, Focal	1 (2%)		1 (2%)	1 (2%)
Pigmentation			1 (2%)	
Capsule, Fibrosis, Focal	1 (2%)		(44)	(49)
Thymus	(48)	(48)		
Atrophy	1 (2%)	1 (2%)		
Cyst, Multiple	1 (2%)			
Hemorrhage	1 (2%)			
Hyperplasia, Lymphoid	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Epithelial Cell, Cyst, Multiple				
Epithelial Cell, Hyperplasia	1 (2%)	1 (2%)		

INTEGUMENTARY SYSTEM

Mammary Gland	(48)	(47)	(45)	(42)
Dilatation	7 (15%)	1 (2%)	3 (7%)	2 (5%)
Ectasia			1 (2%)	
Hyperplasia	2 (4%)			1 (2%)
Hyperplasia, Cystic				

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PETRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

INTEGUMENTARY SYSTEM - CONT

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Epithelium, Pigmentation	(50)	1 (2%) (50)	(50)	(50)
Skin		1 (2%) (50)		
Angiectasis, Focal			1 (2%)	1 (2%)
Cyst Epithelial Inclusion				1 (2%)
Fibrosis, Focal				1 (2%)
Hemorrhage, Focal				1 (2%)
Inflammation, Chronic, Focal			1 (2%)	1 (2%)
Necrosis, Focal				1 (2%)
Pinna, Necrosis, Focal	1 (2%)			1 (2%)
Subcutaneous Tissue, Angiectasis, Focal				1 (2%)
Subcutaneous Tissue, Cyst				1 (2%)
Subcutaneous Tissue, Foreign Body				1 (2%)
Subcutaneous Tissue, Hemorrhage, Focal				1 (2%)

MUSCULOSKELETAL SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Skeletal Muscle	(2)	(1)	(1)	(4)
Fibrosis, Focal				1 (25%)

NERVOUS SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Brain	(50)	(50)	(50)	(50)
Compression, Focal	4 (8%)	2 (4%)	4 (8%)	1 (2%)
Hemorrhage, Focal	2 (4%)	3 (6%)	2 (4%)	1 (2%)
Necrosis, Focal	1 (2%)	1 (2%)		
Spinal Cord	(1)		(1)	
Hemorrhage, Focal			1 (100%)	
Mineralization, Focal			1 (100%)	
Necrosis, Focal			1 (100%)	

RESPIRATORY SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Larynx			(1)	(1)
Glands, Hyperplasia, Focal				1 (100%)
Lung	(50)	(50)	(50)	(50)
Congestion	1 (2%)		1 (2%)	1 (2%)
Hemorrhage, Focal	1 (2%)		1 (2%)	1 (2%)
Hyperplasia, Focal, Histiocytic	4 (8%)	1 (2%)		
Hyperplasia, Histiocytic	3 (6%)	3 (6%)	2 (4%)	2 (4%)
Infiltration Cellular, Focal, Mixed Cell				1 (2%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLIMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

	0PPM	300 PPM	1000 PPM	3000 PPM
RESPIRATORY SYSTEM - CONT				
Infiltration Cellular, Mixed Cell	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Inflammation, Focal		2 (4%)	1 (2%)	2 (4%)
Metaplasia, Focal, Osseous				2 (4%)
Metaplasia, Osseous				2 (4%)
Alveolar Epithelium, Hyperplasia, Focal	2 (4%)	9 (18%)	6 (12%)	5 (10%)
Alveolus, Foreign Body, Focal			1 (2%)	1 (2%)
Interstitialium, Edema	(50)	(50)	(50)	(50)
Nose				
Foreign Body	1 (2%)			
Inflammation, Suppurative	2 (4%)			
Nasolacrimal Duct, Inflammation		2 (4%)	1 (2%)	2 (4%)
Nasolacrimal Duct, Inflammation, Chronic		1 (2%)	1 (2%)	
Nasolacrimal Duct, Inflammation, Suppurative		3 (6%)	1 (2%)	
Sinus, Foreign Body		1 (2%)		
Sinus, Inflammation, Suppurative		1 (2%)		

SPECIAL SENSES SYSTEM

Eye				
Atrophy	(49)	(50)	(46)	(50)
Cataract	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Synechia				1 (2%)
Cornea, Inflammation, Focal		1 (2%)	1 (2%)	
Cornea, Necrosis, Focal		1 (2%)	1 (2%)	
Iris, Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Lens, Cataract				1 (2%)
Retina, Degeneration			1 (2%)	
Retrobulbar, Inflammation, Focal		1 (2%)	(49)	(50)
Harderian Gland	(50)	(50)		2 (4%)
Hyperplasia, Focal		1 (2%)		1 (2%)
Hyperplasia, Focal, Histiocytic				3 (6%)
Hyperplasia, Histiocytic				1 (2%)
Inflammation, Chronic, Focal	1 (2%)		2 (4%)	
Inflammation, Focal, Granulomatous				1 (2%)
Epithelium, Hyperplasia, Focal	3 (6%)			1 (2%)

URINARY SYSTEM

Kidney				
Accumulation, Hyaline Droplet	(49)	(49)	(49)	(50)
Atrophy, Focal	1 (2%)			1 (2%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:19:18

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

URINARY SYSTEM - CONT	OPPM	300 PPM	1000 PPM	3000 PPM
Congestion	1 (2%)	1 (2%)		
Cyst		2 (4%)		2 (4%)
Fibrosis, Focal				1 (2%)
Infarct		1 (2%)		
Inflammation	1 (2%)			
Nephropathy	43 (88%)	43 (88%)	41 (84%)	46 (92%)
Pelvis, Inflammation, Chronic			1 (2%)	
Pelvis, Transitional Epithelium, Hyperplasia			1 (2%)	
Renal Tubule, Accumulation, Hyaline Droplet	1 (2%)	1 (2%)	3 (6%)	2 (4%)
Renal Tubule, Necrosis, Focal	1 (2%)			
Renal Tubule, Pigmentation	5 (10%)	3 (6%)	2 (4%)	3 (6%)
Urinary Bladder	(50)	(50)	(49)	(50)
Hemorrhage			1 (2%)	

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC 2-METHYLMIDAZOLE
Route: DOSED FEED

Report: PEIRPT05
Date: 02/24/03
Time: 14:26:13

FINAL #1/RAFTS

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25019 Moribund Sacrifice 25020 Natural Death
25021 Terminal Sacrifice
Removal Date Range: All
Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

FISCHER 344 RATS FEMALE OPPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Disposition	0 PPM	1000 PPM	2500 PPM	5000 PPM
Animals Initially in Study	60	60	60	60
Early Deaths				
Natural Death	4	3	10	1
Moribund Sacrifice	6	8	12	7
Survivors				
Terminal Sacrifice	40	39	28	41
Natural Death				1
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Colon	(48)	(49)	(48)	(50)
Intestine Large, Rectum	(47)	(48)	(50)	(49)
Intestine Large, Cecum	(48)	(47)	(44)	(50)
Intestine Small, Duodenum	(48)	(49)	(49)	(50)
Intestine Small, Jejunum	(47)	(46)	(44)	(49)
Intestine Small, Ileum	(48)	(46)	(44)	(50)
Liver	(50)	(49)	(50)	(50)
Cholangiocarcinoma	1 (2%)		2 (4%)	1 (2%)
Hepatocellular Adenoma	1 (2%)			3 (6%)
Hepatocellular Adenoma, Multiple				1 (2%)
Mesentery	(8)	(10)	(12)	(9)
Nerve, Schwannoma Malignant				1 (11%)
Pancreas	(50)	(49)	(49)	(50)
Salivary Glands	(50)	(49)	(50)	(50)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma				1 (2%)
Stomach, Glandular	(49)	(49)	(48)	(50)
Tongue	(3)		(1)	
Liposarcoma	1 (33%)			
Squamous Cell Papilloma			1 (100%)	

CARDIOVASCULAR SYSTEM

Heart	(50)	(49)	(50)	(50)
Squamous Cell Carcinoma, Metastatic, Skin			1 (2%)	

FISCHER 344 RATS FEMALE OPPM 1000 PPM 2500 PPM 5000 PPM

ENDOCRINE SYSTEM	0PPM	1000 PPM	2500 PPM	5000 PPM
Adrenal Cortex	(50)	(49)	(50)	(50)
Adenoma	5 (10%)			
Adrenal Medulla	(49)	(49)	(50)	(50)
Pheochromocytoma Malignant			1 (2%)	
Pheochromocytoma Benign		2 (4%)		
Islets, Pancreatic	(50)	(49)	(50)	(50)
Adenoma			1 (2%)	1 (2%)
Carcinoma	2 (4%)			
Pituitary Gland	(50)	(48)	(50)	(50)
Pars Distalis, Adenoma	23 (46%)	24 (50%)	21 (42%)	13 (26%)
Pars Distalis, Carcinoma	2 (4%)	1 (2%)	3 (6%)	
Pars Intermedia, Adenoma		1 (2%)		
Thyroid Gland	(49)	(48)	(42)	(48)
Bilateral, C-Cell, Adenoma	1 (2%)			
Bilateral, C-Cell, Adenoma, Multiple	1 (2%)			1 (2%)
Bilateral, Follicular Cell, Adenoma			8 (19%)	1 (2%)
Bilateral, Follicular Cell, Carcinoma	7 (14%)	8 (17%)		3 (6%)
C-Cell, Adenoma, Multiple		1 (2%)		1 (2%)
C-Cell, Carcinoma		1 (2%)		4 (8%)
Follicular Cell, Adenoma			1 (2%)	6 (13%)
Follicular Cell, Carcinoma	1 (2%)	1 (2%)	1 (2%)	

GENERAL BODY SYSTEM

Tissue NOS	(3)		(4)	(2)
Mediastinum, Squamous Cell Carcinoma,			1 (25%)	
Metastatic, Skin				
Thoracic, Fibrosarcoma	1 (33%)			
Thoracic, Rhabdomyosarcoma			1 (25%)	

GENITAL SYSTEM

Clitoral Gland	(50)	(49)	(50)	(50)
Adenoma	5 (10%)	4 (8%)	5 (10%)	
Carcinoma	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Squamous Cell Papilloma	1 (2%)		1 (2%)	
Bilateral, Adenoma				
Bilateral, Carcinoma, Multiple	(50)	1 (2%)	(50)	(50)
Ovary		(49)		

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLIMIDAZOLE
 Route: DOSED FEED

Report: PE1RPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS FEMALE

0PPM

1000 PPM

2500 PPM

5000 PPM

GENITAL SYSTEM - cont

Granulosa Cell Tumor Benign					1 (2%)
Granulosa-Theca Tumor Benign					(50)
Uterus	(50)	(50)	(50)	(50)	(50)
Endometrium, Polyp Stromal	7 (14%)	6 (12%)	7 (14%)	3 (6%)	
Endometrium, Polyp Stromal, Multiple	1 (2%)				
Vagina	(2)		(2)		

HEMATOPOIETIC SYSTEM

Bone Marrow	(49)	(50)	(50)	(50)	(50)
Lymph Node	(32)	(31)	(34)	(41)	(41)
Lymph Node, Mesenteric	(49)	(49)	(49)	(50)	(50)
Spleen	(50)	(49)	(48)	(50)	(50)
Thymus	(48)	(45)	(49)	(49)	(49)
Thymoma Malignant			1 (2%)		

INTEGUMENTARY SYSTEM

Mammary Gland	(50)	(50)	(50)	(50)	(50)
Carcinoma	4 (8%)	1 (2%)	3 (6%)	1 (2%)	1 (2%)
Fibroadenoma	24 (48%)	18 (36%)	18 (36%)	5 (10%)	5 (10%)
Fibroadenoma, Multiple	2 (4%)	5 (10%)	6 (12%)	1 (2%)	1 (2%)
Skin	(50)	(50)	(50)	(50)	(50)
Basal Cell Adenoma	1 (2%)				
Basal Cell Carcinoma	1 (2%)				
Keratoacanthoma					
Squamous Cell Carcinoma, Multiple			1 (2%)		1 (2%)
Subcutaneous Tissue, Fibroma	1 (2%)		2 (4%)		2 (4%)

MUSCULOSKELETAL SYSTEM

Skeletal Muscle	(1)	(1)	(2)		
Rhabdomyosarcoma		1 (100%)	1 (50%)		

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED

2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

NERVOUS SYSTEM

Brain	(50)	(49)	(50)	(50)
Glioma Malignant, Mixed Cell				
Spinal Cord	(3)	(1)	(4)	(50) 1 (2%)

RESPIRATORY SYSTEM

Lung	(50)	(49)	(50)	(50)
Alveolar/Bronchiolar Adenoma		1 (2%)	1 (2%)	1 (2%)
Rhabdomyosarcoma, Metastatic, Tissue NOS			1 (2%)	
Squamous Cell Carcinoma, Metastatic, Skin			1 (2%)	

SPECIAL SENSERS SYSTEM

Eye	(50)	(49)	(49)	(50)
Harderian Gland	(50)	(49)	(50)	(50)

URINARY SYSTEM

Kidney	(50)	(48)	(47)	(50)
Sarcoma				1 (2%)
Squamous Cell Carcinoma, Metastatic, Skin			1 (2%)	
Urinary Bladder	(50)	(49)	(49)	(50)
Transitional Epithelium, Papilloma	1 (2%)	1 (2%)		

SYSTEMIC LESIONS

Multiple Organs	* (50)	* (50)	* (50)	* (50)
Leukemia Mononuclear	6 (12%)	4 (8%)	9 (18%)	10 (20%)

* Number of animals with any tissue examined microscopically

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMITIDAZOLE

Report: PTRRPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

TUMOR SUMMARY

	0PPM	1000 PPM	2500 PPM	5000 PPM
Total Animals with Primary Neoplasms (b)	45	44	48	38
Total Primary Neoplasms	103	82	97	64
Total Animals with Benign Neoplasms	43	43	40	27
Total Benign Neoplasms	81	71	75	40
Total Animals with Malignant Neoplasms	19	10	21	20
Total Malignant Neoplasms	22	11	22	24
Total Animals with Metastatic Neoplasms			2	
Total Metastatic Neoplasm			5	
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

DISPOSITION SUMMARY

Disposition	0 PPM	300 PPM	1000 PPM	3000 PPM
Animals Initially in Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	13	6	7	13
Natural Death	2	4	7	2
Survivors				
Terminal Sacrifice	34	39	35	35
Moribund Sacrifice	1	1	1	
Natural Death				
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Colon	(50)	(49)	(48)	(50)
Intestine Large, Rectum	(49)	(48)	(48)	(50)
Intestine Large, Cecum	(48)	(45)	(45)	(49)
Lipoma			1 (2%)	
Intestine Small, Duodenum	(49)	(49)	(48)	(50)
Intestine Small, Jejunum	(47)	(45)	(44)	(48)
Leiomyosarcoma			1 (2%)	
Intestine Small, Ileum	(47)	(46)	(45)	(48)
Liver	(50)	(50)	(50)	(50)
Cholangiocarcinoma	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Cholangioma				
Hemangiosarcoma		1 (2%)		
Hepatocellular Carcinoma			1 (2%)	2 (4%)
Hepatocellular Adenoma		1 (2%)	3 (6%)	1 (2%)
Hepatocellular Adenoma, Multiple				1 (2%)
Mesentery	(26)	(46)	(35)	(20)
Hemangiosarcoma	1 (4%)	1 (2%)		
Oral Mucosa			(1)	
Squamous Cell Papilloma			1 (100%)	
Pancreas	(49)	(49)	(50)	(50)
Acinus, Adenoma	1 (2%)			
Salivary Glands	(50)	(50)	(50)	(50)
Stomach, Fore stomach	(50)	(50)	(50)	(49)
Stomach, Glandular	(50)	(50)	(50)	(49)
Adenoma				1 (2%)

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

CARDIOVASCULAR SYSTEM

Heart	(50)	(50)	(50)	(50)
Pericardium, Epicardium,				
Alveolar/Bronchiolar Carcinoma,			1 (2%)	
Metastatic, Lung				

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma		1 (2%)		
Adrenal Medulla	(50)	(50)	(50)	(50)
Pheochromocytoma Malignant		1 (2%)	3 (6%)	1 (2%)
Pheochromocytoma Benign		2 (4%)	6 (12%)	6 (12%)
Schwannoma Malignant, Metastatic, Adrenal				
Medulla		1 (2%)	1 (2%)	
Bilateral, Pheochromocytoma Benign				
Islets, Pancreatic	1 (2%)	1 (2%)	(50)	(50)
Adenoma	(50)	(49)	1 (2%)	3 (6%)
Carcinoma				
Pituitary Gland	(50)	3 (6%)	(50)	(50)
Pars Distalis, Adenoma	9 (18%)	6 (12%)	8 (16%)	8 (16%)
Pars Intermedia, Adenoma				
Thyroid Gland	1 (2%)	(46)	(43)	(50)
Bilateral, C-Cell, Adenoma	(48)			
Bilateral, C-Cell, Adenoma, Multiple	1 (2%)			
C-Cell, Adenoma	8 (17%)	5 (11%)	9 (21%)	6 (12%)
C-Cell, Carcinoma	1 (2%)			
Follicular Cell, Adenoma	1 (2%)		1 (2%)	3 (6%)
Follicular Cell, Carcinoma		2 (4%)		3 (6%)
				2 (4%)

GENERAL BODY SYSTEM

Peritoneum	(1)	(3)	(6)	(4)
Tissue NOS	(7)	(2)		
Sarcoma	1 (14%)			
Mediastinum, Alveolar/Bronchiolar Carcinoma,			1 (17%)	
Metastatic, Lung				
Thoracic, Alveolar/Bronchiolar Carcinoma,			1 (17%)	
Metastatic, Lung				

FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

GENITAL SYSTEM

Epididymis	(50)	(50)	(50)	(50)
Preputial Gland	(50)	(50)	(50)	(50)
Adenoma		1 (2%)	2 (4%)	2 (4%)
Adenoma, Cystic		1 (2%)	1 (2%)	1 (2%)
Carcinoma		1 (2%)	2 (4%)	3 (6%)
Bilateral, Carcinoma		1 (2%)		
Prostate	(50)	(50)	(50)	(50)
Seminal Vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Bilateral, Interstitial Cell, Adenoma	2 (4%)			
Bilateral, Interstitial Cell, Adenoma, Multiple	42 (84%)	36 (72%)	34 (68%)	28 (56%)
Interstitial Cell, Adenoma	3 (6%)	2 (4%)	6 (12%)	7 (14%)
Interstitial Cell, Adenoma, Multiple	1 (2%)	7 (14%)	2 (4%)	8 (16%)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(47)	(50)
Lymph Node	(39)	(49)	(42)	(38)
Deep Cervical, Carcinoma, Metastatic,		1 (2%)		
Zymbal's Gland	(47)	(50)	(50)	(50)
Lymph Node, Mesenteric	(49)	(49)	(50)	(50)
Spleen	(48)	(48)	(44)	(49)
Thymus				

INTEGUMENTARY SYSTEM

Mammary Gland	(48)	(47)	(45)	(42)
Fibroadenoma	(50)	(50)	(50)	2 (5%)
Skin				(50)
Basal Cell Carcinoma	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Keratocanthoma			1 (2%)	4 (8%)
Melanoma Benign			1 (2%)	
Osteosarcoma, Metastatic, Uncertain Primary Site	1 (2%)			
Trichoepithelioma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Dermis, Fibroma				
Pinna, Schwannoma Malignant	1 (2%)	1 (2%)		
Sebaceous Gland, Adenoma				1 (2%)

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLIMIDAZOLE

Report: PETRPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

INTEGUMENTARY SYSTEM - cont

	0PPM	300 PPM	1000 PPM	3000 PPM
Subcutaneous Tissue, Fibroma	1 (2%)	3 (6%)		2 (4%)
Subcutaneous Tissue, Fibroma, Multiple	1 (2%)			
Subcutaneous Tissue, Fibrosarcoma			1 (2%)	1 (2%)

MUSCULOSKELETAL SYSTEM

Bone				
Osteosarcoma	(50)	(50)	(50)	(50)
Cranium, Carcinoma, Metastatic, Zymbal's Gland		1 (2%)		1 (2%)
Cranium, Osteoma	2 (4%)			1 (2%)
Cranium, Osteosarcoma	(2)	(1)	(1)	(4)
Skeletal Muscle				
Hemangiosarcoma	1 (50%)			
Rhabdomyosarcoma				1 (25%)

NERVOUS SYSTEM

Brain				
Astrocytoma Malignant	(50)	(50)	(50)	(50)
Spinal Cord	(1)		(1)	1 (2%)

RESPIRATORY SYSTEM

Lung				
Alveolar/Bronchiolar Adenoma	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma	2 (4%)	2 (4%)	2 (4%)	1 (2%)
Alveolar/Bronchiolar Carcinoma, Multiple	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Carcinoma, Metastatic, Preputial Gland		1 (2%)		1 (2%)
Carcinoma, Metastatic, Zymbal's Gland				
Osteosarcoma, Metastatic, Bone			1 (2%)	1 (2%)
Alveolar Epithelium, Carcinoma	(50)	(50)	(50)	(50)
Nose				
Glands, Adenoma	1 (2%)			

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED

2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

SPECIAL SENSES SYSTEM

Harderian Gland	(50)	(50)	(49)	(50)
Zymbal's Gland		(1)	(2)	
Carcinoma		1 (100%)	2 (100%)	

URINARY SYSTEM

Kidney	(49)	(49)	(49)	(50)
Urinary Bladder	(50)	(50)	(49)	(50)

SYSTEMIC LESIONS

Multiple Organs	*(50)	*(50)	*(50)	*(50)
Leukemia Mononuclear	15 (30%)	14 (28%)	21 (42%)	10 (20%)
Lymphoma Malignant				
Mesothelioma Malignant	2 (4%)	4 (8%)	2 (4%)	1 (2%)

* Number of animals with any tissue examined microscopically

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: P1RPT05
 Date: 02/24/03
 Time: 14:26:13

FISCHER 344 RATS MALE

0PPM

300 PPM

1000 PPM

3000 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	50	49	49	48
Total Primary Neoplasms	111	104	118	115
Total Animals with Benign Neoplasms	49	46	47	45
Total Benign Neoplasms	86	72	80	85
Total Animals with Malignant Neoplasms	22	26	30	25
Total Malignant Neoplasms	25	32	38	30
Total Animals with Metastatic Neoplasms	1	2	2	2
Total Metastatic Neoplasm	1	4	4	2
Total Animals with Malignant Neoplasms Uncertain Primary Site	1			
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 05
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: FARNELL, DANIEL R.

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLMIDAZOLE
CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

REPORT: PEIRPT08
DATE: 02/24/03
TIME: 14:27:17
PAGE: 1
NTP C#: 92012B
CAS: 693-98-1

FINAL #1/RATS

REASONS FOR REMOVAL:
25019 Moribund Sacrifice
25020 Natural Death
25021 Terminal Sacrifice

REMOVAL DATE RANGE: ALL
TREATMENT GROUPS: INCLUDE ALL

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 05
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: FARNELL, DANIEL R.
Rats (FISCHER 344)

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLMIMIDAZOLE

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

FOR ALL DOSES THE TUMOR RATES IN THE FOLLOWING TISSUES/ORGANS ARE
BASED ON NUMBER OF TISSUES EXAMINED. IN OTHER TISSUES/ORGANS RATES
ARE BASED ON THE NUMBER OF ANIMALS NECROPSIED.

-
- Adrenal Cortex
- Adrenal Medulla
- Brain
- Clitoral/Preputial Gland
- Islets, Pancreatic
- Kidney
- Liver
- Lung
- Nose
- Ovary
- Pancreas
- Pituitary Gland
- Testes
- Thymus
- Thyroid Gland
- Urinary Bladder

REPORT: PEIRPT08
DATE: 02/24/03
TIME: 14:27:17
NTP C#: 92012B
CAS: 693-98-1

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 05
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: FARNELL, DANIEL R.

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLIMIDAZOLE
CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

REPORT: PEIRPT08
DATE: 02/24/03
TIME: 14:27:17
NTP C#: 92012B
CAS: 693-98-1

SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS
IN THE ANALYSIS OF 2-METHYLIMIDAZOLE

Male Rats	Morphology
Organ	Osteoma
Bone	Osteosarcoma
Clitoral/Preputial Gland	Carcinoma or Adenoma
Islets, Pancreatic	Adenoma
Mammary Gland	Fibroadenoma
Skin	Fibroma, Fibroadenoma, Carcinoma, or Adenoma
Basal or Sq. Cell Carcinoma, Carcinoma,	Basal Cell Carcinoma
a, Trichoepitheliom	Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthom
Squamous Cell Carcinoma, Basal Cell Carcinoma,	Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthom
Adenoma	Adenoma
Nestes	Carcinoma
Thyroid Gland: C-Cell	Carcinoma or Adenoma
Thyroid Gland: Follicular Cell	Osteoma
All Organs	Osteosarcoma
Female Rats	Morphology
Organ	Adenoma
Adrenal Cortex	Adenoma
Clitoral/Preputial Gland	Carcinoma or Adenoma
Islets, Pancreatic	Carcinoma
Liver	Hepatocellular Adenoma
Mammary Gland	Hepatocellular Carcinoma or Hepatocellular Adenoma
Pituitary Gland: Pars Distalis or Unspecified Site	Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma
	Fibroadenoma
	Fibroma, Fibroadenoma, Carcinoma, or Adenoma
	Adenoma
	Carcinoma or Adenoma
Skin	Adenoma
Basal Cell Carcinoma, Basal Cell Adenoma,	Adenoma
Thyroid Gland: C-Cell	Carcinoma or Adenoma
Thyroid Gland: Follicular Cell	Adenoma
	Carcinoma
	Carcinoma or Adenoma
	Benign Tumors
All Organs	Malignant Tumors
	Malignant and Benign Tumors

Dose	Males			Females			
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
Adrenal Cortex Adenoma							
TUMOR RATES							
OVERALL (a)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	5/50 (10%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	1/45.93	0/44.49	0/43.91	5/46.87	0/44.59	0/48.02
POLY-3 PERCENT (g)	0.0%	2.2%	0.0%	0.0%	10.7%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	0/36 (0%)	0/35 (0%)	3/40 (8%)	0/39 (0%)	0/42 (0%)
FIRST INCIDENCE	---	729 (T)	---	---	588	---	---
STATISTICAL TESTS							
LIFE TABLE							
POLY 3	P=0.586N	P=0.527	(e)	(e)	P=0.015N*	P=0.039N*	P=0.031N*
POLY 1.5	P=0.579N	P=0.499	(e)	(e)	P=0.010N*	P=0.035N*	P=0.044N*
POLY 6	P=0.579N	P=0.500	(e)	(e)	P=0.010N*	P=0.034N*	P=0.038N*
LOGISTIC REGRESSION	(e)	P=0.499	(e)	(e)	P=0.010N*	P=0.036N*	P=0.028N*
COCH-ARM / FISHERS	P=0.576N	P=0.527	(e)	(e)	P=0.011N*	P=0.033N*	P=0.040N*
ORDER RESTRICTED	P=0.389N	P=0.500	(e)	(e)	P=0.012N*	P=0.030N*	P=0.028N*
Adrenal Medulla Pheochromocytoma Benign							
TUMOR RATES							
OVERALL (a)	8/50 (16%)	3/50 (6%)	6/50 (12%)	6/50 (12%)	0/49 (0%)	2/49 (4%)	0/50 (0%)
POLY-3 RATE (b)	8/46.55	3/45.93	6/44.98	6/44.15	0/45.00	2/44.59	0/48.02
POLY-3 PERCENT (g)	17.2%	6.5%	13.3%	13.6%	0.0%	4.5%	0.0%
TERMINAL (d)	5/35 (14%)	3/40 (8%)	5/36 (14%)	4/35 (11%)	0/39 (0%)	2/39 (5%)	0/28 (0%)
FIRST INCIDENCE	689	729 (T)	583	689	---	729 (T)	---
STATISTICAL TESTS							
LIFE TABLE							
POLY 3	P=0.515	P=0.079N	P=0.382N	P=0.407N	P=0.351N	P=0.238	(e)
POLY 1.5	P=0.526	P=0.102N	P=0.413N	P=0.428N	P=0.350N	P=0.235	(e)
POLY 6	P=0.517	P=0.101N	P=0.403N	P=0.414N	P=0.350N	P=0.236	(e)
LOGISTIC REGRESSION	P=0.522	P=0.101N	P=0.407N	P=0.430N	(e)	P=0.238	(e)
COCH-ARM / FISHERS	P=0.562	P=0.100N	P=0.387N	P=0.387N	P=0.348N	P=0.247	(e)
ORDER RESTRICTED	P=0.304N	(e)	(e)	(e)	P=0.233N	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM

Adrenal Medulla
 Pheochromocytoma Malignant

TUMOR RATES						
OVERALL (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)	1/50 (2%)	0/49 (0%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	1/45.93	3/44.49	1/43.91	0/45.00	1/40.77
POLY-3 PERCENT (g)	0.0%	2.2%	6.7%	2.3%	0.0%	2.5%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	3/36 (8%)	1/35 (3%)	0/39 (0%)	1/28 (4%)
FIRST INCIDENCE	---	729 (T)	729 (T)	729 (T)	---	729 (T)

STATISTICAL TESTS

LIFE TABLE						
POLY 3	P=0.491	P=0.527	P=0.126	P=0.500	P=0.677	P=0.434
POLY 1.5	P=0.483	P=0.499	P=0.112	P=0.490	P=0.709	P=0.480
POLY 6	P=0.492	P=0.500	P=0.115	P=0.493	P=0.699	P=0.490
LOGISTIC REGRESSION	P=0.475	P=0.499	P=0.111	P=0.487	P=0.720	P=0.469
COCH-ARM / FISHERS	P=0.512	P=0.527	P=0.126	P=0.500	(e)	P=0.434
ORDER RESTRICTED	P=0.148	P=0.500	P=0.121	P=0.500	P=0.682	P=0.505

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM

Adrenal Medulla
 Pheochromocytoma: Benign, Complex, Malignant, NOS

TUMOR RATES						
OVERALL (a)	8/50 (16%)	4/50 (8%)	9/50 (18%)	7/50 (14%)	0/49 (0%)	2/49 (4%)
POLY-3 RATE (b)	8/46.55	4/45.93	9/44.98	7/44.15	0/45.00	2/44.59
POLY-3 PERCENT (g)	17.2%	8.7%	20.0%	15.9%	0.0%	4.5%
TERMINAL (d)	5/35 (14%)	4/40 (10%)	8/36 (22%)	5/35 (14%)	0/39 (0%)	2/39 (5%)
FIRST INCIDENCE	689	729 (T)	583	689	---	729 (T)

STATISTICAL TESTS

LIFE TABLE						
POLY 3	P=0.440	P=0.140N	P=0.512	P=0.517N	P=0.416N	P=0.434
POLY 1.5	P=0.448	P=0.183N	P=0.469	P=0.544N	P=0.408N	P=0.480
POLY 6	P=0.462	P=0.180N	P=0.481	P=0.529N	P=0.412N	P=0.490
LOGISTIC REGRESSION	P=0.435	P=0.186N	P=0.459	P=0.558N	P=0.402N	P=0.469
COCH-ARM / FISHERS	P=0.442	P=0.178N	P=0.469	P=0.549N	(e)	P=0.434
ORDER RESTRICTED	P=0.493	P=0.178N	P=0.500	P=0.500N	P=0.418N	P=0.505
ORDER RESTRICTED	P=0.405	(e)	(e)	(e)	P=0.299N	(e)

 Dose OPPM 300 PPM 1000 PPM 3000 PPM OPPM 1000 PPM 2500 PPM 5000 PPM
 Males Females
 Osteosarcoma or Osteoma

TUMOR RATES

	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46.14	0/45.93	0/44.49	2/44.60	0/46.00	0/44.99	0/48.02
POLY-3 PERCENT (g)	4.3%	0.0%	0.0%	4.5%	0.0%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	0/40 (0%)	0/36 (0%)	1/35 (3%)	0/40 (0%)	0/39 (0%)	0/28 (0%)
FIRST INCIDENCE	726	---	---	491	---	---	---

STATISTICAL TESTS

LIFE TABLE

POLY 3	P=0.3664	P=0.214N	P=0.237N	P=0.688	(e)	(e)	(e)
POLY 1.5	P=0.375	P=0.238N	P=0.245N	P=0.682	(e)	(e)	(e)
POLY 6	P=0.376	P=0.238N	P=0.242N	P=0.685	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.373	P=0.238N	P=0.247N	P=0.679	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.410	P=0.226N	P=0.241N	P=0.673N	(e)	(e)	(e)
ORDER RESTRICTED	P=0.381	P=0.247N	P=0.247N	P=0.691N	(e)	(e)	(e)

Dose OPPM 300 PPM 1000 PPM 3000 PPM OPPM 1000 PPM 2500 PPM 5000 PPM

Clititoral/Preputial Gland Adenoma

TUMOR RATES

	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)	0/50 (0%)	5/50 (10%)	4/49 (8%)	6/50 (12%)
POLY-3 RATE (b)	0/46.13	1/45.93	3/44.75	0/43.91	5/46.10	4/43.99	6/40.77
POLY-3 PERCENT (g)	0.0%	2.2%	6.7%	0.0%	10.9%	9.1%	14.7%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	1/36 (3%)	0/35 (0%)	4/40 (10%)	4/38 (11%)	6/28 (21%)
FIRST INCIDENCE	---	729 (T)	673	---	703	729 (T)	729 (T)

STATISTICAL TESTS

LIFE TABLE

POLY 3	P=0.520N	P=0.527	P=0.123	P=0.051N	P=0.532N	P=0.263	P=0.030N*
POLY 1.5	P=0.524N	P=0.499	P=0.113	P=0.037N*	P=0.529N	P=0.414	P=0.027N*
POLY 6	P=0.516N	P=0.500	P=0.115	P=0.041N*	P=0.523N	P=0.448	P=0.029N*
LOGISTIC REGRESSION	P=0.513N	P=0.499	P=0.113	P=0.033N*	P=0.535N	P=0.372	P=0.026N*
COCH-ARM / FISHERS	P=0.500N	P=0.527	P=0.117	P=0.043N*	P=0.530N	P=0.304	P=0.027N*
ORDER RESTRICTED	P=0.214	P=0.500	P=0.121	P=0.048N*	P=0.513N	P=0.500	P=0.028N*

Dose	OPPM	Males			Females		
		300 PPM	1000 PPM	3000 PPM	OPPM	1000 PPM	5000 PPM

Clitoreal/Preputial Gland
 Carcinoma

OVERALL (a)	0/50 (0%)	2/50 (4%)	2/50 (4%)	3/50 (6%)	3/50 (6%)	2/49 (4%)	1/50 (2%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	2/46.50	2/44.63	3/44.07	3/46.00	2/44.59	1/40.77	1/48.02
POLY-3 PERCENT (g)	0.0%	4.3%	4.5%	6.8%	6.5%	4.5%	2.5%	2.1%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	1/36 (3%)	2/35 (6%)	3/40 (8%)	1/38 (3%)	1/28 (4%)	1/42 (2%)
FIRST INCIDENCE	---	548	694	687	729 (T)	538	729 (T)	729 (T)

STATISTICAL TESTS

LIFE TABLE	P=0.143	P=0.252	P=0.240	P=0.122	P=0.203N	P=0.522N	P=0.439N	P=0.288N
POLY 3	P=0.142	P=0.239	P=0.230	P=0.111	P=0.194N	P=0.514N	P=0.350N	P=0.290N
POLY 1.5	P=0.146	P=0.239	P=0.233	P=0.113	P=0.197N	P=0.512N	P=0.332N	P=0.296N
POLY 6	P=0.138	P=0.240	P=0.229	P=0.109	P=0.191N	P=0.514N	P=0.373N	P=0.283N
LOGISTIC REGRESSION	P=0.159	P=0.209	P=0.231	P=0.111	P=0.196N	P=0.504N	P=0.439N	P=0.288N
COCH-ARM / FISHERS	P=0.156	P=0.247	P=0.247	P=0.121	P=0.198N	P=0.510N	P=0.309N	P=0.309N
ORDER RESTRICTED	P=0.070	(e)	(e)	(e)	P=0.202N	(e)	(e)	(e)

Dose	OPPM	Males			Females		
		300 PPM	1000 PPM	3000 PPM	OPPM	1000 PPM	2500 PPM

Clitoreal/Preputial Gland
 Carcinoma or Adenoma

OVERALL (a)	0/50 (0%)	3/50 (6%)	5/50 (10%)	3/50 (6%)	8/50 (16%)	6/49 (12%)	7/50 (14%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	3/46.50	5/44.89	3/44.07	8/46.10	6/44.59	7/40.77	1/48.02
POLY-3 PERCENT (g)	0.0%	6.5%	11.1%	6.8%	17.4%	13.5%	17.2%	2.1%
TERMINAL (d)	0/35 (0%)	2/40 (5%)	2/36 (6%)	2/35 (6%)	7/40 (18%)	5/38 (13%)	7/28 (25%)	1/42 (2%)
FIRST INCIDENCE	---	548	673	687	703	538	729 (T)	729 (T)

STATISTICAL TESTS

LIFE TABLE	P=0.267	P=0.138	P=0.036 *	P=0.122	P=0.022N*	P=0.427N	P=0.426	P=0.015N*
POLY 3	P=0.259	P=0.120	P=0.028 *	P=0.111	P=0.015N*	P=0.412N	P=0.603N	P=0.013N*
POLY 1.5	P=0.269	P=0.120	P=0.029 *	P=0.113	P=0.017N*	P=0.409N	P=0.562N	P=0.014N*
POLY 6	P=0.252	P=0.121	P=0.028 *	P=0.109	P=0.013N*	P=0.413N	P=0.569	P=0.012N*
LOGISTIC REGRESSION	P=0.287	P=0.112	P=0.031 *	P=0.111	P=0.017N*	P=0.418N	P=0.478	P=0.013N*
COCH-ARM / FISHERS	P=0.291	P=0.121	P=0.028 *	P=0.121	P=0.020N*	P=0.403N	P=0.500N	P=0.015N*
ORDER RESTRICTED	P=0.052	(e)	(e)	(e)	P=0.012N*	(e)	(e)	(e)

Dose	0PPM	Males			0PPM	Females		
		300 PPM	1000 PPM	3000 PPM		2500 PPM	5000 PPM	

Islets, Pancreatic
 Adenoma

TUMOR RATES								
OVERALL (a)	0/50 (0%)	0/49 (0%)	1/50 (2%)	3/50 (6%)	0/50 (0%)	0/49 (0%)	1/50 (2%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	0/45.35	1/44.49	3/43.91	0/46.00	0/44.59	1/40.77	1/48.02
POLY-3 PERCENT (g)	0.0%	0.0%	2.3%	6.8%	0.0%	0.0%	2.5%	2.1%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	1/36 (3%)	3/35 (9%)	0/40 (0%)	0/39 (0%)	1/28 (4%)	1/42 (2%)
FIRST INCIDENCE	---	---	729 (T)	729 (T)	---	---	729 (T)	729 (T)

STATISTICAL TESTS

LIFE TABLE								
POLY 3	P=0.018 *	(e)	P=0.506	P=0.121	P=0.240	(e)	P=0.429	P=0.510
POLY 1.5	P=0.019 *	(e)	P=0.493	P=0.110	P=0.244	(e)	P=0.476	P=0.509
LOGISTIC REGRESSION	P=0.018 *	(e)	P=0.495	P=0.113	P=0.238	(e)	P=0.485	P=0.505
COCH-ARM / FISHERS	(e)	(e)	P=0.491	P=0.108	P=0.252	(e)	P=0.464	P=0.513
ORDER RESTRICTED	P=0.022 *	(e)	P=0.506	P=0.121	(e)	(e)	P=0.429	P=0.510
	P=0.018 *	(e)	P=0.500	P=0.121	P=0.227	(e)	P=0.500	P=0.500

Dose	0PPM	Males			0PPM	Females		
		300 PPM	1000 PPM	3000 PPM		2500 PPM	5000 PPM	

Islets, Pancreatic
 Carcinoma

TUMOR RATES								
OVERALL (a)	0/50 (0%)	3/49 (6%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/49 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	3/45.35	0/44.49	0/43.91	2/46.22	0/44.59	0/40.77	0/48.02
POLY-3 PERCENT (g)	0.0%	6.6%	0.0%	0.0%	4.3%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	3/40 (8%)	0/36 (0%)	0/35 (0%)	1/40 (3%)	0/39 (0%)	0/28 (0%)	0/42 (0%)
FIRST INCIDENCE	---	729 (T)	---	---	671	---	---	---

STATISTICAL TESTS

LIFE TABLE								
POLY 3	P=0.265N	P=0.146	(e)	(e)	P=0.134N	P=0.243N	P=0.307N	P=0.222N
POLY 1.5	P=0.257N	P=0.116	(e)	(e)	P=0.130N	P=0.245N	P=0.266N	P=0.229N
LOGISTIC REGRESSION	P=0.255N	P=0.116	(e)	(e)	P=0.129N	P=0.244N	P=0.254N	P=0.232N
COCH-ARM / FISHERS	P=0.259N	P=0.116	(e)	(e)	P=0.131N	P=0.246N	P=0.282N	P=0.225N
ORDER RESTRICTED	P=0.253N	P=0.117	(e)	(e)	P=0.128N	P=0.242N	P=0.250N	P=0.244N
	P=0.169N	(e)	(e)	(e)	P=0.027N*	P=0.253N	P=0.247N	(e)

Islets, Pancreatic
 Carcinoma or Adenoma

Dose	PPM	Males			PPM	Females		
		300 PPM	1000 PPM	3000 PPM		1000 PPM	2500 PPM	5000 PPM
TUMOR RATES								
OVERALL (a)	0/50 (0%)	3/49 (6%)	1/50 (2%)	3/50 (6%)	2/50 (4%)	0/49 (0%)	1/50 (2%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	3/45.35	1/44.49	3/43.91	2/46.22	0/44.59	1/40.77	1/48.02
POLY-3 PERCENT (g)	0.0%	6.6%	2.3%	6.8%	4.3%	0.0%	2.5%	2.1%
TERMINAL (d)	0/35 (0%)	3/40 (8%)	1/36 (3%)	3/35 (9%)	1/40 (3%)	0/39 (0%)	1/28 (4%)	1/42 (2%)
FIRST INCIDENCE	---	729 (T)	729 (T)	729 (T)	671	---	729 (T)	729 (T)
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.195	P=0.146	P=0.506	P=0.121	P=0.514N	P=0.243N	P=0.609N	P=0.476N
POLY 3	P=0.203	P=0.116	P=0.493	P=0.110	P=0.519N	P=0.245N	P=0.544N	P=0.487N
POLY 1.5	P=0.209	P=0.116	P=0.495	P=0.113	P=0.522N	P=0.244N	P=0.526N	P=0.492N
POLY 6	P=0.199	P=0.116	P=0.491	P=0.108	P=0.517N	P=0.246N	P=0.565N	P=0.481N
LOGISTIC REGRESSION	(e)	P=0.146	P=0.506	P=0.121	P=0.513N	P=0.242N	P=0.547N	P=0.501N
COCH-ARM / FISHERS	P=0.220	P=0.117	P=0.500	P=0.121	P=0.524N	P=0.253N	P=0.500N	P=0.500N
ORDER RESTRICTED	P=0.069	(e)	(e)	(e)	P=0.272N	(e)	(e)	(e)

Liver
 Cholangiocarcinoma

Dose	PPM	Males			PPM	Females		
		300 PPM	1000 PPM	3000 PPM		1000 PPM	2500 PPM	5000 PPM
TUMOR RATES								
OVERALL (a)	1/50 (2%)	2/50 (4%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	0/49 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 RATE (b)	1/46.13	2/45.93	2/44.49	1/43.91	1/46.00	0/44.59	0/40.77	1/48.02
POLY-3 PERCENT (g)	2.2%	4.4%	4.5%	2.3%	2.2%	0.0%	0.0%	2.1%
TERMINAL (d)	1/35 (3%)	2/40 (5%)	2/36 (6%)	1/35 (3%)	1/40 (3%)	0/39 (0%)	0/28 (0%)	1/42 (2%)
FIRST INCIDENCE	729 (T)	---	---	729 (T)				
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.545N	P=0.547	P=0.510	P=0.762	P=0.576	P=0.505N	P=0.571N	P=0.751N
POLY 3	P=0.541N	P=0.498	P=0.487	P=0.750	P=0.583	P=0.506N	P=0.524N	P=0.751N
POLY 1.5	P=0.534N	P=0.500	P=0.492	P=0.753	P=0.580	P=0.505N	P=0.515N	P=0.755N
POLY 6	P=0.546N	P=0.499	P=0.485	P=0.747	P=0.586	P=0.506N	P=0.536N	P=0.746N
LOGISTIC REGRESSION	P=0.545N	P=0.547	P=0.510	P=0.762	P=0.576	(e)	(e)	P=0.751N
COCH-ARM / FISHERS	P=0.521N	P=0.500	P=0.500	P=0.753N	P=0.576	P=0.505N	P=0.500N	P=0.753N
ORDER RESTRICTED	P=0.536	(e)	(e)	(e)	P=0.599N	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM

Liver
Cholangioma

TUMOR RATES	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	2/45.93	0/44.49	0/46.00	0/44.59	0/40.77
POLY-3 PERCENT (g)	0.0%	4.4%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	2/40 (5%)	0/36 (0%)	0/40 (0%)	0/39 (0%)	0/28 (0%)
FIRST INCIDENCE	---	729 (T)	---	---	---	---

STATISTICAL TESTS

LIFE TABLE	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM
POLY 3	P=0.380N	P=0.268	(e)	(e)	(e)	(e)
POLY 1.5	P=0.375N	P=0.237	(e)	(e)	(e)	(e)
POLY 6	P=0.373N	P=0.236	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.377N	P=0.268	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	(e)	P=0.247	(e)	(e)	(e)	(e)
ORDER RESTRICTED	P=0.369N	(e)	(e)	(e)	(e)	(e)
	P=0.256N	(e)	(e)	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM

Liver
Hepatocellular Adenoma

TUMOR RATES	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM
OVERALL (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)	1/50 (2%)	0/49 (0%)	2/50 (4%)
POLY-3 RATE (b)	0/46.13	1/45.93	3/44.62	1/46.00	0/44.59	2/40.77
POLY-3 PERCENT (g)	0.0%	2.2%	6.7%	2.2%	0.0%	4.9%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	2/36 (6%)	1/40 (3%)	0/39 (0%)	2/28 (7%)
FIRST INCIDENCE	---	729 (T)	696	729 (T)	---	729 (T)

STATISTICAL TESTS

LIFE TABLE	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM
POLY 3	P=0.237	P=0.527	P=0.126	P=0.043 *	P=0.505N	P=0.376
POLY 1.5	P=0.235	P=0.499	P=0.113	P=0.039 *	P=0.506N	P=0.458
POLY 6	P=0.241	P=0.500	P=0.115	P=0.037 *	P=0.505N	P=0.475
LOGISTIC REGRESSION	P=0.229	P=0.499	P=0.112	P=0.041 *	P=0.506N	P=0.437
COCH-ARM / FISHERS	P=0.236	P=0.527	P=0.113	P=0.043 *	(e)	P=0.376
ORDER RESTRICTED	P=0.256	P=0.500	P=0.121	P=0.036 *	P=0.505N	P=0.500
	P=0.103	(e)	(e)	P=0.044 *	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	5000 PPM

Liver
 Hepatocellular Carcinoma

TUMOR RATES						
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	0/45.93	1/44.49	2/43.91	0/46.00	0/48.02
POLY-3 PERCENT (g)	0.0%	0.0%	2.3%	4.6%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	1/36 (3%)	2/35 (6%)	0/40 (0%)	0/42 (0%)
FIRST INCIDENCE	---	---	729 (T)	729 (T)	---	---

STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.075	(e)	P=0.506	P=0.238	(e)	(e)
POLY 1.5	P=0.077	(e)	P=0.493	P=0.226	(e)	(e)
POLY 6	P=0.079	(e)	P=0.230	P=0.230	(e)	(e)
LOGISTIC REGRESSION	P=0.075	(e)	P=0.491	P=0.223	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	P=0.506	P=0.238	(e)	(e)
ORDER RESTRICTED	P=0.084	(e)	P=0.500	P=0.247	(e)	(e)
	P=0.067	(e)	(e)	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM

Liver
 Hepatocellular Carcinoma or Hepatocellular Adenoma

TUMOR RATES						
OVERALL (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)	3/50 (6%)	1/50 (2%)	0/49 (0%)
POLY-3 RATE (b)	0/46.13	1/45.93	3/44.62	3/44.01	1/46.00	0/44.59
POLY-3 PERCENT (g)	0.0%	2.2%	6.7%	6.8%	2.2%	0.0%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	2/36 (6%)	2/35 (6%)	1/40 (3%)	0/39 (0%)
FIRST INCIDENCE	---	729 (T)	696	702	729 (T)	---

STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.095	P=0.527	P=0.126	P=0.121	P=0.043 *	P=0.505N
POLY 1.5	P=0.095	P=0.499	P=0.113	P=0.110	P=0.039 *	P=0.506N
POLY 6	P=0.098	P=0.500	P=0.115	P=0.113	P=0.037 *	P=0.505N
LOGISTIC REGRESSION	P=0.092	P=0.499	P=0.112	P=0.108	P=0.041 *	P=0.506N
COCH-ARM / FISHERS	P=0.093	P=0.527	P=0.113	P=0.109	P=0.043 *	(e)
ORDER RESTRICTED	P=0.107	P=0.500	P=0.121	P=0.121	P=0.036 *	P=0.505N
	P=0.069	(e)	(e)	(e)	P=0.044 *	(e)

Dose	Males					Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

Liver
 Hepatocellular Carcinoma, Hepatocellular Adenoma,
 or Hepatoblastoma

TUMOR RATES								
OVERALL (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)	3/50 (6%)	1/50 (2%)	0/49 (0%)	2/50 (4%)	4/50 (8%)
POLY-3 RATE (b)	0/46.13	1/45.93	3/44.62	3/44.01	1/46.00	0/44.59	2/40.77	4/48.02
POLY-3 PERCENT (g)	0.0%	2.2%	6.7%	6.8%	2.2%	0.0%	4.9%	8.3%
TERMINAL (d)	0/35 (0%)	1/40 (3%)	2/36 (6%)	2/35 (6%)	1/40 (3%)	0/39 (0%)	2/28 (7%)	4/42 (10%)
FIRST INCIDENCE	---	729 (T)	696	702	729 (T)	---	729 (T)	729 (T)

STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.095	P=0.499	P=0.113	P=0.110	P=0.043 *	P=0.505N	P=0.376	P=0.194
POLY 1.5	P=0.098	P=0.500	P=0.112	P=0.113	P=0.039 *	P=0.506N	P=0.458	P=0.192
POLY 6	P=0.092	P=0.499	P=0.112	P=0.108	P=0.041 *	P=0.506N	P=0.475	P=0.187
LOGISTIC REGRESSION	P=0.093	P=0.527	P=0.113	P=0.109	P=0.043 *	(e)	P=0.376	P=0.199
COCH-ARM / FISHERS	P=0.107	P=0.500	P=0.121	P=0.121	P=0.036 *	P=0.505N	P=0.376	P=0.194
ORDER RESTRICTED	(e)	(e)	(e)	(e)	P=0.044 *	(e)	P=0.500	P=0.181

Dose	Males					Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

Lung
 Alveolar/Bronchiolar Adenoma

TUMOR RATES								
OVERALL (a)	2/50 (4%)	2/50 (4%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	1/49 (2%)	1/50 (2%)	1/50 (2%)
POLY-3 RATE (b)	2/46.13	2/46.44	2/44.49	1/43.91	0/46.00	1/44.59	1/40.77	1/48.05
POLY-3 PERCENT (g)	4.3%	4.3%	4.5%	2.3%	0.0%	2.2%	2.5%	2.1%
TERMINAL (d)	2/35 (6%)	1/40 (3%)	2/36 (6%)	1/35 (3%)	0/40 (0%)	1/39 (3%)	1/28 (4%)	0/42 (0%)
FIRST INCIDENCE	729 (T)	572	729 (T)	729 (T)	---	729 (T)	729 (T)	722

STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.403N	P=0.661N	P=0.685N	P=0.500N	P=0.409	P=0.495	P=0.429	P=0.519
POLY 1.5	P=0.402N	P=0.691N	P=0.681	P=0.517N	P=0.415	P=0.494	P=0.476	P=0.509
POLY 6	P=0.395N	P=0.692N	P=0.685	P=0.511N	P=0.407	P=0.495	P=0.485	P=0.505
LOGISTIC REGRESSION	P=0.408N	P=0.689N	P=0.678	P=0.522N	P=0.424	P=0.494	P=0.464	P=0.513
COCH-ARM / FISHERS	P=0.391N	P=0.691N	P=0.685N	P=0.500N	P=0.415	P=0.495	P=0.429	P=0.512
ORDER RESTRICTED	P=0.380N	P=0.691N	P=0.691N	P=0.500N	P=0.396	P=0.495	P=0.500	P=0.500
	(e)	(e)	(e)	(e)	P=0.306	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM

Lung
Alveolar/Bronchiolar Carcinoma

TUMOR RATES						
OVERALL (a)	2/50 (4%)	1/50 (2%)	3/50 (6%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46.13	1/45.93	3/45.22	0/43.91	0/44.59	0/40.77
POLY-3 PERCENT (g)	4.3%	2.2%	6.6%	0.0%	0.0%	0.0%
TERMINAL (d)	2/35 (6%)	1/40 (3%)	2/36 (6%)	0/35 (0%)	0/39 (0%)	0/28 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	471	---	---	---

STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.237N	P=0.453N	P=0.508	P=0.238N	(e)	(e)
POLY 1.5	P=0.240N	P=0.502N	P=0.491	P=0.248N	(e)	(e)
POLY 6	P=0.234N	P=0.500N	P=0.494	P=0.245N	(e)	(e)
LOGISTIC REGRESSION	P=0.244N	P=0.501N	P=0.490	P=0.251N	(e)	(e)
COCH-ARM / FISHERS	P=0.212N	P=0.453N	P=0.519	(e)	(e)	(e)
ORDER RESTRICTED	P=0.223N	P=0.500N	P=0.500	P=0.247N	(e)	(e)
	P=0.193N	(e)	(e)	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM

Lung
Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma

TUMOR RATES						
OVERALL (a)	4/50 (8%)	3/50 (6%)	5/50 (10%)	1/50 (2%)	0/50 (0%)	1/49 (2%)
POLY-3 RATE (b)	4/46.13	3/46.44	5/45.22	1/43.91	0/46.00	1/44.59
POLY-3 PERCENT (g)	8.7%	6.5%	11.1%	2.3%	0.0%	2.2%
TERMINAL (d)	4/35 (11%)	2/40 (5%)	4/36 (11%)	1/35 (3%)	0/40 (0%)	1/39 (3%)
FIRST INCIDENCE	729 (T)	572	471	729 (T)	---	729 (T)

STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.177N	P=0.441N	P=0.514	P=0.178N	P=0.409	P=0.429
POLY 1.5	P=0.180N	P=0.496N	P=0.488	P=0.194N	P=0.415	P=0.476
POLY 6	P=0.173N	P=0.497N	P=0.492	P=0.189N	P=0.407	P=0.485
LOGISTIC REGRESSION	P=0.187N	P=0.493N	P=0.486	P=0.198N	P=0.424	P=0.464
COCH-ARM / FISHERS	P=0.158N	P=0.500N	P=0.498	P=0.178N	P=0.415	P=0.429
ORDER RESTRICTED	P=0.159N	P=0.500N	P=0.500	P=0.181N	P=0.396	P=0.500
	P=0.186N	(e)	(e)	(e)	P=0.306	(e)

Dose	Males				Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM

Mammary Gland
 Carcinoma

TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	4/50 (8%)	1/50 (2%)	3/50 (6%)	1/50 (2%)
POLY-3 RATE (b)	0/46.13	0/45.93	0/44.49	0/43.91	4/46.42	1/44.99	3/41.98	1/48.02
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	0.0%	8.6%	2.2%	7.2%	2.1%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	0/36 (0%)	0/35 (0%)	3/40 (8%)	1/39 (3%)	1/28 (4%)	1/42 (2%)
FIRST INCIDENCE	---	---	---	---	605	729 (T)	332	729 (T)

STATISTICAL TESTS

LIFE TABLE	(e)	(e)	(e)	(e)	P=0.216N	P=0.191N	P=0.633N	P=0.167N
POLY 3	(e)	(e)	(e)	(e)	P=0.198N	P=0.188N	P=0.555N	P=0.169N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.205N	P=0.185N	P=0.532N	P=0.173N
POLY 6	(e)	(e)	(e)	(e)	P=0.192N	P=0.191N	P=0.584N	P=0.164N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.224N	P=0.181N	P=0.404N	P=0.184N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.214N	P=0.181N	P=0.500N	P=0.181N
ORDER RESTRICTED	(e)	(e)	(e)	(e)	P=0.103N	(e)	(e)	(e)

Dose	Males				Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM

Mammary Gland
 Fibroadenoma

TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	26/50 (52%)	23/50 (46%)	24/50 (48%)	6/50 (12%)
POLY-3 RATE (b)	0/46.13	0/45.93	0/44.49	0/43.91	26/47.63	23/47.19	24/42.36	6/48.05
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	0.0%	54.6%	48.7%	56.7%	12.5%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	0/36 (0%)	0/35 (0%)	21/40 (53%)	19/39 (49%)	16/28 (57%)	5/42 (12%)
FIRST INCIDENCE	---	---	---	---	602	483	598	722

STATISTICAL TESTS

LIFE TABLE	P=0.037 *	(e)	(e)	(e)	P=0.238	P=0.399N	P=0.181	P<0.001N**
POLY 3	P=0.038 *	(e)	(e)	(e)	P=0.226	P=0.357N	P=0.506	P<0.001N**
POLY 1.5	P=0.039 *	(e)	(e)	(e)	P=0.230	P=0.349N	P=0.568N	P<0.001N**
POLY 6	P=0.038 *	(e)	(e)	(e)	P=0.223	P=0.370N	P=0.396	P<0.001N**
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.238	P=0.357N	P=0.463	P<0.001N**
COCH-ARM / FISHERS	P=0.042 *	(e)	(e)	(e)	P=0.247	P=0.345N	P=0.421N	P<0.001N**
ORDER RESTRICTED	P=0.026 *	(e)	(e)	(e)	P<0.001N**	(e)	(e)	(e)

Mammary Gland
 Fibroma, Fibroadenoma, Carcinoma, or Adenoma

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	28/50 (56%)	24/50 (48%)	26/50 (52%)	6/50 (12%)
POLY-3 RATE (b)	0/46.13	0/45.93	0/44.49	2/43.91	28/47.63	24/47.19	26/43.57	6/48.05
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	4.6%	58.8%	50.9%	59.7%	12.5%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	0/36 (0%)	2/35 (6%)	23/40 (58%)	20/39 (51%)	16/28 (57%)	5/42 (12%)
FIRST INCIDENCE	---	---	---	729 (T)	602	483	332	722
STATISTICAL TESTS								
LIFE TABLE	#	#	#	#	#	#	#	#
POLY 3	P=0.037 *	(e)	(e)	P=0.238	P<0.001N**	P=0.331N	P=0.167	P<0.001N**
POLY 1.5	P=0.038 *	(e)	(e)	P=0.226	P<0.001N**	P=0.283N	P=0.551	P<0.001N**
POLY 6	P=0.039 *	(e)	(e)	P=0.230	P<0.001N**	P=0.276N	P=0.538N	P<0.001N**
LOGISTIC REGRESSION	(e)	(e)	(e)	P=0.223	P<0.001N**	P=0.295N	P=0.454	P<0.001N**
COCH-ARM / FISHERS	P=0.042 *	(e)	(e)	P=0.238	P<0.001N**	P=0.289N	P=0.549	P<0.001N**
ORDER RESTRICTED	P=0.026 *	(e)	(e)	P=0.247	P<0.001N**	P=0.274N	P=0.421N	P<0.001N**

Pituitary Gland: Pars Distalis or Unspecified Site
 Adenoma

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
OVERALL (a)	9/50 (18%)	6/50 (12%)	8/50 (16%)	9/50 (18%)	23/50 (46%)	24/48 (50%)	21/50 (42%)	13/50 (26%)
POLY-3 RATE (b)	9/46.40	6/45.93	8/46.05	9/44.06	23/46.48	24/46.25	21/44.42	13/48.36
POLY-3 PERCENT (g)	19.4%	13.1%	17.4%	20.4%	49.5%	51.9%	47.3%	26.9%
TERMINAL (d)	7/35 (20%)	6/40 (15%)	5/36 (14%)	8/35 (23%)	21/40 (53%)	18/39 (46%)	10/28 (36%)	11/42 (26%)
FIRST INCIDENCE	694	729 (T)	392	689	658	425	532	644
STATISTICAL TESTS								
LIFE TABLE	#	#	#	#	#	#	#	#
POLY 3	P=0.354	P=0.214N	P=0.489N	P=0.589	P=0.017N*	P=0.458	P=0.252	P=0.020N*
POLY 1.5	P=0.363	P=0.294N	P=0.507N	P=0.556	P=0.006N**	P=0.490	P=0.500N	P=0.018N*
POLY 6	P=0.378	P=0.291N	P=0.504N	P=0.572	P=0.007N**	P=0.463	P=0.477N	P=0.021N*
LOGISTIC REGRESSION	P=0.351	P=0.297N	P=0.508N	P=0.541	P=0.004N**	P=0.532	P=0.515N	P=0.014N*
COCH-ARM / FISHERS	P=0.378	P=0.279N	P=0.488N	P=0.544	P=0.009N**	P=0.413	P=0.565N	P=0.015N*
ORDER RESTRICTED	P=0.409	P=0.288N	P=0.500N	P=0.602N	P=0.010N*	P=0.423	P=0.420N	P=0.030N*

Terminal Sacrifice at 105 weeks

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

Pituitary Gland: Pars Distalis or Unspecified Site
Carcinoma

OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	1/48 (2%)	3/50 (6%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	0/45.93	0/44.49	0/43.91	2/46.71	1/43.78	3/40.77	0/48.02
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	0.0%	4.3%	2.3%	7.4%	0.0%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	0/36 (0%)	0/35 (0%)	0/40 (0%)	1/39 (3%)	3/28 (11%)	0/42 (0%)
FIRST INCIDENCE	---	---	---	---	602	729 (T)	729 (T)	---

STATISTICAL TESTS

LIFE TABLE	(e)	(e)	(e)	(e)	P=0.256N	P=0.516N	P=0.371	P=0.228N
POLY 3	(e)	(e)	(e)	(e)	P=0.236N	P=0.523N	P=0.438	P=0.231N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.242N	P=0.519N	P=0.463	P=0.233N
POLY 6	(e)	(e)	(e)	(e)	P=0.231N	P=0.525N	P=0.407	P=0.229N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.251N	P=0.509N	P=0.493	P=0.292N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.250N	P=0.515N	P=0.500	P=0.247N
ORDER RESTRICTED	(e)	(e)	(e)	(e)	P=0.157N	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

Pituitary Gland: Pars Distalis or Unspecified Site
Carcinoma or Adenoma

OVERALL (a)	9/50 (18%)	6/50 (12%)	8/50 (16%)	9/50 (18%)	25/50 (50%)	25/48 (52%)	24/50 (48%)	13/50 (26%)
POLY-3 RATE (b)	9/46.40	6/45.93	8/46.05	9/44.06	25/47.20	25/46.25	24/44.42	13/48.36
POLY-3 PERCENT (g)	19.4%	13.1%	17.4%	20.4%	53.0%	54.1%	54.0%	26.9%
TERMINAL (d)	7/35 (20%)	6/40 (15%)	5/36 (14%)	8/35 (23%)	21/40 (53%)	19/39 (49%)	13/28 (46%)	11/42 (26%)
FIRST INCIDENCE	694	729 (T)	392	689	602	425	532	644

STATISTICAL TESTS

LIFE TABLE	P=0.354	P=0.214N	P=0.489N	P=0.589	P=0.009N**	P=0.527	P=0.170	P=0.009N**
POLY 3	P=0.363	P=0.294N	P=0.507N	P=0.556	P=0.002N**	P=0.541	P=0.543	P=0.007N**
POLY 1.5	P=0.378	P=0.291N	P=0.504N	P=0.572	P=0.003N**	P=0.525	P=0.582	P=0.008N**
POLY 6	P=0.351	P=0.297N	P=0.508N	P=0.541	P=0.002N**	P=0.564	P=0.506	P=0.006N**
LOGISTIC REGRESSION	P=0.378	P=0.279N	P=0.488N	P=0.544	P=0.004N**	P=0.492	P=0.517	P=0.008N**
COCH-ARM / FISHERS	P=0.409	P=0.288N	P=0.500N	P=0.544	P=0.004N**	P=0.498	P=0.500N	P=0.011N*
ORDER RESTRICTED	P=0.476	(e)	(e)	(e)	P=0.004N**	(e)	(e)	(e)

Dose	Males				Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM

Skin
 Basal Cell Carcinoma

TUMOR RATES	Males		Females	
	#	%	#	%
OVERALL (a)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	2/43.91	1/46.22	0/40.77
POLY-3 PERCENT (g)	0.0%	4.6%	2.2%	0.0%
TERMINAL (d)	0/35 (0%)	2/35 (6%)	0/40 (0%)	0/28 (0%)
FIRST INCIDENCE	---	729 (T)	671	0/42 (0%)

STATISTICAL TESTS

LIFE TABLE	P=0.037 *	(e)	(e)	P=0.238	P=0.316N	P=0.500N	P=0.548N	P=0.478N
POLY 3	P=0.038 *	(e)	(e)	P=0.226	P=0.328N	P=0.505N	P=0.525N	P=0.492N
POLY 1.5	P=0.039 *	(e)	(e)	P=0.230	P=0.326N	P=0.503N	P=0.515N	P=0.495N
POLY 6	P=0.038 *	(e)	(e)	P=0.223	P=0.321N	P=0.507N	P=0.538N	P=0.489N
LOGISTIC REGRESSION	(e)	(e)	(e)	P=0.238	P=0.321N	P=0.494N	P=0.487N	P=0.528N
COCH-ARM / FISHERS	P=0.042 *	(e)	(e)	P=0.247	P=0.321N	P=0.500N	P=0.500N	P=0.500N
ORDER RESTRICTED	P=0.026 *	(e)	(e)	(e)	P=0.113N	(e)	(e)	(e)

Dose	Males				Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM

Skin

Basal Cell Carcinoma, Basal Cell Adenoma, Basosquamous Tumor (benign, malignant or NOS), or Trichoepithelioma

TUMOR RATES	Males		Females	
	#	%	#	%
OVERALL (a)	1/50 (2%)	1/50 (2%)	3/50 (6%)	2/50 (4%)
POLY-3 RATE (b)	1/46.13	1/44.80	3/43.91	2/46.22
POLY-3 PERCENT (g)	2.2%	2.2%	6.8%	4.3%
TERMINAL (d)	1/35 (3%)	0/36 (0%)	3/35 (9%)	1/40 (3%)
FIRST INCIDENCE	729 (T)	644	729 (T)	671

STATISTICAL TESTS

LIFE TABLE	P=0.070	P=0.473N	P=0.758	P=0.305	P=0.134N	P=0.243N	P=0.307N	P=0.222N
POLY 3	P=0.073	P=0.501N	P=0.754	P=0.288	P=0.129N	P=0.243N	P=0.266N	P=0.229N
POLY 1.5	P=0.075	P=0.500N	P=0.756	P=0.294	P=0.129N	P=0.241N	P=0.254N	P=0.232N
POLY 6	P=0.072	P=0.501N	P=0.754	P=0.283	P=0.130N	P=0.245N	P=0.282N	P=0.225N
LOGISTIC REGRESSION	P=0.073	(e)	P=0.758N	P=0.305	P=0.129N	P=0.237N	P=0.250N	P=0.244N
COCH-ARM / FISHERS	P=0.080	P=0.500N	P=0.753N	P=0.309	P=0.129N	P=0.247N	P=0.247N	P=0.247N
ORDER RESTRICTED	P=0.073	(e)	(e)	(e)	P=0.027N*	(e)	(e)	(e)

Dose	Males					Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
Skin Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma									
TUMOR RATES									
OVERALL (a)	#	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	2/50 (4%)	4/50 (8%)	1/50 (2%)	3/50 (6%)	1/50 (2%)	0/50 (0%)	2/50 (4%)	2/41 (11)	2/50 (4%)
POLY-3 PERCENT (g)	2/46.36	4/45.93	1/44.49	3/43.91	1/46.00	0/44.99	0/44.99	2/41.11	2/48.35
TERMINAL (d)	4.3%	8.7%	2.3%	6.8%	2.2%	0.0%	4.9%	0/28 (0%)	4.1%
FIRST INCIDENCE	1/35 (3%)	4/40 (10%)	1/36 (3%)	3/35 (9%)	1/40 (3%)	0/39 (0%)	0/28 (0%)	1/42 (2%)	638
STATISTICAL TESTS	668	729 (T)	729 (T)	729 (T)	729 (T)	---	668	---	638

Dose	Males					Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
Skin Keratoacanthoma									
TUMOR RATES									
OVERALL (a)	#	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	1/50 (2%)	2/50 (4%)	1/50 (2%)	4/50 (8%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 PERCENT (g)	1/46.13	2/45.93	1/44.49	4/44.67	0/46.00	0/44.99	0/40.77	0/40.77	1/48.02
TERMINAL (d)	2.2%	4.4%	2.3%	9.0%	0.0%	0.0%	0.0%	0.0%	2.1%
FIRST INCIDENCE	1/35 (3%)	2/40 (5%)	1/36 (3%)	1/35 (3%)	0/40 (0%)	0/39 (0%)	0/28 (0%)	1/42 (2%)	729 (T)
STATISTICAL TESTS	729 (T)	729 (T)	729 (T)	598	---	---	---	---	729 (T)

Dose	Males					Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
LIFE TABLE									
POLY 3	P=0.531	P=0.388	P=0.499N	P=0.494	P=0.253	P=0.505N	P=0.403	P=0.524	P=0.517
POLY 1.5	P=0.536	P=0.333	P=0.514N	P=0.475	P=0.249	P=0.504N	P=0.461	P=0.510	P=0.510
LOGISTIC REGRESSION	P=0.544	P=0.336	P=0.509N	P=0.484	P=0.240	P=0.503N	P=0.476	P=0.526	P=0.485
COCH-ARM / FISHERS	P=0.528	P=0.331	P=0.519N	P=0.467	P=0.260	P=0.505N	P=0.443	P=0.475	P=0.500
ORDER RESTRICTED	P=0.527	P=0.335	P=0.508N	P=0.474	P=0.224	P=0.500N	P=0.475	P=0.500	P=0.500
	P=0.561	P=0.339	P=0.500N	P=0.500	P=0.226	P=0.500N	P=0.500	P=0.500	P=0.500
	P=0.475	(e)	(e)	(e)	P=0.245	(e)	(e)	(e)	(e)

Dose	Males					Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
LIFE TABLE									
POLY 3	P=0.099	P=0.547	P=0.756N	P=0.177	P=0.208	(e)	(e)	(e)	P=0.510
POLY 1.5	P=0.102	P=0.498	P=0.753	P=0.169	P=0.202	(e)	(e)	(e)	P=0.509
LOGISTIC REGRESSION	P=0.104	P=0.500	P=0.755	P=0.172	P=0.199	(e)	(e)	(e)	P=0.505
COCH-ARM / FISHERS	P=0.102	P=0.499	P=0.751	P=0.169	P=0.205	(e)	(e)	(e)	P=0.513
ORDER RESTRICTED	P=0.104	P=0.547	P=0.756N	P=0.185	(e)	(e)	(e)	(e)	P=0.510
	P=0.108	P=0.500	P=0.753N	P=0.181	P=0.194	(e)	(e)	(e)	P=0.500
	P=0.087	(e)	(e)	(e)	P=0.129	(e)	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM
Skin Squamous Cell Carcinoma, Basal Cell Carcinoma, Basosquamous Tumor (malignant or NOS), or Carcinoma						
TUMOR RATES						
OVERALL (a)	#	#	#	#	#	#
POLY-3 RATE (b)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 PERCENT (g)	0/46.13	0/45.93	0/44.49	1/46.22	0/44.99	1/41.26
TERMINAL (d)	0.0%	0.0%	0.0%	2.2%	0.0%	2.4%
FIRST INCIDENCE	0/35 (0%)	0/40 (0%)	0/36 (0%)	0/40 (0%)	0/39 (0%)	0/28 (0%)
STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.037 *	(e)	(e)	P=0.417N	P=0.500N	P=0.716
POLY 1.5	P=0.038 *	(e)	(e)	P=0.416N	P=0.505N	P=0.735
LOGISTIC REGRESSION	P=0.039 *	(e)	(e)	P=0.420N	P=0.503N	P=0.745
COCH-ARM / FISHERS	P=0.042 *	(e)	(e)	P=0.412N	P=0.507N	P=0.721
ORDER RESTRICTED	P=0.026 *	(e)	(e)	P=0.440N	P=0.494N	P=0.718N
				P=0.425N	P=0.500N	P=0.753N
				P=0.247	P=0.243N	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM
Skin Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma						
TUMOR RATES						
OVERALL (a)	#	#	#	#	#	#
POLY-3 RATE (b)	1/50 (2%)	2/50 (4%)	1/50 (2%)	4/50 (8%)	0/50 (0%)	1/50 (2%)
POLY-3 PERCENT (g)	1/46.13	2/45.93	1/44.49	4/44.67	0/46.00	1/41.26
TERMINAL (d)	2.2%	4.4%	2.3%	9.0%	0.0%	2.4%
FIRST INCIDENCE	1/35 (3%)	2/40 (5%)	1/36 (3%)	1/35 (3%)	0/40 (0%)	0/39 (0%)
STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.099	P=0.547	P=0.756N	P=0.177	P=0.237	P=0.469
POLY 1.5	P=0.102	P=0.498	P=0.753	P=0.169	P=0.243	P=0.478
LOGISTIC REGRESSION	P=0.104	P=0.500	P=0.755	P=0.172	P=0.237	P=0.487
COCH-ARM / FISHERS	P=0.102	P=0.499	P=0.751	P=0.169	P=0.251	P=0.468
ORDER RESTRICTED	P=0.104	P=0.547	P=0.756N	P=0.185	P=0.205	P=0.579
	P=0.108	P=0.500	P=0.753N	P=0.181	P=0.225	P=0.500
	P=0.087	(e)	(e)	(e)	P=0.231	(e)

Dose	Males			Females		
	0PPM	300 PPM	1000 PPM	0PPM	1000 PPM	2500 PPM
Skin Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma						
TUMOR RATES						
OVERALL (a)	#	#	#	#	#	#
POLY-3 RATE (b)	1/50 (2%)	2/50 (4%)	1/50 (2%)	4/50 (8%)	0/50 (0%)	1/50 (2%)
POLY-3 PERCENT (g)	1/46.13	2/45.93	1/44.49	4/44.67	0/46.00	1/41.26
TERMINAL (d)	2.2%	4.4%	2.3%	9.0%	0.0%	2.4%
FIRST INCIDENCE	1/35 (3%)	2/40 (5%)	1/36 (3%)	1/35 (3%)	0/40 (0%)	0/39 (0%)
STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.099	P=0.547	P=0.756N	P=0.177	P=0.237	P=0.469
POLY 1.5	P=0.102	P=0.498	P=0.753	P=0.169	P=0.243	P=0.478
LOGISTIC REGRESSION	P=0.104	P=0.500	P=0.755	P=0.172	P=0.237	P=0.487
COCH-ARM / FISHERS	P=0.102	P=0.499	P=0.751	P=0.169	P=0.251	P=0.468
ORDER RESTRICTED	P=0.104	P=0.547	P=0.756N	P=0.185	P=0.205	P=0.579
	P=0.108	P=0.500	P=0.753N	P=0.181	P=0.225	P=0.500
	P=0.087	(e)	(e)	(e)	P=0.231	(e)

Dose	Males					Females		
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

Thyroid Gland: C-Cell Carcinoma

TUMOR RATES								
OVERALL (a)	1/48 (2%)	0/46 (0%)	0/43 (0%)	3/50 (6%)	0/49 (0%)	1/48 (2%)	0/42 (0%)	1/48 (2%)
POLY-3 RATE (b)	1/45.06	0/43.50	0/40.29	3/44.06	0/45.28	1/44.11	0/35.57	1/46.81
POLY-3 PERCENT (g)	2.2%	0.0%	0.0%	6.8%	0.0%	2.3%	0.0%	2.1%
TERMINAL (d)	1/35 (3%)	0/39 (0%)	0/35 (0%)	2/35 (6%)	0/40 (0%)	0/39 (0%)	0/28 (0%)	1/41 (2%)
FIRST INCIDENCE	729 (T)	---	---	689	---	638	---	729 (T)

STATISTICAL TESTS								
LIFE TABLE	P=0.051	P=0.478N	P=0.500N	P=0.302	P=0.438	P=0.500	(e)	P=0.505
POLY 3	P=0.059	P=0.507N	P=0.522N	P=0.297	P=0.433	P=0.495	(e)	P=0.507
POLY 1.5	P=0.061	P=0.508N	P=0.523N	P=0.304	P=0.428	P=0.495	(e)	P=0.503
POLY 6	P=0.057	P=0.504N	P=0.520N	P=0.293	P=0.439	P=0.496	(e)	P=0.511
LOGISTIC REGRESSION	P=0.054	(e)	(e)	P=0.291	P=0.407	P=0.498	(e)	P=0.505
COCH-ARM / FISHERS	P=0.066	P=0.511N	P=0.527N	P=0.324	P=0.420	P=0.495	(e)	P=0.495
ORDER RESTRICTED	P=0.036	(e)	(e)	(e)	P=0.258	(e)	(e)	(e)

Thyroid Gland: C-Cell Carcinoma or Adenoma

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

OVERALL (a)	10/48 (21%)	5/46 (11%)	9/43 (21%)	10/50 (20%)	9/49 (18%)	10/48 (21%)	8/42 (19%)	3/48 (6%)
POLY-3 RATE (b)	10/45.06	5/43.50	9/40.29	10/44.33	9/45.71	10/44.55	8/36.31	3/46.81
POLY-3 PERCENT (g)	22.2%	11.5%	22.3%	22.6%	19.7%	22.5%	22.0%	6.4%
TERMINAL (d)	10/35 (29%)	5/39 (13%)	9/35 (26%)	7/35 (20%)	8/40 (20%)	7/39 (18%)	5/28 (18%)	3/41 (7%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	689	602	638	638	729 (T)

STATISTICAL TESTS								
LIFE TABLE	P=0.273	P=0.083N	P=0.500N	P=0.593	P=0.039N*	P=0.477	P=0.429	P=0.057N
POLY 3	P=0.318	P=0.144N	P=0.596	P=0.584	P=0.030N*	P=0.475	P=0.505	P=0.054N
POLY 1.5	P=0.337	P=0.148N	P=0.594	P=0.598	P=0.033N*	P=0.476	P=0.528	P=0.058N
POLY 6	P=0.304	P=0.136N	P=0.599N	P=0.579	P=0.027N*	P=0.481	P=0.483	P=0.051N
LOGISTIC REGRESSION	P=0.274	P=0.083N	P=0.500N	P=0.559	P=0.035N*	P=0.472	P=0.508	P=0.056N
COCH-ARM / FISHERS	P=0.382	P=0.150N	P=0.596	P=0.558N	P=0.040N*	P=0.480	P=0.572	P=0.065N
ORDER RESTRICTED	P=0.394	(e)	(e)	(e)	P=0.033N*	(e)	(e)	(e)

Dose	OPPM	Males			OPPM	Females		
		300 PPM	1000 PPM	3000 PPM		2500 PPM	5000 PPM	

Thyroid Gland: Follicular Cell Adenoma

TUMOR RATES	Males						Females		
	OPPM	300 PPM	1000 PPM	3000 PPM	OPPM	1000 PPM	2500 PPM	5000 PPM	
OVERALL (a)	1/48 (2%)	0/46 (0%)	1/43 (2%)	3/50 (6%)	0/49 (0%)	0/48 (0%)	0/42 (0%)	5/48 (10%)	
POLY-3 RATE (b)	1/45.06	0/43.50	1/40.29	3/43.91	0/45.28	0/43.78	0/35.57	5/47.14	
POLY-3 PERCENT (g)	2.2%	0.0%	2.5%	6.8%	0.0%	0.0%	0.0%	10.6%	
TERMINAL (d)	1/35 (3%)	0/39 (0%)	1/35 (3%)	3/35 (9%)	0/40 (0%)	0/39 (0%)	0/28 (0%)	4/41 (10%)	
FIRST INCIDENCE	729 (T)	---	729 (T)	729 (T)	---	---	---	638	

STATISTICAL TESTS

LIFE TABLE	P=0.072	P=0.478N	P=0.762	P=0.305	P<0.001 **	(e)	(e)	P=0.038 *
POLY 3	P=0.083	P=0.507N	P=0.736	P=0.296	P<0.001 **	(e)	(e)	P=0.034 *
POLY 1.5	P=0.087	P=0.508N	P=0.735	P=0.303	P<0.001 **	(e)	(e)	P=0.032 *
POLY 6	P=0.080	P=0.504N	P=0.738	P=0.291	P<0.001 **	(e)	(e)	P=0.036 *
LOGISTIC REGRESSION	P=0.072	(e)	P=0.762	P=0.305	P<0.001 **	(e)	(e)	P=0.028 *
COCH-ARM / FISHERS	P=0.095	P=0.511N	P=0.725	P=0.324	P<0.001 **	(e)	(e)	P=0.027 *
ORDER RESTRICTED	P=0.077	(e)	(e)	(e)	P<0.001 **	(e)	(e)	(e)

Dose	OPPM	Males			OPPM	Females		
		300 PPM	1000 PPM	3000 PPM		2500 PPM	5000 PPM	

Thyroid Gland: Follicular Cell Carcinoma

OVERALL (a)	0/48 (0%)	2/46 (4%)	0/43 (0%)	2/50 (4%)	1/49 (2%)	1/48 (2%)	1/42 (2%)	7/48 (15%)
POLY-3 RATE (b)	0/45.06	2/43.64	0/40.29	2/44.75	1/45.77	1/44.38	1/35.57	7/46.84
POLY-3 PERCENT (g)	0.0%	4.6%	0.0%	4.5%	2.2%	2.3%	2.8%	14.9%
TERMINAL (d)	0/35 (0%)	1/39 (3%)	0/35 (0%)	1/35 (3%)	0/40 (0%)	0/39 (0%)	1/28 (4%)	6/41 (15%)
FIRST INCIDENCE	---	693	---	395	583	538	729 (T)	722

STATISTICAL TESTS

LIFE TABLE	P=0.273	P=0.252	(e)	P=0.240	P=0.005 **	P=0.744	P=0.700	P=0.039 *
POLY 3	P=0.296	P=0.230	(e)	P=0.236	P=0.003 **	P=0.754	P=0.703	P=0.033 *
POLY 1.5	P=0.300	P=0.229	(e)	P=0.239	P=0.003 **	P=0.754	P=0.711	P=0.031 *
POLY 6	P=0.293	P=0.234	(e)	P=0.233	P=0.003 **	P=0.754	P=0.692	P=0.034 *
LOGISTIC REGRESSION	P=0.473	P=0.228	(e)	P=0.403	P=0.002 **	P=0.767	P=0.761	P=0.026 *
COCH-ARM / FISHERS	P=0.310	P=0.237	(e)	P=0.258	P=0.003 **	P=0.747	P=0.713	P=0.028 *
ORDER RESTRICTED	P=0.115	(e)	(e)	(e)	P=0.003 **	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
Zymbal's Gland Carcinoma								

TUMOR RATES	#							
	0/50 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
OVERALL (a)	0/50 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/46.13	1/46.59	2/44.70	0/43.91	0/46.00	0/44.99	0/40.77	0/48.02
POLY-3 PERCENT (g)	0.0%	2.2%	4.5%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/40 (0%)	1/36 (3%)	0/35 (0%)	0/40 (0%)	0/39 (0%)	0/28 (0%)	0/42 (0%)
FIRST INCIDENCE	---	507	673	---	---	---	---	---

STATISTICAL TESTS	P							
	0.528N	0.504	0.238	(e)	(e)	(e)	(e)	(e)
LIFE TABLE	P=0.528N	P=0.504	P=0.238	(e)	(e)	(e)	(e)	(e)
POLY 3	P=0.535N	P=0.502	P=0.230	(e)	(e)	(e)	(e)	(e)
POLY 1.5	P=0.528N	P=0.502	P=0.233	(e)	(e)	(e)	(e)	(e)
POLY 6	P=0.541N	P=0.503	P=0.229	(e)	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.456N	P=0.357	P=0.236	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.515N	P=0.500	P=0.247	(e)	(e)	(e)	(e)	(e)
ORDER RESTRICTED	P=0.319	(e)	(e)	(e)	(e)	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
All Organs								
Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated								

TUMOR RATES	#							
	15/50 (30%)	14/50 (28%)	21/50 (42%)	10/50 (20%)	6/50 (12%)	4/50 (8%)	9/50 (18%)	10/50 (20%)
OVERALL (a)	15/50 (30%)	14/50 (28%)	21/50 (42%)	10/50 (20%)	6/50 (12%)	4/50 (8%)	9/50 (18%)	10/50 (20%)
POLY-3 RATE (b)	15/48.70	14/48.08	21/47.64	10/45.67	6/47.21	4/45.63	9/42.95	10/49.18
POLY-3 PERCENT (g)	30.8%	29.1%	44.1%	21.9%	12.7%	8.8%	21.0%	20.3%
TERMINAL (d)	4/35 (11%)	8/40 (20%)	11/36 (31%)	4/35 (11%)	2/40 (5%)	2/39 (5%)	3/28 (11%)	6/42 (14%)
FIRST INCIDENCE	572	521	439	574	583	598	548	434

STATISTICAL TESTS	P							
	0.222N	0.449N	0.182	0.245N	0.111	0.392N	0.157	0.261
LIFE TABLE	P=0.222N	P=0.449N	P=0.182	P=0.245N	P=0.111	P=0.392N	P=0.157	P=0.261
POLY 3	P=0.193N	P=0.516N	P=0.127	P=0.228N	P=0.090	P=0.391N	P=0.222	P=0.233
POLY 1.5	P=0.172N	P=0.506N	P=0.136	P=0.209N	P=0.083	P=0.383N	P=0.246	P=0.224
POLY 6	P=0.217N	P=0.530N	P=0.120	P=0.251N	P=0.097	P=0.399N	P=0.196	P=0.242
LOGISTIC REGRESSION	P=0.099N	P=0.485N	P=0.179	P=0.146N	P=0.058	P=0.351N	P=0.354	P=0.144
COCH-ARM / FISHERS	P=0.137N	P=0.500N	P=0.149	P=0.178N	P=0.073	P=0.370N	P=0.288	P=0.207
ORDER RESTRICTED	P=0.141N	(e)	(e)	(e)	P=0.135	(e)	(e)	(e)

All Organs
 Mesothelioma: Benign, Malignant, NOS

TUMOR RATES	Males						Females			
	Dose	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
OVERALL (a)	2/50 (4%)	4/50 (8%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/40.77	0/50 (0%)	0/48.02
POLY-3 RATE (b)	2/46.44	4/46.60	2/44.49	0/43.91	0/46.00	0/44.99	0/46.00	0/44.99	0/40.77	0/48.02
POLY-3 PERCENT (g)	4.3%	8.6%	4.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	2/40 (5%)	2/36 (6%)	0/35 (0%)	0/40 (0%)	0/39 (0%)	0/40 (0%)	0/28 (0%)	0/28 (0%)	0/42 (0%)
FIRST INCIDENCE	643	608	729 (T)	---	---	---	---	---	---	---

STATISTICAL TESTS

LIFE TABLE

POLY 3
 P=0.100N P=0.364 P=0.692N P=0.252N (e)
 P=0.097N P=0.339 P=0.678 P=0.250N (e)
 POLY 1.5
 P=0.094N P=0.339 P=0.684 P=0.245N (e)
 P=0.101N P=0.341 P=0.674 P=0.254N (e)
 LOGISTIC REGRESSION
 P=0.085N P=0.330 P=0.689 P=0.230N (e)
 COCH-ARM / FISHERS
 P=0.087N P=0.339 P=0.691N P=0.247N (e)
 ORDER RESTRICTED
 P=0.103N (e)

All Organs
 Mesothelioma: Malignant

TUMOR RATES	Males						Females			
	Dose	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM
OVERALL (a)	2/50 (4%)	4/50 (8%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46.44	4/46.60	2/44.49	0/43.91	0/46.00	0/44.99	0/46.00	0/44.99	0/40.77	0/48.02
POLY-3 PERCENT (g)	4.3%	8.6%	4.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	2/40 (5%)	2/36 (6%)	0/35 (0%)	0/40 (0%)	0/39 (0%)	0/40 (0%)	0/28 (0%)	0/28 (0%)	0/42 (0%)
FIRST INCIDENCE	643	608	729 (T)	---	---	---	---	---	---	---

STATISTICAL TESTS

LIFE TABLE

POLY 3
 P=0.100N P=0.364 P=0.692N P=0.252N (e)
 P=0.097N P=0.339 P=0.678 P=0.250N (e)
 POLY 1.5
 P=0.094N P=0.339 P=0.684 P=0.245N (e)
 P=0.101N P=0.341 P=0.674 P=0.254N (e)
 LOGISTIC REGRESSION
 P=0.085N P=0.330 P=0.689 P=0.230N (e)
 COCH-ARM / FISHERS
 P=0.087N P=0.339 P=0.691N P=0.247N (e)
 ORDER RESTRICTED
 P=0.103N (e)

Dose	Males					Females				
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM	

All Organs
Osteosarcoma or Osteoma

TUMOR RATES	#		#		#		#	
	Overall (a)	Poly-3 Rate (b)						
OVERALL (a)	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 RATE (b)	2/46.14	0/45.93	0/44.49	2/44.60	0/46.00	0/44.99	0/40.77	0/48.02
POLY-3 PERCENT (g)	4.3%	0.0%	0.0%	4.5%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	0/40 (0%)	0/36 (0%)	1/35 (3%)	0/40 (0%)	0/39 (0%)	0/28 (0%)	0/42 (0%)
FIRST INCIDENCE	726	---	---	491	---	---	---	---

STATISTICAL TESTS

LIFE TABLE	#		#		#		#	
	Overall (a)	Poly-3 Rate (b)						
LIFE TABLE	P=0.364	P=0.214N	P=0.237N	P=0.688	(e)	(e)	(e)	(e)
POLY 3	P=0.375	P=0.238N	P=0.245N	P=0.682	(e)	(e)	(e)	(e)
POLY 1.5	P=0.376	P=0.238N	P=0.242N	P=0.685	(e)	(e)	(e)	(e)
POLY 6	P=0.373	P=0.238N	P=0.247N	P=0.679	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.410	P=0.226N	P=0.241N	P=0.673N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.381	P=0.247N	P=0.247N	P=0.691N	(e)	(e)	(e)	(e)
ORDER RESTRICTED	P=0.259	(e)	(e)	(e)	(e)	(e)	(e)	(e)

Dose	Males					Females				
	0PPM	300 PPM	1000 PPM	3000 PPM	5000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM	

All Organs
Benign Tumors

TUMOR RATES	#		#		#		#	
	Overall (a)	Poly-3 Rate (b)	Overall (a)	Poly-3 Rate (b)	Overall (a)	Poly-3 Rate (b)	Overall (a)	Poly-3 Rate (b)
OVERALL (a)	49/50 (98%)	46/50 (92%)	47/50 (94%)	45/50 (90%)	43/50 (86%)	43/50 (86%)	40/50 (80%)	27/50 (54%)
POLY-3 RATE (b)	49/49.08	46/48.27	47/48.49	45/47.50	43/48.60	43/49.21	40/45.84	27/48.69
POLY-3 PERCENT (g)	99.8%	95.3%	96.9%	94.7%	88.5%	87.4%	87.3%	55.5%
TERMINAL (d)	35/35 (100%)	39/40 (98%)	35/36 (97%)	33/35 (94%)	35/40 (88%)	34/39 (87%)	25/28 (89%)	24/42 (57%)
FIRST INCIDENCE	572	548	392	562	588	425	332	638

STATISTICAL TESTS

LIFE TABLE	#		#		#		#	
	Overall (a)	Poly-3 Rate (b)						
LIFE TABLE	P=0.545N	P=0.073N	P=0.387N	P=0.344N	P<0.001N**	P=0.495	P=0.055	P<0.001N**
POLY 3	P=0.220N	P=0.165N	P=0.347N	P=0.154N	P<0.001N**	P=0.558N	P=0.557N	P<0.001N**
POLY 1.5	P=0.201N	P=0.135N	P=0.284N	P=0.113N	P<0.001N**	P=0.567N	P=0.441N	P<0.001N**
POLY 6	P=0.215N	P=0.289N	P=0.451N	P=0.205N	P<0.001N**	P=0.566N	P=0.579	P<0.001N**
LOGISTIC REGRESSION	P=0.361N	P=0.193N	P=0.458N	P=0.205N	P<0.001N**	P=0.588	P=0.591N	P<0.001N**
COCH-ARM / FISHERS	P=0.150N	P=0.181N	P=0.309N	P=0.102N	P<0.001N**	P=0.613N	P=0.298N	P<0.001N**
ORDER RESTRICTED	P=0.082N	(e)	(e)	(e)	P<0.001N**	(e)	(e)	(e)

All Organs
 Malignant Tumors

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

TUMOR RATES

	#	#	#	#	#	#	#	#
OVERALL (a)	22/50 (44%)	26/50 (52%)	30/50 (60%)	25/50 (50%)	19/50 (38%)	10/50 (20%)	21/50 (42%)	20/50 (40%)
POLY-3 RATE (b)	22/49.63	26/50.00	30/48.58	25/47.52	19/49.74	10/46.66	21/46.62	20/49.18
POLY-3 PERCENT (g)	44.3%	52.0%	61.8%	52.6%	38.2%	21.4%	45.0%	40.7%
TERMINAL (d)	9/35 (26%)	16/40 (40%)	18/36 (50%)	15/35 (43%)	10/40 (25%)	5/39 (13%)	10/28 (36%)	16/42 (38%)
FIRST INCIDENCE	315	507	439	395	328	538	244	434

STATISTICAL TESTS

LIFE TABLE	P=0.354	P=0.410	P=0.137	P=0.334	P=0.236	P=0.070N	P=0.153	P=0.569N
POLY 3	P=0.335	P=0.287	P=0.062	P=0.270	P=0.172	P=0.056N	P=0.318	P=0.482
POLY 1.5	P=0.371	P=0.281	P=0.066	P=0.293	P=0.170	P=0.049N*	P=0.362	P=0.490
POLY 6	P=0.300	P=0.296	P=0.060	P=0.248	P=0.168	P=0.065N	P=0.259	P=0.469
LOGISTIC REGRESSION	P=0.548	P=0.196	P=0.108	P=0.419	P=0.106	P=0.023N*	P=0.401N	P=0.308
COCH-ARM / FISHERS	P=0.448	P=0.274	P=0.080	P=0.344	P=0.163	P=0.038N*	P=0.419	P=0.500
ORDER RESTRICTED	P=0.157	(e)	(e)	(e)	P=0.137	(e)	(e)	(e)

All Organs
 Malignant and Benign Tumors

Dose	Males				Females			
	0PPM	300 PPM	1000 PPM	3000 PPM	0PPM	1000 PPM	2500 PPM	5000 PPM

TUMOR RATES

	#	#	#	#	#	#	#	#
OVERALL (a)	50/50 (100%)	49/50 (98%)	49/50 (98%)	48/50 (96%)	45/50 (90%)	44/50 (88%)	48/50 (96%)	38/50 (76%)
POLY-3 RATE (b)	50/50.00	49/50.00	49/50.00	48/49.04	45/50.00	44/49.40	48/49.76	38/49.82
POLY-3 PERCENT (g)	100.0%	98.0%	98.0%	97.9%	90.0%	89.1%	96.5%	76.3%
TERMINAL (d)	35/35 (100%)	39/40 (98%)	35/36 (97%)	34/35 (97%)	35/40 (88%)	34/39 (87%)	27/28 (96%)	32/42 (76%)
FIRST INCIDENCE	315	507	392	395	328	425	244	434

STATISTICAL TESTS

LIFE TABLE	P=0.440	P=0.173N	P=0.465N	P=0.493N	P=0.096N	P=0.567	P=0.005 **	P=0.062N
POLY 3	P=0.463N	P=0.500N	P=0.500N	P=0.480N	P=0.024N*	P=0.570N	P=0.185	P=0.057N
POLY 1.5	P=0.405N	P=0.500N	P=0.500N	P=0.419N	P=0.025N*	P=0.542N	P=0.200	P=0.055N
POLY 6	P=0.477N	P=0.500N	P=0.500N	P=0.495N	P=0.024N*	P=0.598N	P=0.163	P=0.060N
LOGISTIC REGRESSION	P=0.269N	(e)	(e)	P=0.325N	P=0.040N*	P=0.489N	P=0.305	P=0.077N
COCH-ARM / FISHERS	P=0.194N	P=0.500N	P=0.500N	P=0.247N	P=0.030N*	P=0.500N	P=0.218	P=0.054N
ORDER RESTRICTED	P=0.310N	(e)	(e)	(e)	P=0.009N**	(e)	(e)	(e)

(a) Number of tumor-bearing animals / number of animals examined at site.
 (b) Number of tumor-bearing animals / Poly-3 number
 (d) Observed incidence at terminal kill.

(f) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death.

Logistic regression is an alternative method for analyzing the incidence of non-fatal tumors. The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates and for all tests a negative trend is indicated by N

(e) Value of Statistic cannot be computed.

(g) Poly-3 adjusted lifetime tumor incidence.

(I) Interim sacrifice

(T) Terminal sacrifice

Tumor rates based on number of animals necropsied.

* To the right of any statistical result, indicates significance at (P<=0.05).

** To the right of any statistical result, indicates significance at (P<=0.01).

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES (b)
2-METHYLMIDAZOLE

Report: PEIRPT18
Date: 03/14/03
Time: 10:45:10

FINAL#1; REVISION#1

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25019 Moribund Sacrifice 25020 Natural Death
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion
b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Animals Initially In Study 60
 Early Deaths 4
 Natural Death 6
 Moribund Sacrifice 40
 Survivors 39
 Terminal Sacrifice 28
 Natural Death 41
 1

Animals Examined Microscopically 50 50 50 50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(48)	(47)	(44)	(50)
Edema				1 [3.0]
Intestine Small, Jejunum	(47)	(46)	(44)	(49)
Necrosis, Focal				1 [3.0]
Liver	(50)	(49)	(50)	(50)
Angiectasis, Focal	2 [2.0]	1 [2.0]	2 [3.5]	39
Basophilic Focus	42	44	43	1 [2.0]
Cholangiofibrosis				1 [4.0]
Congestion				2 [2.0]
Congestion, Focal		1 [2.0]	1	
Degeneration, Cystic, Focal				2 [2.0]
Rosinophilic Focus		2 [3.0]	1 [2.0]	
Fatty Change				2 [2.0]
Hemorrhage	2 [2.0]			
Hepatodiaphragmatic Nodule		11	14	13
Hyperplasia, Focal, Lymphoid	6		1 [3.0]	1 [2.0]
Infarct				2
Infiltration Cellular, Mixed Cell	42 [1.7]	44 [2.0]	34 [1.9]	38 [1.9]
Inflammation, Granulomatous	18 [1.6]	23 [2.0]	22 [1.5]	42 [2.1]
Mixed Cell Focus	15	14	11	26
Necrosis, Focal		1 [2.0]	1 [2.0]	1 [2.0]
Bile Duct, Cholangiofibrosis, Focal				
Bile Duct, Cyst	2			
Bile Duct, Cyst, Multiple				1
Bile Duct, Hyperplasia	20 [1.3]	29 [1.4]	20 [1.5]	40 [1.9]
Hepatocyte, Necrosis, Focal			1 [2.0]	2 [2.0]
Hepatocyte, Vacuolization Cytoplasmic, Focal	9 [1.4]	10 [1.4]	11 [1.2]	9 [1.8]
Hepatocyte, Periportal, Vacuolization Cytoplasmic				1 [2.0]

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE		0PPM	1000 PPM	2500 PPM	5000 PPM
ALIMENTARY SYSTEM - CONT					
Hepatocyte, Centrilobular, Necrosis				1 [3.0]	1 [3.0]
Hepatocyte, Centrilobular, Vacuolization				4 [3.0]	1 [2.0]
Cytoplasmic	1 [4.0]	(10)		(12)	(9)
Mesentery	(8)	1 [1.0]			
Fibrosis					
Hemorrhage, Focal				1 [2.0]	
Infiltration Cellular, Mixed Cell					
Inflammation, Chronic			1 [2.0]		
Artery, Inflammation, Chronic, Focal					
Fat, Necrosis					
Fat, Necrosis, Focal	5 [2.0]	1 [2.0]		2 [2.5]	1 [3.0]
Pancreas	(50)	7 [2.7]		6 [2.8]	3 [2.0]
Infiltration Cellular, Diffuse, Mixed Cell		(49)		(49)	(50)
Acinus, Atrophy, Diffuse	1 [3.0]	1 [2.0]			1 [2.0]
Acinus, Atrophy, Focal	13 [1.6]	1 [4.0]		13 [1.7]	11 [1.9]
Duct, Cyst, Focal	1 [2.0]	14 [1.2]			1 [2.0]
Duct, Cyst, Focal, Multiple	9 [1.8]			4 [2.0]	5 [1.8]
Salivary Glands	(50)	12 [1.9]		(50)	(50)
Duct, Mineralization, Focal		(49)			2 [2.5]
Stomach, Forestomach	(50)	(50)		(50)	(50)
Diverticulum	1 [2.0]	1 [2.0]			2 [1.5]
Edema					1 [3.0]
Erosion					
Inflammation, Chronic			1 [3.0]		1 [2.0]
Inflammation, Focal				1 [2.0]	
Ulcer			2 [2.5]		1 [2.0]
Epithelium, Hyperplasia	3 [1.3]	1 [2.0]		4 [2.5]	1 [2.0]
Stomach, Glandular	(49)	(49)		(48)	(50)
Erosion		1 [2.0]		1 [2.0]	
Inflammation, Chronic				1 [2.0]	
Necrosis, Focal				1 [2.0]	
Ulcer					
Epithelium, Hyperplasia, Focal	1 [2.0]				
Glands, Degeneration, Cystic, Focal	1 [2.0]				
Glands, Ectasia, Focal				1 [1.0]	
Glands, Hyperplasia, Focal	1 [2.0]				
Tongue					
Epithelium, Hyperplasia, Focal	(3)			(1)	2 [2.0]
Tooth	1 [1.0]				
Peridental Tissue, Inflammation, Chronic	(1)				
	1 [2.0]				

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES^[b]
 2-METHYLMIDAZOLE

Report: PETRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE OPPM 1000 PPM 2500 PPM 5000 PPM

CARDIOVASCULAR SYSTEM

Lesion	1000 PPM	2500 PPM	5000 PPM
Heart	(50)	(49)	(50)
Cardiomyopathy	5 [1.4]	8 [1.9]	6 [1.7]
Infiltration Cellular, Mixed Cell	4 [1.5]	3 [2.0]	2 [1.5]

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(49)	(50)	(50)
Accessory Adrenal Cortical Nodule	2 [1.0]	2 [1.0]	5 [1.2]	5 [1.0]
Angiectasis	1 [2.0]	1 [3.0]	1 [2.0]	2 [2.0]
Cytoplasmic Alteration, Focal	3 [1.7]	1 [2.0]	1 [1.0]	5 [1.4]
Hematopoietic Cell Proliferation		1 [2.0]		
Hemorrhage		1 [2.0]		
Hemorrhage, Focal		1 [2.0]		
Vacuolization Cytoplasmic, Focal	8 [1.8]	3 [2.0]	7 [1.9]	12 [1.6]
Adrenal Medulla	(49)	(49)	(50)	(50)
Hyperplasia, Focal	1 [2.0]	1 [2.0]	1 [1.0]	2 [1.0]
Pituitary Gland	(50)	(48)	(50)	(50)
Angiectasis	5 [2.8]	9 [2.6]	7 [2.7]	2 [3.0]
Cyst		1 [3.0]		
Hemorrhage		1 [3.0]		
Metaplasia, Focal, Lipocyte			1 [2.0]	1 [2.0]
Pars Distalis, Angiectasis				1 [2.0]
Pars Distalis, Cyst	1 [3.0]	3 [2.3]	2 [2.0]	1 [2.0]
Pars Distalis, Cyst, Multiple		2 [2.5]		
Pars Distalis, Cytoplasmic Alteration, Focal	4 [1.5]	4 [1.5]	1 [2.0]	3 [1.7]
Pars Distalis, Degeneration, Cystic	1 [2.0]			
Pars Distalis, Degeneration, Cystic, Focal	9 [2.2]	14 [2.1]	8 [2.4]	5 [2.2]
Pars Distalis, Hemorrhage, Focal	1 [1.0]	3 [2.7]	4 [3.0]	6 [2.7]
Pars Distalis, Hyperplasia, Focal	1 [2.0]	1 [2.0]	1 [3.0]	1 [2.0]
Pars Distalis, Pigmentation, Focal			1 [2.0]	
Pars Intermedia, Cyst				3 [2.0]
Pars Intermedia, Degeneration, Cystic, Focal				1 [2.0]
Pars Intermedia, Hemorrhage				1 [2.0]
Pars Intermedia, Pars Nervosa, Atypia Cellular, Focal	1 [3.0]	1 [2.0]	1 [2.0]	2 [3.0]
Rathke's Cleft, Cyst				(48)
Rathke's Cleft, Hemorrhage	(49)	(48)	(42)	(48)
Thyroid Gland				
Vacuolization Cytoplasmic, Focal	48 [2.2]	1 [1.0]	40 [2.0]	25 [1.7]
C-Cell, Hyperplasia		46 [2.2]		
Follicle, Cyst	2	2	1	1

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLIMIDAZOLE

Report: P18RPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

ENDOCRINE SYSTEM - CONT
 Follicle, Mineralization, Focal 42 [1.0] 47 [1.7] 41 [2.4] 48 [2.7]
 Follicular Cell, Hyperplasia 41 [1.5] 34 [1.7] 46 [2.2]

GENERAL BODY SYSTEM

Tissue NOS (3) (4) (2)
 Mediastinum, Infiltration Cellular, Mixed
 Cell
 Pelvic, Hemorrhage, Focal 1 [3.0]
 Thoracic, Infiltration Cellular, Focal, 1 [3.0]
 Mixed Cell

GENITAL SYSTEM

Clitoral Gland (50) (49) (50) (50)
 Degeneration, Cystic 6 [2.5] 4 [3.0] 1 [2.0] 1 [3.0]
 Fibrosis, Focal 1 [2.0] 1 [2.0]
 Hyperplasia, Cystic 1 [2.0] 4 [2.8] 3 [3.0] 1 [3.0]
 Inflammation, Chronic 2 [3.0] 5 [2.2] 4 [2.3]
 Ovary (50) (49) (50) (50)
 Angiectasis 1 [2.0] 1 [2.0]
 Atrophy 1 [3.0]
 Congestion 5 [2.0] 5 [2.8]
 Cyst 1 [2.0] 1 [2.0]
 Bilateral, Cyst, Multiple 4 [3.3] 5 [3.2] 4 [3.0] 6 [3.0]
 Periovarian Tissue, Cyst 1 [2.0]
 Periovarian Tissue, Cyst, Multiple (50)
 Uterus 3 [2.7] (50)
 Cyst 1 [2.0] 1 [2.0]
 Hemorrhage 2 [2.0]
 Inflammation, Chronic 1 [3.0]
 Cervix, Hyperplasia 1 [3.0]
 Endometrium, Hyperplasia, Cystic 15 [1.6] 15 [1.6]
 Vagina (2)
 Inflammation, Chronic 1 [2.0]
 Epithelium, Cyst 1 [3.0]

HEMATOPOIETIC SYSTEM

Bone Marrow (49) (50) (50) (50)

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLIMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
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FISCHER 344 RATS FEMALE OPPM 1000 PPM 2500 PPM 5000 PPM

HEMATOPOIETIC SYSTEM - CONT

Atrophy	1 [3.0]			
Fibrosis		1 [2.0]		1 [3.0]
Hyperplasia, Focal, Histiocytic				4 [2.3]
Myelofibrosis				1 [3.0]
Necrosis	2 [3.0]	3 [2.7]	5 [2.6]	2 [3.0]
Myeloid Cell, Hyperplasia		2 [2.5]	1 [3.0]	1 [2.0]
Myeloid Cell, Erythroid Cell, Hyperplasia	(32)	(31)	(34)	2 [3.0]
Lymph Node				(41)
Deep Cervical, Hemorrhage	1 [3.0]			2 [3.0]
Mediastinal, Angiectasis			1 [3.0]	
Mediastinal, Congestion	5 [2.8]	3 [2.7]	2 [3.0]	7 [2.9]
Mediastinal, Ectasia	2 [2.0]	3 [3.0]	9 [2.8]	8 [2.9]
Mediastinal, Hemorrhage		1 [3.0]	2 [3.0]	
Mediastinal, Hyperplasia	8 [2.9]	8 [2.9]	5 [3.0]	12 [3.0]
Mediastinal, Hyperplasia, Lymphoid		1 [3.0]	1 [3.0]	1 [3.0]
Mediastinal, Pigmentation	1 [2.0]		2 [3.0]	
Pancreatic, Atrophy		1 [3.0]		
Pancreatic, Ectasia	2 [2.0]	2 [3.0]		11 [2.7]
Pancreatic, Hemorrhage	5 [2.6]	3 [3.0]	2 [2.5]	9 [3.0]
Pancreatic, Hyperplasia, Histiocytic	16 [2.8]	24 [2.8]	17 [3.0]	18 [3.1]
Pancreatic, Hyperplasia, Plasma Cell	1 [3.0]			
Pancreatic, Infiltration Cellular, Mixed Cell		2 [2.5]		1 [3.0]
Pancreatic, Pigmentation	4 [2.8]	(4)	(5)	1 [3.0]
Lymph Node, Mandibular	(5)			(1)
Ectasia	1 [3.0]	(49)	(49)	(50)
Lymph Node, Mesenteric	(49)			
Angiectasis			1 [3.0]	
Ectasia	1 [3.0]			5 [3.0]
Hemorrhage	1 [2.0]		2 [3.0]	2 [3.0]
Hyperplasia, Histiocytic	2 [3.0]	1 [3.0]	2 [3.0]	2 [3.0]
Hyperplasia, Lymphoid		1 [3.0]		
Pigmentation	2 [2.5]			
Spleen	(50)	(49)	(48)	(50)
Accessory Spleen		1 [1.0]	1 [2.0]	
Angiectasis, Focal		1 [2.0]		
Congestion		1 [3.0]		
Fibrosis, Focal		1 [2.0]	1 [2.0]	4 [2.0]
Hematopoietic Cell Proliferation	6 [2.2]	8 [2.4]	5 [2.6]	
Hemorrhage			1 [2.0]	
Infarct				1 [3.0]
Inflammation, Granulomatous	3 [3.3]	2 [3.0]	4 [2.5]	
Pigmentation		1 [3.0]		27 [3.3]

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIMAZOLE

Report: PEIRPT18
 Date: 03/14/03
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FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

HEMATOPOIETIC SYSTEM - CONT	0PPM	1000 PPM	2500 PPM	5000 PPM
Pigmentation, Focal	1 [2.0]	1 [3.0]	1 [3.0]	(49)
Thymus	(48)	(45)	(49)	(49)
Angiectasis			2 [3.0]	
Hyperplasia, Lymphoid	1 [3.0]	1 [3.0]		2 [3.0]

INTEGUMENTARY SYSTEM

Mammary Gland	(50)	(50)	(50)	(50)
Dilatation	33 [2.4]	35 [2.5]	22 [2.6]	19 [2.3]
Ectasia	2 [3.5]	3 [2.3]	7 [2.3]	
Fibrosis		1 [3.0]		
Hyperplasia	3 [2.3]	5 [2.6]	4 [2.0]	3 [2.0]
Hyperplasia, Cystic	1 [3.0]		2 [2.5]	
Inflammation, Focal		1 [3.0]		
Skin	(50)	(50)	(50)	(50)
Necrosis, Focal			1 [3.0]	4 [3.3]
Ulcer				1 [4.0]
Subcutaneous Tissue, Angiectasis, Focal				1 [2.0]
Subcutaneous Tissue, Hemorrhage, Focal				1 [3.0]
Subcutaneous Tissue, Inflammation, Focal, Suppurative				1 [3.0]

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

Brain	(50)	(49)	(50)	(50)
Compression, Focal	10 [2.9]	8 [3.0]	12 [2.9]	4 [3.0]
Hemorrhage, Focal	2 [2.5]	1 [2.0]	2 [3.0]	
Necrosis, Focal			1 [2.0]	
Pigmentation, Focal			1 [3.0]	
Cerebellum, Developmental Malformation				(4)
Spinal Cord	(3)	(1)		
Hemorrhage, Focal	1 [2.0]			
Necrosis, Focal	1 [2.0]			

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

RESPIRATORY SYSTEM

Lesion	0PPM	1000 PPM	2500 PPM	5000 PPM
Lung	(50)	(49)	(50)	(50)
Congestion	2 [1.5]	4 [2.3]	2 [2.0]	2 [1.5]
Emphysema	1 [1.0]	1 [3.0]	1 [3.0]	
Hemorrhage	1 [2.0]			2 [2.5]
Hemorrhage, Focal				1 [3.0]
Hyperplasia, Focal, Histiocytic	6 [1.3]	6 [1.2]	7 [1.0]	1 [2.0]
Hyperplasia, Histiocytic			1 [1.0]	1 [2.0]
Infiltration Cellular, Focal, Mixed Cell			1 [2.0]	6 [2.0]
Infiltration Cellular, Chronic, Focal	1 [1.0]	3 [2.0]	1 [3.0]	1 [1.0]
Inflammation, Chronic, Focal	1 [1.0]	2 [1.0]	1 [2.0]	
Inflammation, Focal, Granulomatous	1 [2.0]			
Pigmentation, Focal	7 [1.6]	5 [1.8]	3 [1.7]	3 [2.0]
Alveolar Epithelium, Hyperplasia, Focal			1 [3.0]	1 [2.0]
Alveolar Inflammation, Focal, Granulomatous				
Interstitialium, Edema	(50)	(49)	(50)	(50)
Nose				
Foreign Body	1 [2.0]	1 [2.0]	1 [3.0]	1 [3.0]
Inflammation, Suppurative	4 [2.8]	2 [2.0]	4 [2.3]	2 [2.5]
Nasolacrimal Duct, Inflammation				

SPECIAL SENSES SYSTEM

Lesion	0PPM	1000 PPM	2500 PPM	5000 PPM
Eye	(50)	(49)	(49)	(50)
Atrophy	1 [3.0]	1 [3.0]	1 [3.0]	1 [3.0]
Cataract	1 [3.0]	2 [3.0]	2 [1.5]	1 [3.0]
Iris, Synchia			1 [3.0]	
Retina, Degeneration		2 [3.0]	1 [3.0]	1 [3.0]
Harderian Gland	(50)	(49)	(50)	(50)
Hyperplasia, Cystic, Focal	1 [2.0]		1 [2.0]	1 [1.0]
Hyperplasia, Focal	2 [1.0]	2 [1.5]	1 [2.0]	4 [1.5]
Hyperplasia, Focal, Histiocytic	1 [2.0]		3 [1.3]	1 [3.0]
Inflammation, Chronic, Focal			1 [1.0]	
Inflammation, Focal, Granulomatous		2 [1.5]	2 [2.0]	1 [1.0]
Epithelium, Hyperplasia, Focal				

URINARY SYSTEM

Lesion	0PPM	1000 PPM	2500 PPM	5000 PPM
Kidney	(50)	(48)	(47)	(50)
Atrophy, Focal		2 [2.0]	1 [2.0]	
Congestion			2 [3.0]	

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

URINARY SYSTEM - CONT

Lesion	0PPM	1000 PPM	2500 PPM	5000 PPM
Cyst				1 [2.0]
Infarct				40 [1.1]
Nephropathy	38 [1.0]	40 [1.0]	38 [1.1]	1 [3.0]
Glomerulus, Amyloid Deposition, Diffuse				4 [2.5]
Pelvis, Inflammation	11 [2.2]	7 [2.0]	3 [2.3]	
Renal Tubule, Accumulation, Hyaline Droplet	8 [1.6]	4 [1.5]	5 [2.2]	
Renal Tubule, Pigmentation				(2)
Urethra				1 [2.0]
Transitional Epithelium, Hyperplasia, Diffuse				(50)
Urinary Bladder	(50)	(49)	(49)	2 [3.0]
Transitional Epithelium, Hyperplasia				

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NTP Experiment-Test: 92012-05
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 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

DISPOSITION SUMMARY

Animals Initially In Study 60
 Early Deaths 60
 Moribund Sacrifice 13
 Natural Death 2
 Survivors 34
 Terminal Sacrifice 1
 Moribund Sacrifice 39
 Natural Death 1

Animals Examined Microscopically 50 50 50 50

ALIMENTARY SYSTEM

Intestine Large, Rectum	(49)	(48)	(48)	(50)
Angiectasis, Focal	(50)	(50)	(50)	(50)
Liver	23	23	8	2
Angiectasis, Focal	1 [4.0]	23	1 [3.0]	1 [2.0]
Basophilic Focus	4 [1.8]	3 [1.3]	2 [3.0]	1 [3.0]
Cholangiofibrosis	3	6	2 [2.0]	7 [1.7]
Congestion			1 [3.0]	1
Degeneration, Cystic, Focal				
Eosinophilic Focus				
Fibrosis, Focal				
Hematopoietic Cell Proliferation	6	5	4	2 [1.0]
Hepatodysplastic Nodule	1 [2.0]		2 [2.0]	1 [3.0]
Hyperplasia, Focal, Lymphoid	25 [2.0]	30 [1.9]	27 [1.9]	36 [1.9]
Infiltration Cellular, Mixed Cell	12 [1.3]	11 [1.2]	4 [1.8]	11 [1.4]
Inflammation, Granulomatous	14	16	23	26
Mixed Cell Focus	2 [2.5]		2 [2.5]	1 [2.0]
Necrosis, Focal				
Pigmentation, Focal				
Bile Duct, Cyst				
Bile Duct, Hyperplasia	49 [2.7]	49 [2.6]	47 [2.7]	49 [2.8]
Centrilobular, Congestion	1 [4.0]	1 [1.0]	1 [3.0]	2 [1.5]
Hepatocyte, Necrosis, Focal				
Hepatocyte, Vacuolization Cytoplasmic, Diffuse				
Hepatocyte, Vacuolization Cytoplasmic, Focal	23 [1.8]	1 [2.0]	26 [1.7]	1 [2.0]
Hepatocyte, Centrilobular, Necrosis				
Hepatocyte, Centrilobular, Vacuolization Cytoplasmic	5 [2.8]	4 [2.8]	2 [2.5]	23 [1.6]
				3 [2.3]

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

ALIMENTARY SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Hepatocyte, Midzonal, Vacuolization	1 [2.0]	1 [2.0]	2 [2.5]	1 [2.0]
Cytoplasmic				
Oval Cell, Hyperplasia				
Serosa, Fibrosis, Focal	(26)	2 [2.5] (46)	(35)	(20)
Mesentery				
Fibrosis, Focal				
Hemorrhage				
Necrosis, Focal				
Artery, Inflammation, Chronic				
Fat, Necrosis	1 [2.0]	1 [3.0]	2 [2.5]	1 [3.0]
Fat, Necrosis, Focal	8 [2.9]	10 [2.7] (49)	16 [2.8] (50)	10 [2.7] (50)
Pancreas				
Atrophy, Diffuse				
Atrophy, Focal	22 [1.9]	1 [4.0]	20 [2.0]	1 [2.0]
Fibrosis, Focal				
Acinus, Atrophy, Diffuse				
Acinus, Atrophy, Focal				
Acinus, Hyperplasia, Focal				
Duct, Cyst	1 [1.0]	1 [4.0]	1 [3.0]	1 [3.0]
Duct, Cyst, Focal				
Duct, Cyst, Focal, Multiple	6 [2.7]	2 [2.0]	5 [2.0]	12 [1.9]
Duct, Hyperplasia, Cystic				
Duct, Hyperplasia, Cystic, Focal				
Duct, Hyperplasia, Focal				
Salivary Glands				
Atrophy, Focal	(50)	(50)	(50)	(50)
Inflammation, Chronic				
Stomach, Forestomach				
Diverticulum				
Edema				
Erosion				
Inflammation, Focal	1 [1.0]	1 [1.0]	2 [1.5]	1 [2.0]
Ulcer	1 [3.0]	1 [2.0]		1 [1.0]
Inflammation, Focal				
Ulcer				
Epithelium, Hyperplasia	1 [2.0]	1 [2.0]	1 [2.0]	1 [2.0]
Epithelium, Hyperplasia, Focal	2 [1.5]	1 [2.0]		1 [2.0]
Serosa, Foreign Body	2 [2.0]	3 [2.7]		4 [2.0]
Serosa, Inflammation, Chronic, Focal				
Stomach, Glandular				
Erosion	(50)	(50)	(50)	(49)
Erosion, Focal	4 [1.8]	1 [1.0]	1 [2.0]	1 [2.0]
Inflammation, Focal	1 [2.0]		1 [3.0]	
Ulcer	1 [2.0]			
Epithelium, Necrosis, Focal	2 [1.0]			1 [1.0]

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAPOLE

Report: PETRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

ALIMENTARY SYSTEM - CONT	OPPM	300 PPM	1000 PPM	3000 PPM
Glands, Hyperplasia, Cystic, Focal		1 [2.0]		
Glands, Hyperplasia, Focal	1 [1.0]	(2)		(1)
Tongue	(1)			1 [2.0]
Epithelium, Hyperplasia, Focal	(1)	(1)	(1)	(2)
Tooth		1 [2.0]		
Malformation				
Periodontal Tissue, Inflammation	1 [3.0]			1 [2.0]
Periodontal Tissue, Inflammation, Chronic				
Periodontal Tissue, Inflammation, Focal, Suppurative			1 [3.0]	

CARDIOVASCULAR SYSTEM

Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	3 [1.7]	5 [1.6]	10 [2.0]	5 [2.0]
Cardiomyopathy, Focal			2 [2.0]	1 [2.0]
Congestion			1 [3.0]	
Fibrosis				1 [2.0]
Infiltration Cellular, Mixed Cell		1 [2.0]		
Thrombosis	1 [3.0]	1 [3.0]		
Endocardium, Myocardium, Fibrosis, Focal	1 [3.0]			

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule	1 [2.0]	4 [1.3]	9 [1.1]	5 [1.6]
Cytoplasmic Alteration, Focal	2 [2.0]	1 [1.0]	1 [1.0]	3 [1.3]
Degeneration, Cystic, Focal			1 [2.0]	
Hemorrhage	2 [1.5]			
Vacuolization Cytoplasmic, Focal	6 [1.5]	9 [1.4]	10 [1.3]	10 [1.4]
Adrenal Medulla	(50)	(50)	(50)	(50)
Angiectasis		1 [2.0]		
Hyperplasia	1 [2.0]	1 [1.0]		1 [2.0]
Hyperplasia, Focal	7 [1.3]	5 [2.2]	3 [1.3]	7 [1.4]
Infiltration Cellular, Lymphoid		1 [2.0]		
Vacuolization Cytoplasmic, Focal		1 [2.0]		
Islets, Pancreatic	(50)	(49)	(50)	(50)
Atrophy		1 [3.0]		
Hyperplasia, Focal		2 [2.0]	1 [3.0]	1 [2.0]
Parathyroid Gland	(47)	(49)	(48)	(49)
Cyst		1 [3.0]		

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMITIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

ENDOCRINE SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Hyperplasia	1 [2.0]		1 [3.0]	1 [3.0]
Hyperplasia, Focal	1 [2.0]			
Bilateral, Hyperplasia, Focal	(50)	(50)	(50)	(50)
Pituitary Gland				
Angiectasis	2 [1.5]	2 [2.5]	3 [2.7]	1 [2.0]
Pars Distalis, Angiectasis	3 [2.3]	2 [2.0]	2 [2.0]	3 [2.0]
Pars Distalis, Cyst	1 [2.0]	4 [1.3]	2 [2.5]	3 [2.0]
Pars Distalis, Cytoplasmic Alteration, Focal	1 [1.0]	4 [1.8]	2 [1.5]	5 [1.0]
Pars Distalis, Degeneration, Cystic, Focal	1 [2.0]	1 [2.0]	1 [2.0]	1 [1.0]
Pars Distalis, Hyperplasia, Focal	2 [1.5]	1 [2.0]		2 [1.5]
Pars Distalis, Inflammation, Chronic, Focal, Granulomatous			1 [2.0]	
Pars Distalis, Pars Intermedia, Angiectasis		1 [3.0]		1 [2.0]
Pars Intermedia, Cyst		2 [1.5]		
Pars Intermedia, Hemorrhage				
Pars Intermedia, Hyperplasia, Focal		1 [1.0]	1 [2.0]	
Pars Nervosa, Infiltration Cellular, Focal, Mixed Cell	(48)	(46)	1 [2.0]	(50)
Thyroid Gland			(43)	
Cyst		1		
C-Cell, Hyperplasia	41 [1.7]	43 [1.7]	38 [1.5]	34 [1.7]
Follicle, Cyst	1			1
Follicle, Mineralization, Focal	48 [1.0]	45 [1.0]	43 [1.9]	49 [2.7]
Follicular Cell, Atrophy, Focal	1 [1.0]			
Follicular Cell, Hyperplasia		17 [1.1]	37 [1.1]	43 [1.8]
Follicular Cell, Hyperplasia, Cystic, Focal	1 [2.0]			1 [2.0]

GENERAL BODY SYSTEM

Tissue NOS	(7)	(2)	(6)	(4)
Mediastinum, Hemorrhage				1 [3.0]
Thoracic, Hemorrhage				1 [3.0]

GENITAL SYSTEM

Epididymis	(50)	(50)	(50)	(50)
Atrophy	1 [3.0]	1 [2.0]	1 [4.0]	1 [2.0]
Granuloma Sperm	1 [2.0]	1 [3.0]	1 [2.0]	1 [2.0]
Inflammation, Chronic	1 [3.0]			
Preputial Gland	(50)	(50)	(50)	(50)
Cyst	1 [3.0]			

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NTP Experiment-Test: 92012-05
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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES^(b)
 2-METHYLMIMDAZOLE

Report: PEIRPT18
 Date: 03/14/03
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FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

GENITAL SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Degeneration, Cystic				2 [2.5]
Hyperplasia			1 [2.0]	
Hyperplasia, Cystic	2 [3.0]		2 [3.0]	1 [4.0]
Hyperplasia, Focal	1 [2.0]			
Inflammation, Chronic	4 [2.0]		10 [1.6]	10 [1.7]
Inflammation, Chronic, Focal			1 [1.0]	1 [3.0]
Inflammation, Suppurative			1 [3.0]	2 [3.5]
Prostate	(50)	(50)	(50)	(50)
Atrophy	1 [3.0]			
Hyperplasia, Focal		1 [1.0]		
Inflammation, Chronic	15 [1.8]	10 [1.9]	17 [1.6]	19 [1.5]
Epithelium, Degeneration, Focal, Mucoid	1 [2.0]			
Epithelium, Hyperplasia, Focal	4 [1.3]	2 [1.5]	(50)	5 [1.2]
Testes	(50)	(50)	(50)	(50)
Atrophy	5 [3.2]	4 [3.8]	13 [3.1]	13 [3.2]
Mineralization, Focal	1 [1.0]			
Bilateral, Atrophy	2 [3.5]			
Bilateral, Interstitial Cell, Hyperplasia,		3 [3.3]	2 [3.0]	
Focal				2 [1.5]
Germinal Epithelium, Atrophy	2 [2.5]	3 [3.3]	1 [3.0]	1 [3.0]
Interstitial Cell, Hyperplasia		2 [1.5]	1 [1.0]	1 [2.0]
Interstitial Cell, Hyperplasia, Focal	1 [1.0]	4 [1.5]	4 [1.5]	9 [1.6]

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(47)	(50)
Fibrosis			1 [3.0]	
Hyperplasia		1 [3.0]		
Hyperplasia, Focal, Histiocytic		1 [3.0]	1 [2.0]	
Myeloid Cell, Hyperplasia	(39)	1 [3.0]		5 [3.0]
Lymph Node		(49)	(42)	(38)
Hemorrhage				1 [2.0]
Hyperplasia, Lymphoid			1 [3.0]	
Mediastinal, Angiectasis		1 [3.0]	1 [4.0]	
Mediastinal, Congestion			3 [3.0]	
Mediastinal, Ectasia	1 [3.0]			1 [3.0]
Mediastinal, Hemorrhage	1 [3.0]	1 [3.0]	5 [3.0]	
Mediastinal, Hyperplasia, Histiocytic	2 [2.5]	1 [3.0]		4 [2.8]
Mediastinal, Hyperplasia, Lymphoid	1 [3.0]	1 [1.0]	1 [3.0]	
Mediastinal, Pigmentation		1 [3.0]		1 [3.0]
Pancreatic, Angiectasis	1 [3.0]			1 [3.0]
Pancreatic, Ectasia	1 [3.0]	3 [3.0]	3 [2.7]	2 [3.0]

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NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLIMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

HEMATOPOIETIC SYSTEM - CONT	OPPM	300 PPM	1000 PPM	3000 PPM
Pancreatic, Hemorrhage	1 [3.0]		1 [2.0]	4 [2.8]
Pancreatic, Hyperplasia, Focal, Histiocytic	1 [3.0]			
Pancreatic, Hyperplasia, Histiocytic	13 [2.8]	12 [3.0]	15 [2.9]	19 [2.9]
Pancreatic, Hyperplasia, Lymphoid		1 [3.0]	1 [3.0]	1 [2.0]
Pancreatic, Pigmentation	1 [3.0]		(2)	(2)
Lymph Node, Mandibular	(2)	(1)		
Hyperplasia, Plasma Cell			1 [4.0]	
Lymph Node, Mesenteric	(47)	(50)	(50)	(50)
Ectasia		2 [2.5]		2 [3.0]
Hemorrhage			1 [3.0]	1 [3.0]
Hyperplasia, Histiocytic	1 [3.0]	2 [3.0]	1 [3.0]	4 [2.8]
Hyperplasia, Lymphoid	2 [3.0]	1 [3.0]		
Spleen	(49)	(49)	(50)	(50)
Angiectasis, Focal	1 [3.0]		1 [2.0]	
Congestion				1 [3.0]
Cyst		1		
Fibrosis, Focal	2 [2.5]			
Hematopoietic Cell Proliferation	4 [2.5]	4 [2.5]		1 [2.0]
Hemorrhage			1 [3.0]	6 [2.5]
Hemorrhage, Focal			1 [3.0]	
Hyperplasia, Lymphoid			2 [2.5]	1 [3.0]
Infarct	1 [2.5]	1 [2.0]		
Inflammation, Granulomatous		1 [3.0]		
Necrosis, Focal	1 [4.0]		2 [3.0]	3 [1.7]
Pigmentation			1 [2.0]	1 [3.0]
Capsule, Fibrosis, Focal	1 [2.0]		1 [2.0]	
Thymus	(48)	(48)	(44)	(49)
Atrophy	1 [3.0]	1 [3.0]		
Cyst, Multiple	1 [4.0]			
Hemorrhage	1 [3.0]			
Hyperplasia, Lymphoid	2 [3.0]	1 [3.0]	1 [3.0]	1 [2.0]
Epithelial Cell, Cyst, Multiple			1 [3.0]	
Epithelial Cell, Hyperplasia	1 [3.0]			

INTEGUMENTARY SYSTEM

Mammary Gland	(48)	(47)	(45)	(42)
Dilatation	7 [2.1]	1 [2.0]	3 [2.3]	2 [2.5]
Ectasia			1 [3.0]	
Hyperplasia	2 [2.0]			
Hyperplasia, Cystic		1 [2.0]		1 [3.0]
Epithelium, Pigmentation				

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NTP Experiment-Test: 92012-05
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 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

INTEGUMENTARY SYSTEM - CONT

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Skin	(50)	(50)	(50)	(50)
Angiectasis, Focal		1 [1.0]		
Cyst Epithelial Inclusion			1 [1.0]	1 [3.0]
Fibrosis, Focal	1 [3.0]			1 [2.0]
Hemorrhage, Focal	1 [2.0]			1 [2.0]
Inflammation, Chronic, Focal	1 [2.0]		1 [2.0]	1 [2.0]
Necrosis, Focal				1 [2.0]
Pinna, Necrosis, Focal	1 [3.0]			1 [2.0]
Subcutaneous Tissue, Angiectasis, Focal				1 [2.0]
Subcutaneous Tissue, Cyst				1 [3.0]
Subcutaneous Tissue, Foreign Body				1 [2.0]
Subcutaneous Tissue, Hemorrhage, Focal				1 [2.0]

MUSCULOSKELETAL SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Skeletal Muscle	(2)	(1)	(1)	(4)
Fibrosis, Focal				1 [1.0]

NERVOUS SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Brain	(50)	(50)	(50)	(50)
Compression, Focal	4 [3.0]	2 [2.5]	4 [3.0]	1 [2.0]
Hemorrhage, Focal	2 [2.5]	3 [3.3]	2 [3.0]	1 [2.0]
Necrosis, Focal	1 [3.0]	1 [3.0]		
Spinal Cord	(1)		(1)	
Hemorrhage, Focal			1 [3.0]	
Mineralization, Focal			1 [2.0]	
Necrosis, Focal			1 [3.0]	

RESPIRATORY SYSTEM

Lesion	0PPM	300 PPM	1000 PPM	3000 PPM
Larynx			(1)	(1)
Glands, Hyperplasia, Focal				1 [3.0]
Lung	(50)	(50)	(50)	(50)
Congestion	1 [3.0]			1 [2.0]
Hemorrhage, Focal	1 [2.0]		1 [3.0]	1 [2.0]
Hyperplasia, Focal, Histiocytic	4 [2.3]	1 [2.0]		
Hyperplasia, Histiocytic	3 [1.3]	3 [1.7]	2 [1.0]	2 [1.0]
Infiltration Cellular, Focal, Mixed Cell				1 [3.0]
Infiltration Cellular, Mixed Cell	2 [2.5]	1 [2.0]		

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NTP Experiment-Test: 92012-05
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 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

RESPIRATORY SYSTEM - CONT	0PPM	300 PPM	1000 PPM	3000 PPM
Inflammation, Focal				1 [3.0]
Metaplasia, Focal, Osseous		2 [1.5]	1 [1.0]	2 [1.0]
Metaplasia, Osseous				2 [1.0]
Alveolar Epithelium, Hyperplasia, Focal	2 [1.0]	9 [1.6]	6 [1.7]	5 [1.8]
Alveolus, Foreign Body, Focal				1 [2.0]
Interstitialium, Edema				1 [2.0]
Nose	(50)	(50)	(50)	(50)
Foreign Body	1 [2.0]			
Inflammation, Suppurative	2 [2.0]			
Nasolacrimal Duct, Inflammation		2 [2.0]	1 [2.0]	2 [3.0]
Nasolacrimal Duct, Inflammation, Chronic		1 [2.0]		
Nasolacrimal Duct, Inflammation, Suppurative		3 [2.3]		
Sinus, Foreign Body		1 [3.0]		
Sinus, Inflammation, Suppurative		1 [3.0]		

SPECIAL SENSES SYSTEM

Eye	(49)	(50)	(46)	(50)
Atrophy		1 [3.0]		
Cataract	1 [3.0]		1 [2.0]	
Synechia			1 [3.0]	
Cornea, Inflammation, Focal				
Cornea, Necrosis, Focal		1 [2.0]		
Iris, Hyperplasia	1 [2.0]	1 [1.0]		
Lens, Cataract		1 [2.0]		
Retina, Degeneration				
Retinobulbar, Inflammation, Focal		1 [2.0]	1 [3.0]	
Harderian Gland	(50)	(50)	(49)	(50)
Hyperplasia, Focal		1 [1.0]		
Hyperplasia, Focal, Histiocytic				2 [1.0]
Hyperplasia, Histiocytic				1 [1.0]
Inflammation, Chronic, Focal	1 [1.0]		1 [2.0]	3 [1.7]
Inflammation, Focal, Granulomatous			2 [1.0]	1 [1.0]
Epithelium, Hyperplasia, Focal	3 [1.3]			1 [3.0]

URINARY SYSTEM

Kidney	(49)	(49)	(49)	(50)
Accumulation, Hyaline Droplet	1 [3.0]			
Atrophy, Focal				1 [2.0]
Congestion	1 [2.0]	1 [3.0]		

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIMDIAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 10:45:10

URINARY SYSTEM - CONT	FISCHER 344 RATS MALE			
	0PPM	300 PPM	1000 PPM	3000 PPM
Cyst		2 [2.5]		2 [2.0]
Fibrosis, Focal		1 [3.0]		1 [2.0]
Infarct				
Inflammation	1 [2.0]			
Nephropathy	43 [1.3]	43 [1.3]	41 [1.2]	46 [1.2]
Pelvis, Inflammation, Chronic			1 [3.0]	
Pelvis, Transitional Epithelium, Hyperplasia		1 [1.0]	1 [3.0]	
Renal Tubule, Accumulation, Hyaline Droplet	1 [3.0]		3 [3.0]	2 [3.0]
Renal Tubule, Necrosis, Focal	1 [2.0]			
Renal Tubule, Pigmentation	5 [2.8]	3 [2.0]	2 [2.5]	3 [2.3]
Urinary Bladder	(50)	(50)	(49)	(50)
Hemorrhage			1 [3.0]	

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLMIDAZOLE

Report: PEIRPT03
Date: 02/24/03
Time: 14:01:01

27 WEEK SSAC

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: All

Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: P2IRPT03
 Date: 02/24/03
 Time: 14:01:01

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hepatodiphragmatic Nodule	1 (10%)		1 (10%)	
Inflammation, Granulomatous	10 (100%)	10 (100%)	10 (100%)	10 (100%)

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule				1 (10%)
Pituitary Gland	(10)	(10)	(10)	(10)
Pars Distalis, Cyst	1 (10%)	2 (20%)	2 (20%)	1 (10%)
Pars Distalis, Mitotic Alteration	1 (10%)	2 (20%)	2 (20%)	2 (20%)
Pars Intermedia, Cyst		1 (10%)	1 (10%)	
Thyroid Gland	(10)	(10)	(10)	(10)
Follicle, Mineralization, Focal	1 (10%)	6 (60%)	10 (100%)	10 (100%)
Follicular Cell, Hyperplasia		5 (50%)	10 (100%)	10 (100%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)
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a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIMIDAZOLE

Report: PRIRPF03
 Date: 02/24/03
 Time: 14:01:01

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

GENITAL SYSTEM - CONT	0PPM	1000 PPM	2500 PPM	5000 PPM
Cyst	1 (10%)		1 (10%)	
Periovarian Tissue, Cyst	1 (10%)			
Uterus	(10)	(10)	(10)	(10)
Hydrometra	1 (10%)			

HEMATOPOIETIC SYSTEM

Lymph Node	(3)	(4)	(1)	(3)
Mediastinal, Hemorrhage	1 (33%)	1 (25%)		2 (67%)
Pancreatic, Hemorrhage		2 (50%)		1 (33%)
Pancreatic, Hyperplasia, Lymphoid	2 (67%)	1 (25%)	1 (100%)	
Spleen	(10)	(10)	(10)	(10)
Accessory Spleen			1 (10%)	

INTEGUMENTARY SYSTEM

Skin	(10)	(10)	(10)	(10)
Cyst Epithelial Inclusion			1 (10%)	

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

Eye	(10)	(10)	(10)	(10)
Retrolubar, Inflammation, Focal		1 (10%)		
Harderian Gland	(10)	(10)	(10)	(10)
Hyperplasia, Focal, Lymphoid				1 (10%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLMIDAZOLE

Report: PEIRPT03
Date: 02/24/03
Time: 14:01:01

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

SPECIAL SENSES SYSTEM - CONT
Inflammation, Focal, Granulomatous 1 (10%) 5 (50%)

URINARY SYSTEM

Kidney (10) (10) (10) (10)
Cyst 1 (10%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:01:01

FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

DISPOSITION SUMMARY

	0PPM	300 PPM	1000 PPM	3000 PPM
Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hepatodistalagmatic Nodule	2 (20%)		1 (10%)	
Hyperplasia, Focal, Mast Cell			1 (10%)	
Infiltration Cellular, Focal,				
Polymorphonuclear				
Inflammation, Granulomatous	9 (90%)	7 (70%)	1 (10%)	10 (100%)
Mesentery			10 (100%)	
Fat, Necrosis			1 (100%)	

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule				2 (20%)
Pituitary Gland	(10)	(10)	(10)	(10)
Pars Distalis, Cyst	1 (10%)	2 (20%)	1 (10%)	1 (10%)
Pars Distalis, Mitotic Alteration				
Pars Distalis, Vacuolization Cytoplasmic,				
Focal				
Pars Intermedia, Cyst	(10)	(10)	(10)	1 (10%)
Thyroid Gland	1 (10%)	4 (40%)	9 (90%)	2 (20%)
Follicle, Mineralization, Focal		7 (70%)	10 (100%)	(10)
Follicular Cell, Hyperplasia				9 (90%)
				10 (100%)

GENERAL BODY SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion

MTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:01:01

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

Lymph Node	(1)	1 (100%)	(1)	(1)
Mediastinal, Hemorrhage			1 (100%)	1 (100%)
Pancreatic, Hemorrhage	(10)	(10)	(10)	(10)
Lymph Node, Mesenteric Hemorrhage	(10)	(10)	(10)	1 (10%)
Spleen	(10)	2 (20%)	(10)	(10)
Accessory Spleen	(10)	(10)	(10)	(10)
Thymus	(10)	(10)	(10)	(10)
Hemorrhage	(10)	1 (10%)	1 (10%)	(10)

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSRD FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLMIDAZOLE

Report: PEIRPT03
Date: 02/24/03
Time: 14:01:01

FISCHER 344 RATS MALE	0PPM	300 PPM	1000 PPM	3000 PPM
SPECIAL SENSES SYSTEM - CONT				
Harderian Gland	(10)	(10)	(10)	(10)
Inflammation, Focal, Granulomatous	1 (10%)			
Necrosis, Focal	1 (10%)			

URINARY SYSTEM

None

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED

2-METHYLDIMIDAZOLE

27 WEEK SSAC

Report: PEIRPT05
Date: 02/24/03
Time: 14:09:20

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25017 Scheduled Sacrifice
Removal Date Range: All
Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Thyroid Gland	(10)	(10)	(10)	(10)
Follicular Cell, Adenoma				2 (20%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED

Report: PTRP105
Date: 02/24/03
Time: 14:09:20

FISCHER 344 RATS FEMALE

0PPM

1000 PPM

2500 PPM

5000 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b) 2
 Total Primary Neoplasms 2
 Total Animals with Benign Neoplasms 2
 Total Benign Neoplasms 2
 Total Animals with Malignant Neoplasms
 Total Malignant Neoplasms
 Total Animals with Metastatic Neoplasms
 Total Metastatic Neoplasm
 Total Animals with Malignant Neoplasms
 Uncertain Primary Site
 Total Animals with Neoplasms Uncertain-
 Benign or Malignant
 Total Uncertain Neoplasms

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLMIDAZOLE
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS MALE

0PPM 300 PPM 1000 PPM 3000 PPM

DISPOSITION SUMMARY

Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED
2-METHYLIMIDAZOLE

Report: PEIRPT05
Date: 02/24/03
Time: 14:09:20

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC 2-METHYLMIDAZOLE
Route: DOSED FEED

Report: PEIRPT05
Date: 02/24/03
Time: 14:09:20

27 WEEK SSAC

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25017 Scheduled Sacrifice
Removal Date Range: All
Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

	0PPM	1000 PPM	2500 PPM	5000 PPM
Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Thyroid Gland (10) (10) (10) (10)
 Follicular Cell, Adenoma 2 (20%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED

2-METHYLMIDAZOLE

Report: PEIRPT05
Date: 02/24/03
Time: 14:09:20

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSHD FEED

2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	2
Total Primary Neoplasms	2
Total Animals with Benign Neoplasms	2
Total Benign Neoplasms	2
Total Animals with Malignant Neoplasms	
Total Malignant Neoplasms	
Total Animals with Metastatic Neoplasms	
Total Metastatic Neoplasms	
Total Animals with Malignant Neoplasms Uncertain Primary Site	
Total Animals with Neoplasms Uncertain- Benign or Malignant	
Total Uncertain Neoplasms	

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLMIDAZOLE
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:09:20

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

DISPOSITION SUMMARY

	OPPM	300 PPM	1000 PPM	3000 PPM
Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED

Report: PEIRP05
Date: 02/24/03
Time: 14:09:20

FISCHER 344 RATS MALE OPPM 300 PPM 1000 PPM 3000 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
2-METHYLLIMITDAZOLE

Report: PEIRPT18
Date: 02/24/03
Time: 14:17:53

27 WEEK SSAC

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: All

Treatment Groups: Include All

- a Number of animals examined microscopically at site and number of animals with lesion
- b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLIMIDAZOLE

Report: PEIRPR18
 Date: 02/24/03
 Time: 14:17:53

FISCHER 344 RATS FEMALE

0PPM 1000 PPM 2500 PPM 5000 PPM

DISPOSITION SUMMARY

Disposition	0 PPM	1000 PPM	2500 PPM	5000 PPM
Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Lesion	0 PPM	1000 PPM	2500 PPM	5000 PPM
Liver	(10)	(10)	(10)	(10)
Hepatodiaphragmatic Nodule	1		1	
Inflammation, Granulomatous	10 [1.1]	10 [1.3]	10 [1.5]	10 [1.8]

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Lesion	0 PPM	1000 PPM	2500 PPM	5000 PPM
Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule				1 [1.0]
Pituitary Gland	(10)	(10)	(10)	(10)
Pars Distalis, Cyst	1 [1.0]	2 [1.0]	2 [1.5]	1 [1.0]
Pars Distalis, Mitotic Alteration	1 [1.0]	1 [1.0]	1 [2.0]	2 [2.0]
Pars Intermedia, Cyst	(10)	(10)	(10)	(10)
Thyroid Gland		6 [1.0]	10 [1.0]	10 [1.0]
Follicle, Mineralization, Focal	1 [1.0]	5 [1.6]	10 [1.7]	10 [3.0]
Follicular Cell, Hyperplasia				

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

System	0 PPM	1000 PPM	2500 PPM	5000 PPM
Ovary	(10)	(10)	(10)	(10)

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 14:17:53

FISCHER 344 RATS FEMALE

OPPM 1000 PPM 2500 PPM 5000 PPM

GENITAL SYSTEM - CONT	OPPM	1000 PPM	2500 PPM	5000 PPM
Cyst	1 [3.0]		1 [3.0]	
Periovarian Tissue, Cyst	1 [3.0]			
Uterus	(10)	(10)	(10)	(10)
Hydrometra	1 [1.0]			

HEMATOPOIETIC SYSTEM

Lymph Node	(3)	(4)	(1)	(3)
Mediastinal, Hemorrhage	1 [3.0]	1 [3.0]		2 [2.5]
Pancreatic, Hemorrhage		2 [3.0]		1 [3.0]
Pancreatic, Hyperplasia, Lymphoid	2 [2.5]	1 [2.0]	1 [3.0]	
Spleen	(10)	(10)	(10)	(10)
Accessory Spleen			1 [1.0]	

INTEGUMENTARY SYSTEM

Skin				
Cyst Epithelial Inclusion	(10)	(10)	(10)	(10)

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

Eye	(10)	(10)	(10)	(10)
Retrolbulbar, Inflammation, Focal		1 [1.0]		
Harderian Gland	(10)	(10)	(10)	(10)
Hyperplasia, Focal, Lymphoid				1 [2.0]

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
2-METHYLIMIDAZOLE

Report: PEIRPT18
Date: 02/24/03
Time: 14:17:53

FISCHER 344 RATS FEMALE 0PPM 1000 PPM 2500 PPM 5000 PPM

SPECIAL SENSES SYSTEM - CONT
Inflammation, Focal, Granulomatous 1 [2.0] 5 [1.6]

URINARY SYSTEM

Kidney (10) (10) (10) (10)
Cyst 1 [2.0]

a Number of animals examined microscopically at site and number of animals with lesion
b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIMDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 14:17:53

FISCHER 344 RATS MALE

OPPM 300 PPM 1000 PPM 3000 PPM

DISPOSITION SUMMARY

Disposition	OPPM	300 PPM	1000 PPM	3000 PPM
Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hepatodiaphragmatic Nodule	2		1	
Hyperplasia, Focal, Mast Cell			1 [2.0]	
Infiltration Cellular, Focal,				
Polymorphonuclear			1 [2.0]	
Inflammation, Granulomatous	9 [1.0]	7 [1.0]	10 [1.0]	
Mesenterly			10 [1.0]	
Fat, Necrosis			1 [4.0]	

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule				2 [2.0]
Pituitary Gland	(10)	(10)	(10)	(10)
Pars Distalis, Cyst	1 [2.0]	2 [1.5]	1 [1.0]	1 [2.0]
Pars Distalis, Mitotic Alteration				
Pars Distalis, Vacuolization Cytoplasmic,				
Focal				1 [1.0]
Pars Intermedia, Cyst	(10)	(10)	(10)	1 [1.0]
Thyroid Gland	1 [1.0]	4 [1.0]	9 [1.0]	2 [1.0]
Follicle, Mineralization, Focal		7 [1.1]	10 [1.0]	10 [2.8]
Follicular Cell, Hyperplasia				10 [2.0]

GENERAL BODY SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
 Study Type: CHRONIC
 Route: DOSED FBDD

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PRIRPT18
 Date: 02/24/03
 Time: 14:17:53

FISCHER 344 RATS MALE 0PPM 300 PPM 1000 PPM 3000 PPM

None

GENTRAL SYSTEM

None

HEMATOPOIETIC SYSTEM

Lymph Node	(1)	(1)	(1)
Mediastinal, Hemorrhage	1 [3.0]	1 [3.0]	1 [3.0]
Pancreatic, Hemorrhage	(10)	(10)	(10)
Lymph Node, Mesenteric Hemorrhage	(10)	(10)	1 [2.0]
Spleen	(10)	(10)	(10)
Accessory Spleen	2 [2.0]	(10)	(10)
Thymus	(10)	(10)	(10)
Hemorrhage	1 [2.0]	1 [1.0]	(10)

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-05
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
2-METHYLMIMDAZOLE

Report: PEIRPT18
Date: 02/24/03
Time: 14:17:53

FISCHER 344 RATS MALE OPPM 300 PPM 1000 PPM 3000 PPM

SPECIAL SENSES SYSTEM - CONT	(10)	(10)	(10)	(10)
Harderian Gland	1 [1.0]			
Inflammation, Focal, Granulomatous	1 [2.0]			
Necrosis, Focal				

URINARY SYSTEM

None

- a Number of animals examined microscopically at site and number of animals with lesion
- b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

**PATHOLOGY WORKING GROUP
CHAIRPERSON'S REPORT**

**TWO YEAR CHRONIC STUDY OF 2-METHYLIMIDAZOLE (2-MI)
(C92012B/92012-06) ADMINISTERED BY DOSED FEED IN MALE AND
FEMALE B6C3F1 MICE**

DATE OF FIRST MEETING OF PWG: October 17, 2002

DATE OF SECOND MEETING OF PWG: November 1, 2002

LOCATION OF REVIEWS: NIEHS, Research Triangle Park, NC

PARTICIPANTS IN FIRST AND SECOND PWGS:

Drs. Robert Sills (NIEHS – Co-NTP Study Pathologist), Georgette Hill (NIEHS-Co-NTP Study Pathologist), Ronald Herbert (NIEHS), Gordon Flake (NIEHS), Gail Pearse (NIEHS), Abraham Nyska (NIEHS), John Peckham (EPL), Cynthia Shackelford (EPL-QA Pathologist), Catherine Picut (ILS-PWG Chairperson), and Yoshiro Tani (NIEHS – observer).

SUMMARY OF FINDINGS FROM THE PWG MEETINGS

The PWG convened to evaluate selected H&E slides from this two-year chronic study in B6C3F1 mice exposed to 2-Methylimidazole (2-MI) in food. The target organs are the thyroid gland, liver, spleen, and bone marrow of both sexes; and the epididymis/testis and kidney in males. The following is a summary of treatment-related lesions.

- **THYROID GLAND:** Chronic exposure of mice to 2-MI caused increased incidences and severities of follicular cell hypertrophy and follicular cell hyperplasia in both sexes, and an increased incidence of follicular cell adenomas in males.

- **LIVER:** Treatment with 2-MI resulted in increased incidences and severities of karyomegaly and cytoplasmic alteration in males; increased incidences and severities of iron-containing pigment in males; increased incidences of hepatocellular adenoma or carcinoma in males; and an increased incidence of hepatocellular adenoma in females.
- **SPLEEN:** Chronic exposure of mice to 2-MI caused increased incidences and severities of hematopoietic cell proliferation in males and females, increased incidences and severities of lymphoid follicular atrophy in males and females, increased incidences of splenic atrophy in males, and increased severities of iron-containing pigment in males.
- **BONE MARROW:** 2-MI exposure caused increased incidences and severities of bone marrow hyperplasia in males and females.
- **EPIDIDYMIS/TESTIS:** Chronic exposure to 2-MI caused increased incidences and severities of chronic inflammation of the epididymis and atrophy of the germinal epithelium of the testis.
- **KIDNEY:** 2-MI exposure in mice was associated with increased incidences and severities of iron-containing pigment in the proximal convoluted tubules of the kidney in males.

INTRODUCTION

2-Methylimidazole (2-MI) is an imidazole derivative used as an intermediate in the production of pharmaceuticals, photographic chemicals, dyes and pigments. 2-MI is also present in tobacco smoke, wine, soy sauce and other food products. It is formed when ammonia or molasses is added to livestock feed to enhance the nutritional value of food, and as a result, 2-MI is a contaminant of meat from livestock fed such enhanced feed.

STUDY DESIGN

2-MI was administered to male and female B6C3F1 mice at dose levels of 0 ppm, 625 ppm, 1250 ppm, or 2500 ppm for two years. There were 60 animals per dose group. Ten of these animals in each dose group were sacrificed at 27 weeks (interim sacrifice).

The study was conducted at Southern Research Institute, Birmingham, Alabama. The Study Pathologist (SP) was Dr. Daniel R. Farnell. The Quality Assessment Pathologist (QAP) was Dr. Cynthia Shackelford of EPL.

CONDUCT OF THE PWG

The PWG convened twice to review selected slides from B6C3F1 mice exposed to 2-MI in food for two years.

Before the first PWG meeting, the chairperson reviewed the laboratory reports and the SP's pathology narratives, the summary and individual animal pathology tables, the individual animal necropsy records, the pathology data review, the quality assessment reports, and microslides from the study. The PWG chairperson selected a set of slides for review by the PWG which included examples of treatment related lesions as well as slides for which there were differences of opinion in diagnoses among the SP, QAP or PWG chairperson. The PWG consensus opinion for each slide examined, including any additional diagnoses made by the PWG, was recorded on the PWG chairperson's worksheets attached to this report.

STUDY RESULTS

Morbidity, Mortality, Clinical Signs, Organ Weights, Body Weight

Treatment of mice with 2-MI had no significant dose related effect on survival in any dose group of either sex. There was a mild deficit in body weight gain in the high dose males and females compared to controls, and this reduction in body weight gain was attributed to the toxic effects of 2-MI. There were no clinical signs of toxicity observed in this study that were considered to be due to administration of 2-MI.

2-MI administration caused a dose-related increase in absolute and relative liver, thyroid and spleen weights in male and female mice at study termination. 2-MI was also associated with an increase in absolute and relative pituitary weights for male mice, yet this increase was present only at the 6 months time point.

Histopathology

Thyroid Gland

Follicular Cell Hypertrophy: There were dose related increased incidences and severities of follicular cell hypertrophy in animals of both sexes, and this change was seen in the 27 week and chronic sacrifice groups.

The QAP agreed with the SP in the finding of follicular cell hypertrophy in males at 2500 ppm and females at 1000ppm and 2500 ppm. The PWG chairperson identified additional cases of hypertrophy in the 625 ppm and 1000 ppm males.

The PWG reviewed examples of the following: 1) normal thyroid gland from control animals; 2) follicular cell hypertrophy for which there were no discrepancies in diagnoses; 3) two-way discrepancies in the diagnosis of follicular cell hypertrophy; and

4) additional cases of hypertrophy identified by the PWG chairperson in the 1000 ppm group of males. The PWG agreed by consensus with the diagnosis of follicular cell hypertrophy, resolved all discrepancies, and confirmed the additional cases of hypertrophy in the 1000 ppm group of males.

Follicular cell hypertrophy was locally extensive to diffuse and characterized by an increase in the size of the follicular epithelial cells due to distended cytoplasm. The cytoplasm of these enlarged cells was foamy and vacuolated. Commonly, the hypertrophy was associated with basophilic floccular colloid. In the interim sacrifice males and females, follicular cell hypertrophy was seen without concomitant hyperplasia. In the chronic sacrifice animals, however, follicular cell hypertrophy was typically accompanied by follicular cell hyperplasia.

Follicular Cell Hyperplasia: There were increased incidences and severities of follicular cell hyperplasia in the chronic sacrifice male and female mice. There was good agreement between the pathologists regarding the diagnosis of follicular cell hyperplasia. Additional cases of hyperplasia were identified by the PWG chairperson.

The PWG reviewed several examples of follicular cell hyperplasia, as well as 2-way and 3-way discrepancies in diagnosis of this lesion. The PWG agreed with the diagnosis of follicular cell hyperplasia and resolved those discrepancies presented.

Follicular cell hyperplasia was characterized by an increase in the number of follicular cells, frequently resulting in infolding of cells into the follicular lumina. The hyperplastic lesions did not cause compression of the surrounding thyroid parenchyma. Follicular cell hyperplasia occurred focally-to-multifocally and was commonly seen bilaterally.

Thyroid Gland Adenoma: Chronic administration of 2-MI caused increased incidences of follicular cell adenomas in male mice, and to a lesser extent, female mice. There was excellent agreement between the SP, QAP and PWG chairperson regarding the diagnosis of follicular cell adenomas. The PWG reviewed all cases involving a diagnosis of thyroid follicular cell adenoma and agreed with each diagnosis by consensus opinion.

The adenomas were compressive, non-encapsulated masses of cuboidal epithelial cells forming colloid-containing follicles of variable size. The neoplastic epithelial cells generally had an increased nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, and increased cytoplasmic basophilia compared to normal follicular epithelium. The follicular cell adenomas in this study were mostly unilateral (6 out of 7) and invariably associated with follicular cell hyperplasia elsewhere in the thyroid gland.

Liver

Eosinophilic Foci and Hepatocellular Adenomas/ Carcinomas: There were increased incidences of eosinophilic foci, hepatocellular adenomas, and hepatocellular carcinomas in male mice at chronic sacrifice, and an increased incidence of hepatocellular adenomas in female mice at chronic sacrifice.

There was considerable disagreement between the SP, QAP and PWG chairperson regarding the diagnoses of eosinophilic foci, hepatocellular adenoma and hepatocellular carcinoma. The PWG reviewed examples of foci, adenomas and carcinomas where there was full agreement between the SP, QAP and PWG chairperson in diagnosis of these three lesions. The PWG confirmed unanimously the diagnosis in each case. The PWG also reviewed all cases involving a 2-way or 3-way discrepancy in the diagnosis of these three lesions. The PWG resolved each discrepancy by consensus opinion.

The criteria used by the PWG for classifying proliferative lesions as hepatocellular foci, adenomas or carcinomas were those outlined in *Pathology of the Mouse*, (Maronpot, R.R., ed., Cache Valley Press, 1999, pp. 140-149).

Hepatocellular Karyomegaly: Treatment with 2-MI caused increased incidences of karyomegaly in the male mice at the interim and chronic sacrifices. There was excellent agreement between the SP, QAP, and PWG chairperson regarding karyomegaly. The data was presented to the PWG members. The members unanimously elected not to evaluate the slides of karyomegaly, since there was excellent agreement between the three pathologists.

Karyomegaly was characterized by enlargement of the nuclei of hepatocytes. These karyomegalic cells were commonly seen in the centrilobular regions and were commonly associated with cytoplasmic alteration.

Cytoplasmic Alteration: Treatment with 2-MI was associated with cytoplasmic alteration in male mice at chronic sacrifice. There was excellent agreement between the SP, QAP and PWG chairperson regarding this lesion. The PWG members unanimously elected not to review slides of this lesion in light of the excellent agreement between the three pathologists.

This lesion consisted of increased cytoplasmic eosinophilia and apparent loss of normal glycogenic vacuolization of hepatocytes in the centrilobular and midzonal areas of the hepatic lobules. This change was commonly seen in association with karyomegaly.

Pigmentation: There were increased incidences and severities of Kupffer cell pigmentation in the high dose group of male mice at two years. This pigment was consistent with hemosiderin, as it was iron-containing, globular, and golden brown. Given the excellent agreement between the SP, QAP and PWG chairperson regarding the

diagnosis of pigment in the liver, this lesion was only discussed with the PWG members. No slides were reviewed during the PWG.

Bone Marrow

Bone Marrow Hyperplasia: There were increased incidences and severities of bone marrow hyperplasia in males at the interim sacrifice, and in both sexes at the chronic sacrifice. There was good correlation regarding this diagnosis between the SP and QAP, however the QAP identified additional cases of bone marrow hyperplasia in the males at chronic sacrifice.

In view of the good agreement with the diagnosis of bone marrow hyperplasia between the SP, QAP and PWG chairperson, the PWG members unanimously decided not to review slides of this lesion. There was discussion among members of the PWG to subclassify the bone marrow hyperplasia into erythroid and myeloid. The PWG members unanimously decided that such subclassification was not desirable or valid without access to bone marrow smears.

Bone marrow hyperplasia was characterized by an overall increase in cellularity of the bone marrow. The severities ranged from minimal to marked.

Spleen

Pigmentation and Hematopoietic Cell Proliferation: There was an increase in the incidences and severities of pigmentation and hematopoietic cell proliferation in the spleens of males and females at the six month and chronic sacrifices. There was excellent agreement between the SP, QAP and PWG chairperson regarding the diagnoses of pigmentation and hematopoietic cell proliferation. The lesions were discussed with the PWG. No slides were presented to the PWG to specifically exemplify pigmentation or hematopoietic cell proliferation.

Lymphoid Follicular Atrophy and Splenic Atrophy: Administration of 2-MI was associated with dose-related increased severities and incidences of lymphoid follicular atrophy of the spleen in males and females at the interim and chronic sacrifices. Administration of 2-MI was also associated with dose-related increased incidences and severities of splenic atrophy in males at chronic sacrifice.

Regarding lymphoid follicular atrophy, the QAP generally agreed with the diagnoses made by the SP, yet QAP identified more cases of lymphoid follicular atrophy in both males and females in the interim and chronic sacrifice time points. Moreover, the QAP thought several cases of lymphoid atrophy, as diagnosed by the SP, were more appropriately classified as splenic atrophy.

Splenic atrophy was a diagnosis made only by the QAP. The SP did not make a diagnosis of splenic atrophy in this study.

During the first PWG on October 17, 2002, the PWG members examined three examples of lymphoid follicular atrophy where there was 3-way agreement between the SP, QAP and PWG chairperson, and a fourth case where there was a 3-way discrepancy in diagnosis. The PWG refrained from making any consensus opinion about lymphoid follicular atrophy from these slides. The PWG members were of the opinion that the diagnosis of splenic atrophy may be a more appropriate diagnosis than lymphoid atrophy in two of these four cases. In the other two cases, the PWG members were concerned that lymphoid follicles only *appeared* small because of the expansion of red pulp due to extramedullary hematopoiesis. The PWG members unanimously decided to withhold any decision on these four slides; have the PWG chairperson more closely review the slides of lymphoid follicular atrophy and splenic atrophy; and to convene a second meeting of the PWG to review the splenic lesions.

During the second meeting of the PWG on November 1, 2002, the PWG members examined examples of normal spleen from control animals where there was no discrepancy between the SP and QAP; examples of lymphoid atrophy where there was 3-way agreement between the SP, QAP and PWG chairperson; and examples of discrepancies between the SP and QAP regarding the diagnoses of splenic atrophy and lymphoid atrophy. Photomicrographs of these slides were presented to the PWG prior to the slide examination. The PWG members agreed by overwhelming consensus with the diagnoses in those cases involving no discrepancies, and resolved the discrepancies by consensus opinion.

Lymphoid follicular atrophy was graded minimal to marked, and characterized by a smaller size of the periarteriolar lymphoid sheaths with occasionally decreased cell density, a thin or indiscernible pale mantle zone and reduction in the number of germinal centers compared to controls.

Splenic atrophy was graded mild to moderate and characterized by a decrease in the cross section of the spleen and a decrease in the size of both the white and red pulp when compared to controls.

There was discussion that in all cases of splenic atrophy the animals were either natural deaths or moribund sacrifices. In all but one case, the animals died early in the study (i.e., at or prior to day 21). In the majority of these cases, splenic atrophy was accompanied by thymic atrophy and lymph node atrophy. On the other hand, lymphoid follicular atrophy was seen in animals that survived to, or died close to, termination of the study.

Lymphoid Hyperplasia: The SP reported a dose related increased incidence of lymphoid hyperplasia in females at chronic sacrifice. The QAP agreed with these diagnoses but also made additional diagnoses in the control females, and made more diagnoses in control and treated males. These additional findings of lymphoid hyperplasia by the QAP essentially eliminated any dose-related increase in incidence. The PWG chairperson agreed with the QAP's additional findings of lymphoid

hyperplasia. In view of the agreement between the PWG chairperson and the QAP, the PWG chairperson and the NTP-pathologist agreed that lymphoid follicular hyperplasia in the spleen was not a 2-MI treatment related effect and was not an issue to be presented at the PWG.

Testis/Epididymis

Epididymal Inflammation: There were increased incidences and severities of chronic active inflammation and sperm granulomas of the epididymis in chronic sacrifice males.

There was good correlation between the SP and QAP regarding the epididymal lesions, however, the SP and QAP referred to the epididymal lesion as epididymal "degeneration". While there was some degeneration of epithelial cells in the epididymis, the PWG members were of unanimous decision that the lesion represented an inflammatory process and elected to replace the term "degeneration" with "inflammation".

The PWG members reviewed cases of normal epididymal tissue from control males, examples of the epididymal inflammation, examples of sperm granuloma, and all discrepancies involving the diagnosis of the epididymal lesion. Photomicrographs of these same lesions were presented at the PWG. The PWG agreed by consensus opinion on the diagnosis of the epididymal lesions (i.e., chronic active inflammation and sperm granuloma) and resolved all discrepancies. The possible pathogenesis of the epididymal inflammation was discussed. It was agreed that the epididymal lesions may be associated with administration of 2-MI.

The inflammation of the epididymis was generally unilateral and characterized by focal to locally extensive infiltrates of mononuclear inflammatory cells, engorgement of ducts with spermatozoa, multinucleated spermatozoa in duct lumina, marked vacuolization and disruption of the cells lining the epididymal ducts, and ducts containing coagulated protein and cell debris. Interstitial fibrosis and edema were seen to variable degrees. The inflammatory lesion was commonly seen with sperm granulomas. In these sperm granulomas, there was rupture of the epididymal ducts with a focal aggregation of macrophages in the interstitium.

Germinal Epithelial Atrophy: There were dose related increased incidences of atrophy of the germinal epithelium in chronic sacrifice males.

The PWG reviewed 6 cases of normal testicular tissue from control males, and nine cases of germinal epithelial atrophy where there was 3-way agreement between the SP, QAP and PWG chairperson. The PWG unanimously affirmed the diagnoses.

The atrophy was unilateral and commonly associated with ipsilateral epididymal inflammation and/or a sperm granuloma. The atrophy was locally extensive to diffuse

and characterized by a minimal to moderate decrease in the numbers of spermatogenic epithelium. Many tubules were lined only by Sertoli cells.

There was discussion that the lesion of germinal epithelial atrophy in this study had features of degeneration rather than atrophy; in that, the lesion was locally extensive rather than diffuse, unilateral rather than bilateral, and individual tubules were variably affected within the confines of a single lesion. However, the PWG agreed that the term "atrophy" was more appropriate than the term "degeneration". There was discussion as to the pathogenesis of the testicular lesion. The PWG members were of the general opinion that the unilateral testicular lesion was secondary to the ipsilateral epididymal inflammation, rather than due to a direct toxic effect of 2-MI.

Pituitary Gland

There was no macroscopic or microscopic lesion in the pituitary that was considered related to 2-MI administration. The QAP did not evaluate pituitary glands from the interim sacrifice animals. Since there was "mitotic alteration" in the pars distalis of pituitaries of *rats* at the interim sacrifice, the PWG chairperson examined the pituitary glands from all mice sacrificed at interim sacrifice. No lesion and in particular, no alteration in the mitotic rate, was seen.

Kidney

Pigmentation: There were increased incidences and severities of pigmentation in the proximal convoluted tubules of the kidneys of male mice at the interim and chronic sacrifices. There was excellent correlation regarding this diagnosis between the SP, QAP and PWG chairperson. No slides were presented to the PWG.

The pigment was consistent with hemosiderin, as it was globular, golden brown and iron-containing. The pigment was consistent with that in the spleen and liver and compatible with 2-MI treatment-related hemolysis. The finding of pigment in the males and not the females is also consistent with the finding of more hemosiderin pigment in male liver and spleen compared to females and increased severity and incidence of bone marrow hyperplasia in the males compared to females.

Uterus

The SP diagnosed "inflammation, lymphocytic" when there was minimal to marked lymphocytic inflammation of the uterus. The SP used a no threshold approach for rendering this diagnosis. This lesion was commonly associated with endometrial cystic hyperplasia. The QAP was of the opinion that "inflammation, lymphocytic" coincided with the presence of prolonged aged related estrous and therefore deleted this diagnosis in many instances. The PWG unanimously decided to maintain the diagnosis of "inflammation, lymphocytic" in the uterus even if many cases were considered normal

background change associated with estrous. The PWG reasoned that as long as the grading was consistent by the SP, the desirable approach was to grade and identify all cases of lymphocytic inflammation.

Lymph Node

Hyperplasia: The original pathology tables revealed the presence of a higher incidence of lymphoid cell hyperplasia of the mandibular lymph nodes in the 1250 ppm and 2500 ppm groups of female mice. This QAP confirmed the majority of the diagnoses made by the SP, and made additional findings of lymphoid hyperplasia in control and in the 625 ppm group of females. The QAP's additional findings essentially eliminated the dose related trend in incidences. The PWG chairperson agreed with the QAP, regarding the diagnoses of lymphoid hyperplasia, and with QAP's conclusion that the lesion was unrelated to 2-MI administration. At the advice of the NTP pathologist, the lesion was not presented to the PWG.

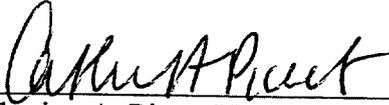
Miscellaneous Issues

The Harderian gland tumors were out of historical control range in both the males and females. Five Harderian gland neoplasms involving a 2-way or 3-way discrepancy in diagnoses were presented to the PWG and the PWG resolved the discrepancies by consensus opinion.

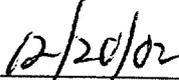
The alveolar bronchiolar neoplasms of the lung (adenomas, carcinomas or adenomas/carcinomas combined) were at the upper end of historical control range in the control males. The PWG reviewed three cases involving a 2-way discrepancy in tumor diagnosis of the lung, and resolved each discrepancy by consensus opinion.

HISTOTECHNIQUE QUALITY

The histotechnique quality assessment indicated that the overall histological processing and slide preparation was good, with no artifacts that would interfere with the interpretation of tissue sections.



Catherine A. Picut, VMD, JD
Diplomate, ACVP
PWG Chairperson



Date

NTP Experiment-Test: 92012-06
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLMIDAZOLE

Report: PEIRPT03
Date: 03/14/03
Time: 11:37:08

FINAL#1; REVISION#1

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25022 Accidentally Killed
25019 Moribund Sacrifice
25026 Other

25023 Missing
25020 Natural Death
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLIMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Early Deaths				
Morbund Sacrifice	2	3	4	4
Natural Death	2	3	2	1
Survivors				
Terminal Sacrifice	46	42	42	45
Morbund Sacrifice				
Natural Death		1	1	
Other		1	1	
Animals Examined Microscopically	50	49	49	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(50)	(48)	(48)	(50)
Edema	2 (4%)		2 (4%)	2 (4%)
Intestine Small, Jejunum	(50)	(46)	(48)	(49)
Hyperplasia, Lymphoid		1 (2%)		1 (2%)
Peyer's Patch, Infiltration Cellular, Polymorphonuclear	(47)	(49)	(47)	1 (2%)
Intestine Small, Ileum	1 (2%)			(48)
Hyperplasia, Lymphoid				
Peyer's Patch, Infiltration Cellular, Polymorphonuclear	(50)	(49)	(49)	1 (2%)
Liver				
Angiectasis	1 (2%)			(50)
Basophilic Focus		4 (8%)		1 (2%)
Clear Cell Focus	1 (2%)		1 (2%)	4 (8%)
Eosinophilic Focus			1 (2%)	1 (2%)
Hematopoietic Cell Proliferation	3 (6%)	3 (6%)	5 (10%)	3 (6%)
Hemorrhage		1 (2%)		3 (6%)
Hepatodiphragmatic Nodule			1 (2%)	2 (4%)
Hyperplasia, Lymphoid	3 (6%)	3 (6%)		6 (12%)
Infarct		1 (2%)		10 (20%)
Infiltration Cellular, Mixed Cell	13 (26%)	5 (10%)	12 (24%)	4 (8%)
Mixed Cell Focus	4 (8%)	1 (2%)	3 (6%)	
Necrosis, Focal	5 (10%)	2 (4%)	3 (6%)	
Tension Lipidosis			2 (4%)	
Bile Duct, Hyperplasia		1 (2%)		
Hepatocyte, Vacuolization			1 (2%)	
Kupffer Cell, Pigmentation		2 (4%)		

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

ALIMENTARY SYSTEM - CONT

Mesentery	(3)	(4)	(6)	(6)
Inflammation, Chronic	1 (33%)	1 (25%)		
Fat, Angiectasis	2 (67%)	3 (75%)	1 (17%)	1 (17%)
Fat, Necrosis	(50)	(49)	6 (100%)	6 (100%)
Pancreas	1 (2%)		(48)	(50)
Atrophy	1 (2%)	1 (2%)		
Cyst			1 (2%)	2 (4%)
Acinus, Cytoplasmic Alteration			2 (4%)	1 (2%)
Salivary Glands	2 (4%)	(49)	(49)	(49)
Atrophy			5 (10%)	1 (2%)
Hyperplasia, Lymphoid	(50)	(49)	(49)	(50)
Stomach, Forestomach	1 (2%)	(49)	(49)	(50)
Inflammation, Chronic Active	1 (2%)	1 (2%)		5 (10%)
Diverticulum	1 (2%)			
Epithelium, Hyperplasia	1 (2%)		1 (2%)	1 (2%)

CARDIOVASCULAR SYSTEM

Heart	(50)	(49)	(49)	(50)
Cardiomyopathy				2 (4%)
Thrombosis				1 (2%)
Myocardium, Necrosis				

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(49)	(49)	(50)
Accessory Adrenal Cortical Nodule	7 (14%)	5 (10%)	4 (8%)	6 (12%)
Hyperplasia, Focal				2 (4%)
Capsule, Hyperplasia	3 (6%)	(49)	(49)	(50)
Adrenal Medulla	(50)			
Hyperplasia			1 (2%)	(50)
Islets, Pancreatic	(50)	(48)	(48)	(50)
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Parathyroid Gland	(48)	(46)	(45)	(48)
Cyst			1 (2%)	1 (2%)
Pituitary Gland	(50)	(49)	(47)	(49)
Pars Distalis, Angiectasis			3 (6%)	1 (2%)
Pars Distalis, Cyst	1 (2%)	3 (6%)	1 (2%)	2 (4%)
Pars Distalis, Hyperplasia, Focal	1 (2%)	2 (4%)	1 (2%)	
Thyroid Gland	(49)	(48)	(48)	(50)
Degeneration, Cystic	15 (31%)	14 (29%)	12 (25%)	9 (18%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

ENDOCRINE SYSTEM - CONT	0PPM	625 PPM	1250 PPM	2500 PPM
Follicle, Cyst	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Follicular Cell, Hyperplasia	6 (12%)	3 (6%)	1 (2%)	9 (18%)
Follicular Cell, Hypertrophy			23 (48%)	46 (92%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Clitoral Gland	(50)	(48)	(48)	(50)
Inflammation, Chronic				1 (2%)
Ovary	(50)	(49)	(49)	(48)
Angiectasis	12 (24%)	7 (14%)	8 (16%)	8 (17%)
Cyst	10 (20%)	11 (22%)	15 (31%)	10 (21%)
Inflammation, Chronic	3 (6%)		2 (4%)	1 (2%)
Thrombosis				1 (2%)
Corpus Luteum, Hyperplasia	(50)	(49)	(49)	(50)
Uterus				1 (2%)
Angiectasis	3 (6%)	2 (4%)	2 (4%)	6 (12%)
Inflammation, Chronic	6 (12%)	2 (4%)	9 (18%)	4 (8%)
Metaplasia, Squamous	5 (10%)		5 (10%)	1 (2%)
Cervix, Cyst Epithelial Inclusion		1 (2%)		
Endometrium, Fibrosis				1 (2%)
Endometrium, Hyperplasia, Cystic	48 (96%)	47 (96%)	46 (94%)	45 (90%)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(49)	(48)	(50)
Hyperplasia	10 (20%)	5 (10%)	13 (27%)	16 (32%)
Lymph Node	(12)	(6)	(8)	(9)
Bronchial, Hyperplasia, Lymphoid	1 (8%)			2 (22%)
Iliac, Ectasia			1 (13%)	
Iliac, Hematopoietic Cell Proliferation	2 (17%)	1 (17%)	1 (13%)	2 (22%)
Iliac, Hyperplasia, Lymphoid	5 (42%)	3 (50%)	4 (50%)	
Iliac, Pigmentation		1 (17%)		
Inguinal, Hyperplasia, Lymphoid			1 (13%)	
Lumbar, Hyperplasia, Lymphoid	1 (8%)	1 (17%)	2 (25%)	2 (22%)
Lumbar, Pigmentation		1 (17%)		
Mediastinal, Hyperplasia, Lymphoid	1 (8%)			

a Number of animals examined microscopically at site and number of animals with lesion

B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

HEMATOPOIETIC SYSTEM - CONT

Pancreatic, Hyperplasia, Lymphoid	1 (8%)	1 (17%)	1 (13%)	1 (2%)
Renal, Hematopoietic Cell Proliferation	3 (25%)	2 (25%)	1 (13%)	15 (31%)
Renal, Hyperplasia, Lymphoid	(48)	(48)	2 (25%)	
Lymph Node, Mandibular			(46)	(48)
Atrophy	3 (6%)	2 (4%)		
Hematopoietic Cell Proliferation				1 (2%)
Hemorrhage	11 (23%)	12 (25%)	10 (22%)	15 (31%)
Hyperplasia, Lymphoid	2 (4%)	1 (2%)	4 (9%)	
Hyperplasia, Plasma Cell	24 (50%)	20 (42%)	21 (46%)	21 (44%)
Pigmentation	(48)	(48)	(47)	(48)
Lymph Node, Mesenteric				1 (2%)
Ectasia	5 (10%)	3 (6%)	4 (9%)	3 (6%)
Hematopoietic Cell Proliferation		1 (2%)	1 (2%)	1 (2%)
Hemorrhage	3 (6%)	7 (15%)		6 (13%)
Hyperplasia, Lymphoid	(50)	(49)	(49)	(50)
Hyperplasia, Plasma Cell		1 (2%)	1 (2%)	
Spleen	2 (4%)	20 (41%)	24 (49%)	39 (78%)
Angiectasis	15 (30%)	1 (2%)	1 (2%)	
Atrophy		4 (8%)	11 (22%)	34 (68%)
Congestion		3 (6%)	5 (10%)	4 (8%)
Hematopoietic Cell Proliferation		14 (29%)	13 (27%)	16 (32%)
Hyperplasia, Plasma Cell	1 (2%)	(48)	(48)	(50)
Pigmentation	12 (24%)	2 (4%)	7 (15%)	3 (6%)
Lymphoid Follicle, Atrophy	(50)			4 (8%)
Lymphoid Follicle, Hyperplasia				
Thymus				
Atrophy				
Hyperplasia, Lymphoid				

INTEGUMENTARY SYSTEM

Mammary Gland	(49)	(49)	(49)	(50)
Hyperplasia		2 (4%)		2 (4%)
Skin	(50)	(49)	(49)	(50)
Edema			1 (2%)	

MUSCULOSKELETAL SYSTEM

Bone	(50)	(49)	(49)	(50)
Hyperostosis	9 (18%)	13 (27%)	10 (20%)	11 (22%)
Skeletal Muscle	(1)	(1)		

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

MUSCULOSKELETAL SYSTEM - CONT
 Necrosis 1 (100%)

NERVOUS SYSTEM

Brain (50)
 Hemorrhage (49)
 Inflammation, Chronic Active 1 (2%)
 Vacuolization Cytoplasmic 1 (2%)
 1 (2%)

RESPIRATORY SYSTEM

Lung (50)
 Edema 2 (4%)
 Foreign Body (49)
 Hemorrhage 2 (4%)
 Hyperplasia, Lymphoid 3 (6%)
 Infiltration Cellular, Histiocyte 6 (12%)
 Thrombosis 2 (4%)
 Alveolar Epithelium, Hyperplasia 1 (2%)
 Nose (49)
 Foreign Body 1 (2%)

SPECIAL SENSES SYSTEM

Eye (50)
 Atrophy (49)
 Cataract 1 (2%)
 Inflammation, Chronic 2 (4%)
 Harderian Gland (49)
 Hyperplasia (49)
 Hyperplasia, Focal 2 (4%)
 1 (2%)

URINARY SYSTEM

Kidney (50)
 Cyst 1 (2%)
 Hyperplasia, Lymphoid (49)
 Infarct 2 (4%)
 Inflammation, Chronic 16 (33%)
 8 (16%)
 1 (2%)
 2 (4%)
 8 (16%)
 4 (8%)
 2 (4%)
 1 (2%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE FEMALE	0PPM	625 PPM	1250 PPM	2500 PPM
URINARY SYSTEM - CONT				
Metaplasia, Osseous		1 (2%)		2 (4%)
Nephropathy	27 (54%)	17 (35%)	21 (43%)	19 (38%)
Papilla, Necrosis		1 (2%)		1 (2%)
Renal Tubule, Accumulation, Hyaline Droplet			1 (2%)	1 (2%)
Renal Tubule, Dilatation			1 (2%)	
Renal Tubule, Necrosis		2 (4%)		1 (2%)
Renal Tubule, Pigmentation	(50)	(49)	(49)	(50)
Urinary Bladder	16 (32%)	16 (33%)	6 (12%)	11 (22%)
Hyperplasia, Lymphoid	1 (2%)	1 (2%)		
Inflammation, Chronic		1 (2%)		
Transitional Epithelium, Hyperplasia		1 (2%)		

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Disposition	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	4	1	5	5
Natural Death	3	3	9	5
Survivors				
Terminal Sacrifice	43	46	36	40
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(49)	(49)	(47)	(50)
Edema	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Intestine Small, Duodenum	(49)	(49)	(45)	(50)
Epithelium, Hyperplasia				1 (2%)
Intestine Small, Jejunum	(50)	(49)	(46)	(50)
Hyperplasia, Lymphoid		1 (2%)	1 (2%)	1 (2%)
Infiltration Cellular, Polymorphonuclear	(49)	(50)	(45)	(49)
Intestine Small, Ileum		1 (2%)		1 (2%)
Hyperplasia, Lymphoid				1 (2%)
Infiltration Cellular, Polymorphonuclear	(50)	(50)	(50)	(50)
Liver				
Angiectasis	2 (4%)	3 (6%)	1 (2%)	3 (6%)
Basophilic Focus	2 (4%)	2 (4%)	1 (2%)	3 (6%)
Clear Cell Focus	6 (12%)	9 (18%)	6 (12%)	8 (16%)
Cyst		1 (2%)		6 (12%)
Eosinophilic Focus	3 (6%)	3 (6%)	2 (4%)	2 (4%)
Hematopoietic Cell Proliferation	1 (2%)		2 (4%)	2 (4%)
Hepatodiphragmatic Nodule				1 (2%)
Infarct	1 (2%)	7 (14%)	7 (14%)	7 (14%)
Infiltration Cellular, Mixed Cell	5 (10%)	3 (6%)	4 (8%)	4 (8%)
Mixed Cell Focus	4 (8%)			1 (2%)
Necrosis, Diffuse		6 (12%)	2 (4%)	6 (12%)
Necrosis, Focal	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Pension Lipidosis				11 (22%)
Hepatocyte, Cytoplasmic Alteration				10 (20%)
Hepatocyte, Karyomegaly		1 (2%)		1 (2%)
Hepatocyte, Vacuolization Cytoplasmic		1 (2%)		1 (2%)
Kupffer Cell, Pigmentation	(6)	(2)	(5)	(2)
Mesentery				
Angiectasis		1 (50%)		

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE MALE

0PPM

625 PPM

1250 PPM

2500 PPM

ALIMENTARY SYSTEM - CONT	0PPM	625 PPM	1250 PPM	2500 PPM
Inflammation, Chronic	4 (67%)	1 (50%)	3 (60%)	2 (100%)
Fat, Necrosis	(50)	(50)	(49)	(50)
Pancreas	1 (2%)		1 (2%)	
Atrophy	2 (4%)		3 (6%)	2 (4%)
Cyst			2 (4%)	1 (2%)
Acinus, Cytoplasmic Alteration	(50)	(50)	(50)	(50)
Salivary Glands	2 (4%)	2 (4%)	(50)	(50)
Hyperplasia, Lymphoid	(50)	(49)	(50)	(50)
Stomach, Fore stomach	1 (2%)	2 (4%)		1 (2%)
Diverticulum		1 (2%)		1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)		1 (2%)
Ulcer		1 (2%)		1 (2%)
Epithelium, Hyperplasia	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Stomach, Glandular	(50)	(49)	(49)	(50)
Glands, Dysplasia	1 (2%)		1 (2%)	
Tooth				1 (100%)
Inflammation, Chronic				

CARDIOVASCULAR SYSTEM

Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	1 (2%)			1 (2%)
Perivascular, Inflammation, Chronic	3 (6%)			

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule	2 (4%)	6 (12%)	8 (16%)	6 (12%)
Hyperplasia, Focal	2 (4%)	4 (8%)	3 (6%)	1 (2%)
Hyper trophy, Focal	13 (26%)	18 (36%)	10 (20%)	10 (20%)
Capsule, Hyperplasia	1 (2%)	2 (4%)	3 (6%)	2 (4%)
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	(50)	(50)	2 (4%)	(50)
Islets, Pancreatic	(50)	(50)	(49)	(50)
Hyperplasia	(49)	2 (4%)	(45)	1 (2%)
Parathyroid Gland	3 (6%)	(47)	2 (4%)	(48)
Cyst	(49)	1 (2%)	2 (4%)	1 (2%)
Pituitary Gland	2 (4%)	(48)	(48)	(50)
Pars Distalis, Cyst		1 (2%)	2 (4%)	2 (4%)
Pars Distalis, Hyperplasia, Focal		1 (2%)		
Thyroid Gland	(50)	(50)	(50)	(50)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

ENDOCRINE SYSTEM - CONT	0PPM	625 PPM	1250 PPM	2500 PPM
Degeneration, Cystic	10 (20%)	2 (4%)	3 (6%)	4 (8%)
Follicular Cell, Hyperplasia	1 (2%)	2 (4%)	3 (6%)	33 (66%)
Follicular Cell, Hypertrophy			6 (12%)	25 (50%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Epididymis	(50)	(50)	(50)	(50)
Fibrosis	1 (2%)			
Granuloma Sperm			2 (4%)	5 (10%)
Hyperplasia, Lymphoid			2 (4%)	1 (2%)
Hypospertma			1 (2%)	
Inflammation, Chronic Active	1 (2%)	3 (6%)	7 (14%)	8 (16%)
Penis	(1)		(1)	(1)
Angiectasis	(50)	(50)	1 (100%)	1 (100%)
Preputial Gland	18 (36%)	23 (46%)	16 (32%)	21 (42%)
Cyst	14 (28%)	10 (20%)	14 (28%)	7 (14%)
Inflammation, Chronic	(49)	(50)	(49)	(50)
Prostate				2 (4%)
Inflammation, Chronic	(50)	(50)	(50)	(50)
Seminal Vesicle	1 (2%)			
Atrophy	(50)	(50)	(50)	(50)
Testes	1 (2%)	4 (8%)	8 (16%)	14 (28%)
Germinal Epithelium, Atrophy	(50)	(50)	(50)	(50)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(50)	(50)
Hyperplasia	4 (8%)	10 (20%)	20 (40%)	42 (84%)
Lymph Node	(2)	(3)		(1)
Bronchial, Hyperplasia, Lymphoid		1 (33%)		
Lymph Node, Mandibular	(48)	(46)	(45)	(50)
Atrophy	1 (2%)		2 (4%)	4 (8%)
Ectasia			1 (2%)	
Hyperplasia, Lymphoid	10 (21%)	14 (30%)	9 (20%)	13 (26%)
Pigmentation	8 (17%)	6 (13%)	9 (20%)	6 (12%)
Lymph Node, Mesenteric	(47)	(47)	(46)	(48)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM - CONT

Angiectasis	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Atrophy	4 (8%)	2 (4%)	2 (4%)	2 (4%)
Hemorrhage	7 (15%)	7 (15%)	15 (33%)	10 (21%)
Hyperplasia, Lymphoid	1 (2%)	(50)	(49)	1 (2%)
Necrosis	(50)	(50)	(49)	(50)
Spleen				
Angiectasis				
Atrophy				
Hematopoietic Cell Proliferation	10 (20%)	1 (2%)	4 (8%)	3 (6%)
Pigmentation	1 (2%)	21 (42%)	38 (78%)	45 (90%)
Lymphoid Follicle, Atrophy		16 (32%)	33 (67%)	43 (86%)
Lymphoid Follicle, Hyperplasia	5 (10%)	4 (8%)	14 (29%)	30 (60%)
Thymus	(47)	2 (4%)	2 (4%)	2 (4%)
Atrophy	7 (15%)	(46)	(46)	(47)
Cyst	1 (2%)	5 (11%)	9 (20%)	8 (17%)
Hyperplasia, Lymphoid		1 (2%)	1 (2%)	1 (2%)

INTEGUMENTARY SYSTEM

Skin	(50)	(50)	(50)	(50)
Inflammation, Chronic		1 (2%)		

MUSCULOSKELETAL SYSTEM

Skeletal Muscle	(1)	(1)		(2)
Atrophy				1 (50%)

NERVOUS SYSTEM

Brain	(50)	(50)	(50)	(50)
Compression		1 (2%)		
Peripheral Nerve	(1)			(1)
Atrophy				1 (100%)

RESPIRATORY SYSTEM

Lung	(50)	(50)	(50)	(50)
Edema	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Hemorrhage	4 (8%)	8 (16%)	4 (8%)	2 (4%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PETRPT03
 Date: 03/14/03
 Time: 11:37:08

B6C3F1 MICE MALE

	0PPM	625 PPM	1250 PPM	2500 PPM
RESPIRATORY SYSTEM - CONT				
Hyperplasia, Lymphoid	1 (2%)	2 (4%)	2 (4%)	4 (8%)
Infiltration Cellular, Histiocyte	4 (8%)	4 (8%)	4 (8%)	2 (4%)
Inflammation, Chronic			1 (2%)	2 (4%)
Metaplasia, Osseous			2 (4%)	
Thrombosis	1 (2%)	3 (6%)	1 (2%)	1 (2%)
Alveolar Epithelium, Hyperplasia	5 (10%)			3 (6%)
Alveolar Epithelium, Multifocal	1 (2%)	(50)	(50)	(50)
Nose	1 (2%)	3 (6%)	3 (6%)	2 (4%)
Foreign Body	1 (2%)	4 (8%)	3 (6%)	2 (4%)
Inflammation, Chronic				

SPECIAL SENSES SYSTEM

Eye	(50)	(50)	(50)	(50)
Cataract			1 (2%)	1 (2%)
Inflammation, Chronic	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Cornea, Hyperplasia	1 (2%)	(50)	1 (2%)	(50)
Harderian Gland	(50)		(48)	
Hyperplasia, Focal	1 (2%)		2 (4%)	
Inflammation, Chronic	3 (6%)	4 (8%)		2 (4%)

URINARY SYSTEM

Kidney	(50)	(50)	(50)	(50)
Cyst	13 (26%)	11 (22%)	12 (24%)	19 (38%)
Hydronephrosis	1 (2%)	3 (6%)	3 (6%)	3 (6%)
Hyperplasia, Lymphoid	1 (2%)	6 (12%)	6 (12%)	1 (2%)
Infarct	6 (12%)			1 (2%)
Inflammation, Suppurative				3 (6%)
Metaplasia, Osseous	5 (10%)	3 (6%)	2 (4%)	3 (6%)
Nephropathy	34 (68%)	43 (86%)	32 (64%)	31 (62%)
Papilla, Necrosis				1 (2%)
Renal Tubule, Hyperplasia	1 (2%)	1 (2%)	2 (4%)	3 (6%)
Renal Tubule, Pigmentation	1 (2%)		2 (4%)	45 (90%)
Urethra				(1)
Angiectasis				1 (100%)
Inflammation, Suppurative				1 (100%)
Urinary Bladder	(50)	(50)	(50)	(50)
Transitional Epithelium, Hyperplasia				1 (2%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC 2-METHYLMIDAZOLE
Route: DOSED FEED

Report: PEIRPT05
Date: 02/25/03
Time: 07:34:38

FINAL#1/MICE

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25019 Moribund Sacrifice 25020 Natural Death
25021 Terminal Sacrifice
Removal Date Range: All
Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

2-METHYLMIDAZOLE

B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

DISPOSITION SUMMARY

Disposition	0 PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially in Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	2	3	4	4
Natural Death	2	3	2	1
Survivors				
Terminal Sacrifice	46	42	42	45
Moribund Sacrifice				
Natural Death		1	1	
Animals Examined Microscopically	50	49	49	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(50)	(48)	(48)	(50)
Intestine Small, Duodenum	(50)	(49)	(48)	(49)
Carcinoma				1 (2%)
Polyp Adenomatous		1 (2%)		
Intestine Small, Jejunum	(50)	(46)	(48)	(49)
Serosa, Histiocytic Sarcoma				1 (2%)
Liver				
Hepatocellular Carcinoma	(50)	(49)	(49)	(50)
Hepatocellular Adenoma	2 (4%)	3 (6%)	6 (12%)	9 (18%)
Hepatocellular Adenoma, Multiple	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Histiocytic Sarcoma	1 (2%)		1 (2%)	1 (2%)
Pancreas	(50)	(49)	(48)	(50)
Histiocytic Sarcoma				1 (2%)
Salivary Glands	(50)	(49)	(49)	(49)
Stomach, Forestomach	(50)	(49)	(49)	(50)
Squamous Cell Papilloma	1 (2%)	1 (2%)		2 (4%)
Squamous Cell Papilloma, Multiple	1 (2%)			
Stomach, Glandular	(50)	(49)	(48)	(50)

CARDIOVASCULAR SYSTEM

Heart	(50)	(49)	(49)	(50)
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B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

ENDOCRINE SYSTEM

Adrenal Medulla	(50)	(49)	(49)	(50)
Pheochromocytoma Malignant			1 (2%)	
Islets, Pancreatic	(50)	(48)	(48)	(50)
Adenoma		1 (2%)		
Pituitary Gland	(50)	(49)	(47)	(49)
Pars Distalis, Adenoma	1 (2%)	1 (2%)		
Thyroid Gland	(49)	(48)	(48)	(50)
Unilateral, Follicular Cell, Adenoma	1 (2%)			1 (2%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(50)	(49)	(49)	(48)
Cystadenoma		1 (2%)		
Granulosa-Theca Tumor Benign		1 (2%)		
Histiocytic Sarcoma			1 (2%)	1 (2%)
Luteoma			(49)	(50)
Uterus	(50)		(49)	(49)
Hemangiosarcoma	1 (2%)			1 (2%)
Histiocytic Sarcoma				(50)
Polyp Stromal			2 (4%)	
Sarcoma Stromal	1 (2%)			1 (2%)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(49)	(48)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic Sarcoma			1 (2%)	
Lymph Node	(12)	(6)	(8)	(9)
Lymph Node, Mandibular	(48)	(48)	(46)	(48)
Lymph Node, Mesenteric	(48)	(48)	(47)	(48)
Histiocytic Sarcoma				1 (2%)
Spleen	(50)	(49)	(49)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic Sarcoma	(50)	(48)	(48)	(50)

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/25/03
 Time: 07:34:38

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM - cont

INTEGUMENTARY SYSTEM

Mammary Gland	(49)	(49)	(49)	(50)
Carcinoma	1 (2%)	(49)	(49)	2 (4%)
Skin	(50)	(49)	(49)	(50)
Basal Cell Carcinoma		1 (2%)	1 (2%)	
Keratoacanthoma				
Subcutaneous Tissue, Fibrosarcoma			3 (6%)	1 (2%)
Subcutaneous Tissue, Fibrous Histiocytoma			1 (2%)	
Subcutaneous Tissue, Hemangiosarcoma	1 (2%)	1 (2%)		

MUSCULOSKELETAL SYSTEM

Bone	(50)	(49)	(49)	(50)
Osteoma				1 (2%)
Osteosarcoma	1 (2%)	(1)	(1)	
Skeletal Muscle				

NERVOUS SYSTEM

Brain	(50)	(49)	(49)	(50)
Cranial Nerve, Schwannoma Malignant			1 (2%)	

RESPIRATORY SYSTEM

Lung	(50)	(49)	(49)	(50)
Alveolar/Bronchiolar Adenoma	4 (8%)	2 (4%)	2 (4%)	1 (2%)
Alveolar/Bronchiolar Carcinoma		2 (4%)		
Histiocytic Sarcoma			1 (2%)	

SPECIAL SENSES SYSTEM

Harderian Gland	(50)	(49)	(49)	(50)
Adenoma	3 (6%)	2 (4%)	6 (12%)	6 (12%)
Carcinoma	1 (2%)		1 (2%)	1 (2%)

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLMIDAZOLE
 Route: DOSED FEED

Report: PETRPT05
 Date: 02/25/03
 Time: 07:34:38

B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

URINARY SYSTEM

Kidney
 Urinary Bladder

(50)
 (50)

(49)
 (49)

(49)
 (49)

(50)
 (50)

SYSTEMIC LESIONS

Multiple Organs
 Histiocytic Sarcoma
 Lymphoma Malignant

*(50)
 6 (12%)

*(49)
 8 (16%)

*(49)
 1 (2%)
 6 (12%)

*(50)
 1 (2%)
 8 (16%)

* Number of animals with any tissue examined microscopically

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLMIDAZOLE
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/25/03
 Time: 07:34:38

B6C3F1 MICE FEMALE 0PPM 625 PPM 1250 PPM 2500 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	23	20	23	29
Total Primary Neoplasms	28	28	30	36
Total Animals with Benign Neoplasms	13	12	14	20
Total Benign Neoplasms	14	15	15	22
Total Animals with Malignant Neoplasms	12	12	15	14
Total Malignant Neoplasms	14	13	15	14
Total Animals with Metastatic Neoplasms				
Total Metastatic Neoplasms				
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

B6C3F1 MICE MALE

OPPM

625 PPM

1250 PPM

2500 PPM

DISPOSITION SUMMARY

Disposition	OPPM	625 PPM	1250 PPM	2500 PPM
Animals Initially in Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	4	1	5	5
Natural Death	3	3	9	5
Survivors				
Terminal Sacrifice	43	46	36	40
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(49)	(49)	(47)	(50)
Intestine Small, Duodenum	(49)	(49)	(45)	(50)
Polyp Adenomatous	1 (2%)		1 (2%)	(50)
Intestine Small, Jejunum	(50)	(49)	(46)	(50)
Carcinoma	1 (2%)	1 (2%)	1 (2%)	(50)
Liver	(50)	(50)	(50)	(50)
Hemangioma	1 (2%)			1 (2%)
Hemangiosarcoma	4 (8%)	5 (10%)	8 (16%)	2 (4%)
Hepatocellular Carcinoma		3 (6%)	6 (12%)	5 (10%)
Hepatocellular Carcinoma, Multiple	5 (10%)	11 (22%)	9 (18%)	1 (2%)
Hepatocellular Adenoma	2 (4%)	3 (6%)	4 (8%)	15 (30%)
Hepatocellular Adenoma, Multiple	1 (2%)		1 (2%)	3 (6%)
Histiocytic Sarcoma				
Liposarcoma, Metastatic, Uncertain Primary Site		1 (2%)		1 (2%)
Osteosarcoma, Metastatic, Bone	(50)	(50)	(49)	1 (2%)
Pancreas	(50)	(50)	(50)	(50)
Salivary Glands	(50)	(49)	(50)	(50)
Stomach, Forestomach	(50)	(49)	(50)	(50)
Squamous Cell Papilloma		1 (2%)		1 (2%)

CARDIOVASCULAR SYSTEM

Heart	(50)	(50)	(50)	(50)
Liposarcoma, Metastatic, Uncertain Primary Site				1 (2%)

B6C3F1 MICE MALE OPPM 625 PPM 1250 PPM 2500 PPM

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(50)	(50)	(50)
Capsule, Adenoma		2 (4%)		1 (2%)
Islets, Pancreatic	(50)	(50)	(49)	(50)
Adenoma				1 (2%)
Pituitary Gland	(49)	(48)	(48)	(50)
Thyroid Gland	(50)	(50)	(50)	(50)
Bilateral, Follicular Cell, Adenoma				1 (2%)
Follicular Cell, Adenoma				
Unilateral, Follicular Cell, Adenoma				6 (12%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Epididymis	(50)	(50)	(50)	(50)
Preputial Gland	(50)	(50)	(50)	(50)
Histiocytic Sarcoma			1 (2%)	(50)
Testes	(50)	(50)	(50)	(50)
Sertoli Cell Tumor Malignant				1 (2%)
Interstitial Cell, Adenoma				1 (2%)

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)	1 (2%)		
Histiocytic Sarcoma	1 (2%)			
Lymph Node	(2)	(3)		(1)
Inguinal, Histiocytic Sarcoma	1 (50%)			
Inguinal, Osteosarcoma, Metastatic, Bone				1 (100%)
Mediastinal, Osteosarcoma, Metastatic, Bone				1 (100%)
Lymph Node, Mandibular	(48)	(46)	(45)	(50)
Histiocytic Sarcoma	1 (2%)			
Lymph Node, Mesenteric	(47)	(47)	(46)	(48)
Histiocytic Sarcoma	1 (2%)			
Spleen	(50)	(50)	(49)	(50)
Hemangiosarcoma	1 (2%)			
Histiocytic Sarcoma	1 (2%)			

B6C3F1 MICE MALE

0PPM

625 PPM

1250 PPM

2500 PPM

HEMATOPOIETIC SYSTEM - cont

Tymus	0PPM	625 PPM	1250 PPM	2500 PPM
Histiocytic Sarcoma	(47) 1 (2%)	(46)	(46)	(47)
Osteosarcoma, Metastatic, Bone				1 (2%)

INTEGUMENTARY SYSTEM

Skin	0PPM	625 PPM	1250 PPM	2500 PPM
Subcutaneous Tissue, Fibrous Histiocytoma	(50)	(50)	(50)	(50)
Subcutaneous Tissue, Hemangiosarcoma	1 (2%)	1 (2%)		
Subcutaneous Tissue, Sarcoma	1 (2%)			
Subcutaneous Tissue, Schwannoma Benign			1 (2%)	

MUSCULOSKELETAL SYSTEM

Bone	0PPM	625 PPM	1250 PPM	2500 PPM
Liposarcoma, Metastatic, Uncertain Primary Site	(50)	(50)	(50)	(50)
Osteoma		1 (2%)		1 (2%)
Osteosarcoma		(1)	1 (100%)	(2)
Skeletal Muscle	(1)			
Hemangiosarcoma				
Liposarcoma, Metastatic, Uncertain Primary Site				1 (50%)

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung	0PPM	625 PPM	1250 PPM	2500 PPM
Alveolar/Bronchiolar Adenoma	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma, Multiple	11 (22%)	7 (14%)	6 (12%)	4 (8%)
Alveolar/Bronchiolar Carcinoma	5 (10%)	2 (4%)	4 (8%)	1 (2%)
Alveolar/Bronchiolar Carcinoma, Multiple	1 (2%)	1 (2%)	1 (2%)	4 (8%)
Carcinoma, Metastatic, Harderian Gland	1 (2%)			1 (2%)
Carcinoma, Metastatic, Kidney			1 (2%)	
Hemangiosarcoma, Metastatic, Liver		3 (6%)	6 (12%)	1 (2%)
Hepatocellular Carcinoma, Metastatic, Liver				2 (4%)

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/25/03
 Time: 07:34:38

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

RESPIRATORY SYSTEM - cont
 Histiocytic Sarcoma 1 (2%)
 Liposarcoma, Metastatic, Uncertain Primary
 Site
 Osteosarcoma, Metastatic, Bone 1 (2%)

SPECIAL SENSES SYSTEM
 Harderian Gland (50)
 Adenoma 9 (18%)
 Carcinoma 1 (2%)
 Histiocytic Sarcoma 1 (2%)
 (50) 6 (12%) (48) (50)
 5 (10%) 3 (6%)
 1 (2%) 2 (4%)

URINARY SYSTEM
 Kidney (50)
 Histiocytic Sarcoma 1 (2%)
 Liposarcoma, Metastatic, Uncertain Primary (50)
 Site (50)
 Renal Tubule, Adenoma 1 (2%)
 Renal Tubule, Carcinoma 1 (2%)
 Urinary Bladder (50) (50)

SYSTEMIC LESIONS
 Multiple Organs *(50)
 Histiocytic Sarcoma 1 (2%) *(50)
 Leukemia Granulocytic 1 (2%) 1 (2%)
 Lymphoma Malignant 2 (4%) 3 (6%) 1 (2%)

* Number of animals with any tissue examined microscopically

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/25/03
 Time: 07:34:38

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	32	34	34	38
Total Primary Neoplasms	50	53	52	56
Total Animals with Benign Neoplasms	23	25	24	30
Total Benign Neoplasms	28	32	27	39
Total Animals with Malignant Neoplasms	20	16	21	14
Total Malignant Neoplasms	22	21	25	17
Total Animals with Metastatic Neoplasms	1	3	7	5
Total Metastatic Neoplasms	1	3	7	14
Total Animals with Malignant Neoplasms Uncertain Primary Site				1
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 06
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: HEATH, JAMES E.

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLMIMIDAZOLE
CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

REPORT: PEIRPT08
DATE: 02/25/03
TIME: 07:34:56
PAGE: 1
NTP C#: 92012B
CAS: 693-98-1

FINAL#1/MICE

REASONS FOR REMOVAL: 25019 Moribund Sacrifice
25020 Natural Death
25021 Terminal Sacrifice

REMOVAL DATE RANGE: ALL
TREATMENT GROUPS: INCLUDE ALL

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 06
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: HEATH, JAMES E.
Mice(B6C3F1)

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLMIMIDAZOLE

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

FOR ALL DOSES THE TUMOR RATES IN THE FOLLOWING TISSUES/ORGANS ARE
BASED ON NUMBER OF TISSUES EXAMINED. IN OTHER TISSUES/ORGANS RATES
ARE BASED ON THE NUMBER OF ANIMALS NECROPSIED.

Adrenal Cortex
Adrenal Medulla
Bone Marrow
Brain
Islets, Pancreatic
Kidney
Liver
Lung
Ovary
Pituitary Gland
Spleen
Testes
Thyroid Gland

REPORT: PEIRPT08
DATE: 02/25/03
TIME: 07:34:56
NTP C#: 92012B
CAS: 693-98-1

NTP
LAB: Southern Research Inst
EXPERIMENT: 92012 TEST: 06
TEST TYPE: CHRONIC
CONT: N01-ES-85420
PATHOLOGIST: HEATH, JAMES E.

STATISTICAL ANALYSIS OF PRIMARY TUMORS
2-METHYLMIDAZOLE
CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED FEED

REPORT: PEIRPT08
DATE: 02/25/03
TIME: 07:34:56
NTP C#: 92012B
CAS: 693-98-1

SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS
IN THE ANALYSIS OF 2-METHYLMIDAZOLE

Male Mice

Organ

Harderian Gland
Liver

Morphology

Adenoma
Hepatocellular Adenoma
Hepatocellular Carcinoma
Hepatocellular Carcinoma, or Hepatocellular Adenoma
Hepatocellular Adenoma, or Hepatoblastoma

Thyroid Gland: Follicular Cell
All Organs

Benign Tumors
Malignant and Benign Tumors

Female Mice

Organ

Liver

Morphology

Hepatocellular Adenoma
Hepatocellular Carcinoma
Hepatocellular Carcinoma, or Hepatocellular Adenoma
Hepatocellular Adenoma, or Hepatoblastoma
Alveolar/Bronchiolar Adenoma

Lung

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
Adrenal Cortex Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/49 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	0/47.43	2/48.59	0/41.44	1/44.45	0/48.25	0/46.83	0/46.63	0/48.64
POLY-3 PERCENT (g)	0.0%	4.1%	0.0%	2.3%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/43 (0%)	2/46 (4%)	0/36 (0%)	1/40 (3%)	0/46 (0%)	0/43 (0%)	0/43 (0%)	0/45 (0%)
FIRST INCIDENCE	---	729 (T)	---	729 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.509	P=0.253	(e)	P=0.486	(e)	(e)	(e)	(e)
POLY 3	P=0.513	P=0.243	(e)	P=0.487	(e)	(e)	(e)	(e)
POLY 1.5	P=0.513	P=0.240	(e)	P=0.487	(e)	(e)	(e)	(e)
POLY 6	P=0.513	P=0.247	(e)	P=0.487	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	(e)	P=0.253	(e)	P=0.486	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.539	P=0.247	(e)	P=0.500	(e)	(e)	(e)	(e)
ORDER RESTRICTED	P=0.314	(e)						

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
Harderian Gland Adenoma								
TUMOR RATES								
OVERALL (a)	9/50 (18%)	6/50 (12%)	5/50 (10%)	3/50 (6%)	3/50 (6%)	2/49 (4%)	6/49 (12%)	6/50 (12%)
POLY-3 RATE (b)	9/47.43	6/48.59	5/41.71	3/45.07	3/48.25	2/46.83	6/46.63	6/48.64
POLY-3 PERCENT (g)	19.0%	12.4%	12.0%	6.7%	6.2%	4.3%	12.9%	12.3%
TERMINAL (d)	9/43 (21%)	6/46 (13%)	4/36 (11%)	2/40 (5%)	3/46 (7%)	2/43 (5%)	6/43 (14%)	6/45 (13%)
FIRST INCIDENCE	729 (T)	729 (T)	654	531	729 (T)	729 (T)	729 (T)	729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.072N	P=0.240N	P=0.304N	P=0.081N	P=0.106	P=0.531N	P=0.210	P=0.232
POLY 3	P=0.060N	P=0.271N	P=0.271N	P=0.072N	P=0.113	P=0.514N	P=0.226	P=0.247
POLY 1.5	P=0.060N	P=0.279N	P=0.262N	P=0.074N	P=0.112	P=0.511N	P=0.227	P=0.246
POLY 6	P=0.060N	P=0.259N	P=0.278N	P=0.069N	P=0.113	P=0.518N	P=0.223	P=0.246
LOGISTIC REGRESSION	P=0.061N	P=0.240N	P=0.284N	P=0.073N	P=0.106	P=0.531N	P=0.210	P=0.232
COCH-ARM / FISHERS	P=0.046N*	P=0.288N	P=0.194N	P=0.061N	P=0.109	P=0.510N	P=0.233	P=0.243
ORDER RESTRICTED	P=0.052N	(e)	(e)	(e)	P=0.156	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
Harderian Gland Carcinoma								
TUMOR RATES								
OVERALL (a)	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	1/50 (2%)	3/50 (6%)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/49 (0%)	1/49 (2%)	1/50 (2%)
POLY-3 PERCENT (g)	1/47.70	3/48.59	1/41.81	2/44.45	1/48.25	0/46.83	1/47.00	1/48.64
TERMINAL (d)	2.1%	6.2%	2.4%	4.5%	2.1%	0.0%	2.1%	2.1%
FIRST INCIDENCE	0/43 (0%)	3/46 (7%)	0/36 (0%)	2/40 (5%)	1/46 (2%)	0/43 (0%)	0/43 (0%)	1/45 (2%)
	657	729 (T)	623	729 (T)	729 (T)		623	729 (T)
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.480	P=0.329	P=0.722	P=0.473	P=0.538	P=0.513N	P=0.750	P=0.757
POLY 1.5	P=0.485	P=0.312	P=0.730	P=0.475	P=0.544	P=0.506N	P=0.755	P=0.759N
POLY 6	P=0.488	P=0.309	P=0.734	P=0.476	P=0.543	P=0.508N	P=0.754	P=0.759N
LOGISTIC REGRESSION	P=0.483	P=0.317	P=0.727	P=0.475	P=0.545	P=0.508N	P=0.755	P=0.759N
COCH-ARM / FISHERS	P=0.506	P=0.305	P=0.753N	P=0.487	P=0.536	(e)	P=0.754N	P=0.757
ORDER RESTRICTED	P=0.526	P=0.309	P=0.753N	P=0.500	P=0.540	P=0.505N	P=0.747	P=0.753N
	P=0.435	(e)	(e)	(e)	P=0.534	(e)	(e)	(e)
Dose								
	0PPM	625 PPM	Males 1250 PPM	2500 PPM	0PPM	625 PPM	Females 1250 PPM	2500 PPM
Harderian Gland Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	10/50 (20%)	9/50 (18%)	6/50 (12%)	5/50 (10%)	4/50 (8%)	2/49 (4%)	7/49 (14%)	7/50 (14%)
POLY-3 PERCENT (g)	10/47.70	9/48.59	6/42.09	5/45.07	4/48.25	2/46.83	7/47.00	7/48.64
TERMINAL (d)	21.0%	18.5%	14.3%	11.1%	8.3%	4.3%	14.9%	14.4%
FIRST INCIDENCE	9/43 (21%)	9/46 (20%)	4/36 (11%)	4/40 (10%)	4/46 (9%)	2/43 (5%)	6/43 (14%)	7/45 (16%)
	657	729 (T)	623	531	729 (T)	729 (T)	623	729 (T)
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.128N	P=0.437N	P=0.334N	P=0.170N	P=0.102	P=0.369N	P=0.229	P=0.249
POLY 1.5	P=0.108N	P=0.482N	P=0.292N	P=0.157N	P=0.107	P=0.351N	P=0.247	P=0.267
POLY 6	P=0.107N	P=0.490N	P=0.282N	P=0.159N	P=0.106	P=0.349N	P=0.246	P=0.266
LOGISTIC REGRESSION	P=0.108N	P=0.470N	P=0.298N	P=0.155N	P=0.108	P=0.356N	P=0.247	P=0.265
COCH-ARM / FISHERS	P=0.105N	P=0.470N	P=0.280N	P=0.152N	P=0.107	P=0.369N	P=0.245	P=0.249
ORDER RESTRICTED	P=0.080N	P=0.500N	P=0.207N	P=0.131N	P=0.103	P=0.349N	P=0.251	P=0.262
	P=0.153N	(e)	(e)	(e)	P=0.137	(e)	(e)	(e)

Liver
 Hemangiosarcoma

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	1/47.66	0/48.59	2/44.45	0/48.25	0/46.83	0/48.64
POLY-3 PERCENT (g)	2.1%	0.0%	4.5%	0.0%	0.0%	0.0%
TERMINAL (d)	0/43 (0%)	0/46 (0%)	2/40 (5%)	0/46 (0%)	0/43 (0%)	0/45 (0%)
FIRST INCIDENCE	668	---	729 (T)	---	---	---

Liver
 Hepatocellular Adenoma

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
OVERALL (a)	7/50 (14%)	14/50 (28%)	13/50 (26%)	3/50 (6%)	4/49 (8%)	6/49 (12%)
POLY-3 RATE (b)	7/47.43	14/48.59	13/42.27	3/48.27	4/46.99	6/46.63
POLY-3 PERCENT (g)	14.8%	28.8%	30.8%	6.2%	8.5%	12.9%
TERMINAL (d)	7/43 (16%)	14/46 (30%)	10/36 (28%)	2/46 (4%)	3/43 (7%)	6/43 (14%)
FIRST INCIDENCE	729 (T)	729 (T)	611	723	688	729 (T)

LIFE TABLE

POLY 3	P=0.005 **	P=0.094	P=0.048 *	P=0.005 **	P=0.015 *	P=0.464	P=0.212
POLY 1.5	P=0.006 **	P=0.077	P=0.058	P=0.005 **	P=0.015 *	P=0.485	P=0.037 *
POLY 6	P=0.006 **	P=0.073	P=0.061	P=0.005 **	P=0.014 *	P=0.487	P=0.227
LOGISTIC REGRESSION	P=0.006 **	P=0.083	P=0.056	P=0.006 **	P=0.015 *	P=0.482	P=0.223
COCH-ARM / FISHERS	P=0.015 *	P=0.094	P=0.056	P=0.006 **	P=0.015 *	P=0.485	P=0.215
ORDER RESTRICTED	P=0.003 **	P=0.070	P=0.105	P=0.010 *	P=0.014 *	P=0.489	P=0.233

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM

Liver
 Hepatocellular Carcinoma

TUMOR RATES	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
OVERALL (a)	4/50 (8%)	8/50 (16%)	14/50 (28%)	2/50 (4%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	4/47.84	8/49.00	14/42.82	2/48.27	0/46.83	0/48.64
POLY-3 PERCENT (g)	8.4%	16.3%	32.7%	4.1%	0.0%	0.0%
TERMINAL (d)	3/43 (7%)	5/46 (11%)	9/36 (25%)	1/46 (2%)	0/43 (0%)	0/45 (0%)
FIRST INCIDENCE	611	657	531	723	---	---

STATISTICAL TESTS

LIFE TABLE	P=0.267	P=0.219	P=0.005 **	P=0.332	P=0.120N	P=0.257N	P=0.257N	P=0.245N
POLY 3	P=0.261	P=0.190	P=0.003 **	P=0.330	P=0.114N	P=0.244N	P=0.245N	P=0.236N
POLY 1.5	P=0.264	P=0.184	P=0.003 **	P=0.330	P=0.114N	P=0.243N	P=0.245N	P=0.236N
POLY 6	P=0.260	P=0.199	P=0.003 **	P=0.332	P=0.113N	P=0.246N	P=0.246N	P=0.236N
LOGISTIC REGRESSION	P=0.302	P=0.178	P=0.005 **	P=0.345	P=0.115N	P=0.246N	P=0.246N	P=0.236N
COCH-ARM / FISHERS	P=0.348	P=0.178	P=0.009 **	P=0.370	P=0.115N	P=0.253N	P=0.253N	P=0.247N
ORDER RESTRICTED	P=0.043 *	(e)	(e)	(e)	P=0.029N*	(e)	(e)	(e)

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM

Liver
 Hepatocellular Carcinoma or Hepatocellular Adenoma

TUMOR RATES	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
OVERALL (a)	10/50 (20%)	22/50 (44%)	22/50 (44%)	4/50 (8%)	4/49 (8%)	6/49 (12%)
POLY-3 RATE (b)	10/47.84	22/49.00	22/43.23	4/48.27	4/46.99	6/46.63
POLY-3 PERCENT (g)	20.9%	44.9%	50.9%	8.3%	8.5%	12.9%
TERMINAL (d)	9/43 (21%)	19/46 (41%)	16/36 (44%)	3/46 (7%)	3/43 (7%)	6/43 (14%)
FIRST INCIDENCE	611	657	531	723	688	729 (T)

STATISTICAL TESTS

LIFE TABLE	P=0.010 *	P=0.020 **	P=0.003 **	P=0.005 **	P=0.030 *	P=0.0604	P=0.328
POLY 3	P=0.007 **	P=0.009 **	P=0.002 **	P=0.003 **	P=0.030 *	P=0.0628	P=0.348
POLY 1.5	P=0.007 **	P=0.008 **	P=0.002 **	P=0.003 **	P=0.030 *	P=0.0630	P=0.350
POLY 6	P=0.007 **	P=0.011 *	P=0.002 **	P=0.003 **	P=0.031 *	P=0.0624	P=0.345
LOGISTIC REGRESSION	P=0.010 *	P=0.010 *	P=0.003 **	P=0.004 **	P=0.030 *	P=0.0628	P=0.333
COCH-ARM / FISHERS	P=0.024 *	P=0.009 **	P=0.009 **	P=0.009 **	P=0.029 *	P=0.0631	P=0.357
ORDER RESTRICTED	P=0.002 **	(e)	(e)	(e)	P=0.048 *	(e)	(e)

Liver
 Hepatocellular Carcinoma, Hepatocellular Adenoma,
 or Hepatoblastoma

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	10/50 (20%)	22/50 (44%)	22/50 (44%)	22/50 (44%)	4/50 (8%)	4/49 (8%)	6/49 (12%)	10/50 (20%)
POLY-3 RATE (b)	10/47.84	22/49.00	22/43.23	22/44.86	4/48.27	4/46.99	6/46.63	10/48.88
POLY-3 PERCENT (g)	20.9%	44.9%	50.9%	49.0%	8.3%	8.5%	12.9%	20.5%
TERMINAL (d)	9/43 (21%)	19/46 (41%)	16/36 (44%)	20/40 (50%)	3/46 (7%)	3/43 (7%)	6/43 (14%)	9/45 (20%)
FIRST INCIDENCE	611	657	531	656	723	688	729 (T)	664
STATISTICAL TESTS								
LIFE TABLE	P=0.010 *	P=0.020 *	P=0.003 **	P=0.005 **	P=0.030 *	P=0.604	P=0.328	P=0.074
POLY 3	P=0.007 **	P=0.002 **	P=0.002 **	P=0.003 **	P=0.030 *	P=0.628	P=0.348	P=0.077
POLY 1.5	P=0.007 **	P=0.008 **	P=0.002 **	P=0.003 **	P=0.030 *	P=0.630	P=0.350	P=0.076
POLY 6	P=0.007 **	P=0.011 *	P=0.002 **	P=0.003 **	P=0.031 *	P=0.624	P=0.345	P=0.077
LOGISTIC REGRESSION	P=0.010 *	P=0.010 *	P=0.003 **	P=0.004 **	P=0.030 *	P=0.628	P=0.333	P=0.077
COCH-ARM / FISHERS	P=0.024 **	P=0.009 **	P=0.009 **	P=0.009 **	P=0.029 *	P=0.631	P=0.357	P=0.074
ORDER RESTRICTED	P=0.002 **	(e)	(e)	(e)	P=0.048 *	(e)	(e)	(e)

Lung
 Alveolar/Bronchiolar Adenoma

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	11/50 (22%)	7/50 (14%)	6/50 (12%)	5/50 (10%)	4/50 (8%)	2/49 (4%)	0/49 (0%)	1/50 (2%)
POLY-3 RATE (b)	11/47.93	7/48.59	6/41.44	5/44.45	4/48.25	2/47.22	0/46.63	1/48.64
POLY-3 PERCENT (g)	23.0%	14.4%	14.5%	11.3%	8.3%	4.2%	0.0%	2.1%
TERMINAL (d)	9/43 (21%)	7/46 (15%)	6/36 (17%)	5/40 (13%)	4/46 (9%)	1/43 (2%)	0/43 (0%)	1/45 (2%)
FIRST INCIDENCE	657	729 (T)	729 (T)	729 (T)	729 (T)	620	---	729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.114N	P=0.180N	P=0.255N	P=0.117N	P=0.090N	P=0.366N	P=0.072N	P=0.187N
POLY 3	P=0.103N	P=0.208N	P=0.229N	P=0.113N	P=0.085N	P=0.348N	P=0.065N	P=0.177N
POLY 1.5	P=0.099N	P=0.212N	P=0.214N	P=0.111N	P=0.085N	P=0.347N	P=0.065N	P=0.177N
POLY 6	P=0.108N	P=0.201N	P=0.245N	P=0.115N	P=0.085N	P=0.349N	P=0.066N	P=0.177N
LOGISTIC REGRESSION	P=0.104N	P=0.208N	P=0.224N	P=0.108N	P=0.086N	P=0.345N	(e)	P=0.187N
COCH-ARM / FISHERS	P=0.072N	P=0.218N	P=0.143N	P=0.086N	P=0.086N	P=0.349N	P=0.061N	P=0.181N
ORDER RESTRICTED	P=0.093N	(e)	(e)	(e)	P=0.038N*	(e)	(e)	(e)

STATISTICAL TESTS

LIFE TABLE

POLY 3

POLY 1.5

POLY 6

LOGISTIC REGRESSION

COCH-ARM / FISHERS

ORDER RESTRICTED

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

Lung
 Alveolar/Bronchiolar Carcinoma

TUMOR RATES	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	6/50 (12%)	3/50 (6%)	5/50 (10%)	5/50 (10%)	0/50 (0%)	2/49 (4%)	0/49 (0%)	0/50 (0%)
POLY-3 RATE (b)	6/47.43	3/48.59	5/41.71	5/44.45	0/48.25	2/47.16	0/46.63	0/48.64
POLY-3 PERCENT (g)	12.7%	6.2%	12.0%	11.3%	0.0%	4.2%	0.0%	0.0%
TERMINAL (d)	6/43 (14%)	3/46 (7%)	4/36 (11%)	5/40 (13%)	0/46 (0%)	1/43 (2%)	0/43 (0%)	0/45 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	654	729 (T)	---	639	---	---

STATISTICAL TESTS

LIFE TABLE	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
POLY 3	P=0.502	P=0.210N	P=0.621N	P=0.551N	P=0.406N	P=0.228	(e)	(e)
POLY 1.5	P=0.521	P=0.231N	P=0.589N	P=0.545N	P=0.404N	P=0.232	(e)	(e)
POLY 6	P=0.525	P=0.236N	P=0.579N	P=0.545N	P=0.404N	P=0.233	(e)	(e)
LOGISTIC REGRESSION	P=0.516	P=0.223N	P=0.596N	P=0.544N	P=0.405N	P=0.231	(e)	(e)
COCH-ARM / FISHERS	P=0.516	P=0.210N	P=0.601N	P=0.551N	P=0.407N	P=0.234	(e)	(e)
ORDER RESTRICTED	P=0.549N	P=0.243N	P=0.500N	P=0.500N	P=0.405N	P=0.242	(e)	(e)
	P=0.502N	(e)	(e)	(e)	P=0.241N	(e)	(e)	(e)

Lung
 Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma

TUMOR RATES	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	14/50 (28%)	9/50 (18%)	10/50 (20%)	9/50 (18%)	4/50 (8%)	4/49 (8%)	0/49 (0%)	1/50 (2%)
POLY-3 RATE (b)	14/47.93	9/48.59	10/41.71	9/44.45	4/48.25	4/47.54	0/46.63	1/48.64
POLY-3 PERCENT (g)	29.2%	18.5%	24.0%	20.3%	8.3%	8.4%	0.0%	2.1%
TERMINAL (d)	12/43 (28%)	9/46 (20%)	9/36 (25%)	9/40 (23%)	4/46 (9%)	2/43 (5%)	0/43 (0%)	1/45 (2%)
FIRST INCIDENCE	657	729 (T)	654	729 (T)	729 (T)	620	---	729 (T)

STATISTICAL TESTS

LIFE TABLE	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
POLY 3	P=0.287N	P=0.133N	P=0.420N	P=0.227N	P=0.064N	P=0.609	P=0.072N	P=0.187N
POLY 1.5	P=0.264N	P=0.160N	P=0.376N	P=0.226N	P=0.059N	P=0.635	P=0.065N	P=0.177N
POLY 6	P=0.256N	P=0.165N	P=0.355N	P=0.223N	P=0.059N	P=0.634	P=0.065N	P=0.177N
LOGISTIC REGRESSION	P=0.275N	P=0.154N	P=0.395N	P=0.231N	P=0.059N	P=0.635	P=0.066N	P=0.177N
COCH-ARM / FISHERS	P=0.264N	P=0.158N	P=0.373N	P=0.216N	P=0.060N	P=0.636	(e)	P=0.187N
ORDER RESTRICTED	P=0.189N	P=0.171N	P=0.241N	P=0.171N	P=0.060N	P=0.631	P=0.061N	P=0.181N
	P=0.242N	(e)	(e)	(e)	P=0.063N	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
Mammary Gland Carcinoma								
TUMOR RATES								
OVERALL (a)	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/49 (0%)	0/49 (0%)	2/50 (4%)
POLY-3 PERCENT (g)	0/47.43	0/48.59	0/41.44	0/44.45	1/48.25	0/46.83	0/46.63	2/48.65
TERMINAL (d)	0.0%	0.0%	0.0%	0.0%	2.1%	0.0%	0.0%	4.1%
FIRST INCIDENCE	0/43 (0%)	0/46 (0%)	0/36 (0%)	0/40 (0%)	1/46 (2%)	0/43 (0%)	0/43 (0%)	1/45 (2%)
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	(e)	(e)	(e)	(e)	P=0.249	P=0.513N	P=0.513N	P=0.495
POLY 1.5	(e)	(e)	(e)	(e)	P=0.249	P=0.506N	P=0.507N	P=0.503
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.249	P=0.505N	P=0.507N	P=0.502
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.250	P=0.508N	P=0.508N	P=0.502
ORDER RESTRICTED	(e)	(e)	(e)	(e)	P=0.251	P=0.505N	P=0.505N	P=0.500
Dose	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
Skin Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES								
OVERALL (a)	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	4/49 (8%)	1/50 (2%)
POLY-3 PERCENT (g)	1/47.43	1/48.59	0/41.44	0/44.45	0/48.25	0/46.83	4/46.77	1/48.67
TERMINAL (d)	2.1%	2.1%	0.0%	0.0%	0.0%	0.0%	8.6%	2.1%
FIRST INCIDENCE	1/43 (2%)	1/46 (2%)	0/36 (0%)	0/40 (0%)	0/46 (0%)	0/43 (0%)	3/43 (7%)	0/45 (0%)
STATISTICAL TESTS								
LIFE TABLE								
POLY 3	P=0.256N	P=0.747N	P=0.535N	P=0.514N	P=0.250	(e)	P=0.058	P=0.500
POLY 1.5	P=0.249N	P=0.755N	P=0.527N	P=0.513N	P=0.252	(e)	P=0.057	P=0.502
LOGISTIC REGRESSION	P=0.247N	P=0.757N	P=0.523N	P=0.513N	P=0.250	(e)	P=0.057	P=0.501
COCH-ARM / FISHERS	P=0.250N	P=0.751N	P=0.530N	P=0.513N	P=0.253	(e)	P=0.056	P=0.502
ORDER RESTRICTED	P=0.256N	P=0.747N	P=0.500N	P=0.500N	P=0.249	(e)	P=0.059	P=0.500
Dose	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

Skin
 Fibrosarcoma

TUMOR RATES	Males				Females			
	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	3/49 (6%)	1/50 (2%)
POLY-3 RATE (b)	0/47.43	0/48.59	0/41.44	0/44.45	0/48.25	0/46.83	3/46.77	1/48.67
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	6.4%	2.1%
TERMINAL (d)	0/43 (0%)	0/46 (0%)	0/36 (0%)	0/40 (0%)	0/46 (0%)	0/43 (0%)	2/43 (5%)	0/45 (0%)
FIRST INCIDENCE	---	---	---	---	---	---	693	720

STATISTICAL TESTS

LIFE TABLE	(e)	(e)	(e)	(e)	(e)	(e)	(e)	(e)
POLY 3	(e)	(e)	(e)	(e)	P=0.253	(e)	P=0.113	P=0.500
POLY 1.5	(e)	(e)	(e)	(e)	P=0.254	(e)	P=0.113	P=0.502
POLY 6	(e)	(e)	(e)	(e)	P=0.253	(e)	P=0.113	P=0.501
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.255	(e)	P=0.113	P=0.502
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.250	(e)	P=0.116	P=0.500
ORDER RESTRICTED	(e)	(e)	(e)	(e)	P=0.249	(e)	P=0.117	P=0.500

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

Skin
 Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma

TUMOR RATES	Males				Females			
	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	4/49 (8%)	1/50 (2%)
POLY-3 RATE (b)	1/47.43	1/48.59	0/41.44	0/44.45	0/48.25	0/46.83	4/46.77	1/48.67
POLY-3 PERCENT (g)	2.1%	2.1%	0.0%	0.0%	0.0%	0.0%	8.6%	2.1%
TERMINAL (d)	1/43 (2%)	1/46 (2%)	0/36 (0%)	0/40 (0%)	0/46 (0%)	0/43 (0%)	3/43 (7%)	0/45 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	---	---	---	---	693	720

STATISTICAL TESTS

LIFE TABLE	P=0.256N	P=0.747N	P=0.535N	P=0.514N	P=0.250	(e)	P=0.058	P=0.500
POLY 3	P=0.249N	P=0.755N	P=0.527N	P=0.513N	P=0.252	(e)	P=0.057	P=0.502
POLY 1.5	P=0.247N	P=0.757N	P=0.523N	P=0.513N	P=0.250	(e)	P=0.057	P=0.501
POLY 6	P=0.250N	P=0.751N	P=0.530N	P=0.513N	P=0.253	(e)	P=0.056	P=0.502
LOGISTIC REGRESSION	P=0.256N	P=0.747N	P=0.530N	P=0.513N	P=0.249	(e)	P=0.059	P=0.500
COCH-ARM / FISHERS	P=0.236N	P=0.753N	P=0.500N	P=0.500N	P=0.248	(e)	P=0.056	P=0.500
ORDER RESTRICTED	P=0.265N	(e)	(e)	(e)	P=0.074	(e)	(e)	(e)

Stomach, Forestomach
 Squamous Cell Papilloma

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
TUMOR RATES								
OVERALL (a)	#	#	#	#	#	#	#	#
POLY-3 RATE (b)	0/50 (0%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	1/49 (2%)	0/49 (0%)	2/50 (4%)
POLY-3 PERCENT (g)	0/47.43	1/48.59	0/41.44	1/44.45	2/48.25	1/46.83	0/46.63	2/49.07
TERMINAL (d)	0.0%	2.1%	0.0%	2.3%	4.2%	2.1%	0.0%	4.1%
FIRST INCIDENCE	0/43 (0%)	1/46 (2%)	0/36 (0%)	1/40 (3%)	2/46 (4%)	1/43 (2%)	0/43 (0%)	1/45 (2%)
STATISTICAL TESTS								
LIFE TABLE	P=0.381	P=0.513	(e)	P=0.486	P=0.589	P=0.524N	P=0.253N	P=0.689
POLY 3	P=0.385	P=0.505	(e)	P=0.487	P=0.596	P=0.510N	P=0.245N	P=0.687N
POLY 1.5	P=0.385	P=0.503	(e)	P=0.487	P=0.594	P=0.509N	P=0.245N	P=0.689N
LOGISTIC REGRESSION	(e)	P=0.508	(e)	P=0.487	P=0.598	P=0.514N	P=0.246N	P=0.686N
COCH-ARM / FISHERS	P=0.405	P=0.513	(e)	P=0.486	P=0.589	P=0.524N	(e)	P=0.676
ORDER RESTRICTED	P=0.239	P=0.500	(e)	P=0.500	P=0.592	P=0.508N	P=0.253N	P=0.691N
Dose								
	0PPM	625 PPM	Males 1250 PPM	2500 PPM	0PPM	625 PPM	Females 1250 PPM	2500 PPM

Thyroid Gland: Follicular Cell
 Adenoma

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
TUMOR RATES								
OVERALL (a)	0/50 (0%)	1/50 (2%)	0/50 (0%)	7/50 (14%)	1/49 (2%)	0/48 (0%)	0/48 (0%)	1/50 (2%)
POLY-3 RATE (b)	0/47.43	1/48.86	0/41.44	7/44.45	1/47.25	0/45.83	0/45.89	1/48.64
POLY-3 PERCENT (g)	0.0%	2.1%	0.0%	15.8%	2.1%	0.0%	0.0%	2.1%
TERMINAL (d)	0/43 (0%)	1/46 (0%)	0/36 (0%)	7/40 (18%)	1/45 (2%)	0/42 (0%)	0/43 (0%)	1/45 (2%)
FIRST INCIDENCE	---	657	---	729 (T)	729 (T)	---	---	729 (T)
STATISTICAL TESTS								
LIFE TABLE	P<0.001 **	P=0.508	(e)	P=0.007 **	P=0.597	P=0.514N	P=0.509N	P=0.761
POLY 3	P<0.001 **	P=0.506	(e)	P=0.006 **	P=0.602	P=0.506N	P=0.506N	P=0.754N
POLY 1.5	P<0.001 **	P=0.503	(e)	P=0.006 **	P=0.601	P=0.505N	P=0.506N	P=0.754N
LOGISTIC REGRESSION	P<0.001 **	P=0.510	(e)	P=0.006 **	P=0.603	P=0.508N	P=0.506N	P=0.754N
COCH-ARM / FISHERS	P<0.001 **	P=0.496	(e)	P=0.007 **	P=0.597	(e)	(e)	P=0.761
ORDER RESTRICTED	P<0.001 **	P=0.500	(e)	P=0.006 **	P=0.599	P=0.505N	P=0.505N	P=0.747N

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
Uterus						
Polyp Stromal						

TUMOR RATES	#	#	#	#	#	#
OVERALL (a)						
POLY-3 RATE (b)						
POLY-3 PERCENT (g)						
TERMINAL (d)						
FIRST INCIDENCE						

STATISTICAL TESTS						

LIFE TABLE						
POLY 3						
POLY 1.5						
POLY 6						
LOGISTIC REGRESSION						
COCH-ARM / FISHERS						
ORDER RESTRICTED						

Dose	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM
			Males			Females
			1250 PPM	2500 PPM		1250 PPM
						2500 PPM
Uterus						
Sarcoma Stromal or Polyp Stromal						

TUMOR RATES	#	#	#	#	#	#
OVERALL (a)						
POLY-3 RATE (b)						
POLY-3 PERCENT (g)						
TERMINAL (d)						
FIRST INCIDENCE						

STATISTICAL TESTS						

LIFE TABLE						
POLY 3						
POLY 1.5						
POLY 6						
LOGISTIC REGRESSION						
COCH-ARM / FISHERS						
ORDER RESTRICTED						

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM

All Organs
 Hemangiosarcoma

TUMOR RATES	#		#		#	
	OVERALL (a)	POLY-3 RATE (b)	OVERALL (a)	POLY-3 RATE (b)	OVERALL (a)	POLY-3 RATE (b)
2/50 (4%)	2/47.66	1/50 (2%)	1/41.44	2/50 (4%)	2/50 (4%)	2/48.86
4.2%	1/43 (2%)	2.1%	2.4%	4.5%	4.1%	1/46 (2%)
668	726	0/46 (0%)	729 (T)	2/40 (5%)	533	0/43 (0%)
STATISTICAL TESTS						
LIFE TABLE	P=0.512	P=0.477N	P=0.563N	P=0.668	P=0.089N	P=0.676
POLY 3	P=0.522	P=0.493N	P=0.548N	P=0.668	P=0.087N	P=0.682
POLY 1.5	P=0.525	P=0.496N	P=0.542N	P=0.669	P=0.087N	P=0.684
POLY 6	P=0.518	P=0.488N	P=0.555N	P=0.668	P=0.088N	P=0.679
LOGISTIC REGRESSION	P=0.526	P=0.500N	P=0.535N	P=0.677	P=0.081N	P=0.696
COCH-ARM / FISHERS	P=0.556	P=0.500N	P=0.500N	P=0.691N	P=0.086N	P=0.684
ORDER RESTRICTED	P=0.526	(e)	(e)	(e)	P=0.111N	(e)

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM

All Organs
 Hemangiosarcoma or Hemangioma

TUMOR RATES	#		#		#	
	OVERALL (a)	POLY-3 RATE (b)	OVERALL (a)	POLY-3 RATE (b)	OVERALL (a)	POLY-3 RATE (b)
2/50 (4%)	2/47.66	1/50 (2%)	1/41.44	3/50 (6%)	2/50 (4%)	2/49 (4%)
4.2%	1/43 (2%)	2.1%	2.4%	6.8%	4.1%	4.2%
668	726	0/46 (0%)	729 (T)	3/40 (8%)	533	0/43 (0%)
STATISTICAL TESTS						
LIFE TABLE	P=0.285	P=0.477N	P=0.563N	P=0.468	P=0.089N	P=0.676
POLY 3	P=0.294	P=0.493N	P=0.548N	P=0.468	P=0.087N	P=0.682
POLY 1.5	P=0.297	P=0.496N	P=0.542N	P=0.469	P=0.087N	P=0.684
POLY 6	P=0.290	P=0.488N	P=0.555N	P=0.467	P=0.088N	P=0.679
LOGISTIC REGRESSION	P=0.295	P=0.500N	P=0.535N	P=0.474	P=0.081N	P=0.696
COCH-ARM / FISHERS	P=0.324	P=0.500N	P=0.500N	P=0.500	P=0.086N	P=0.684
ORDER RESTRICTED	P=0.268	(e)	(e)	(e)	P=0.111N	(e)

All Organs
 Malignant Lymphoma: Histiocytic, Lymphocytic, Mixed,
 NOS, or Undifferentiated Cell Type

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
TUMOR RATES						
OVERALL (a)	2/50 (4%)	3/50 (6%)	0/50 (0%)	1/50 (2%)	6/49 (12%)	8/50 (16%)
POLY-3 RATE (b)	2/47.43	3/48.59	0/41.44	1/44.45	6/48.25	8/48.64
POLY-3 PERCENT (g)	4.2%	6.2%	0.0%	2.3%	12.4%	16.5%
TERMINAL (d)	2/43 (5%)	3/46 (7%)	0/36 (0%)	1/40 (3%)	6/46 (13%)	8/45 (18%)
FIRST INCIDENCE	729 (T)	729 (T)	---	729 (T)	729 (T)	729 (T)
STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.277N	P=0.531	P=0.278N	P=0.525N	P=0.389	P=0.338
POLY 1.5	P=0.266N	P=0.511	P=0.269N	P=0.523N	P=0.403	P=0.575
LOGISTIC REGRESSION	P=0.264N	P=0.506	P=0.264N	P=0.523N	P=0.402	P=0.600
COCH-ARM / FISHERS	P=0.277N	P=0.519	P=0.272N	P=0.522N	P=0.403	P=0.599
ORDER RESTRICTED	P=0.242N	P=0.531	(e)	P=0.525N	P=0.404	P=0.598
	P=0.217N	P=0.500	P=0.247N	P=0.500N	P=0.396	P=0.606
		(e)	(e)	(e)	P=0.456	(e)
Dose						
	0PPM	625 PPM	Males 1250 PPM	2500 PPM	0PPM	Females 1250 PPM
						2500 PPM

All Organs
 Benign Tumors

Dose	Males			Females		
	0PPM	625 PPM	2500 PPM	0PPM	625 PPM	2500 PPM
TUMOR RATES						
OVERALL (a)	23/50 (46%)	25/50 (50%)	24/50 (48%)	30/50 (60%)	13/50 (26%)	12/49 (24%)
POLY-3 RATE (b)	23/48.07	25/48.86	24/42.55	30/45.48	13/48.27	12/47.41
POLY-3 PERCENT (g)	47.9%	51.2%	56.4%	66.0%	26.9%	25.3%
TERMINAL (d)	20/43 (47%)	24/46 (52%)	20/36 (56%)	27/40 (68%)	12/46 (26%)	9/43 (21%)
FIRST INCIDENCE	657	657	611	531	723	620
STATISTICAL TESTS						
LIFE TABLE						
POLY 3	P=0.030 *	P=0.546	P=0.213	P=0.063	P=0.054	P=0.421
POLY 1.5	P=0.037 *	P=0.451	P=0.273	P=0.057	P=0.058	P=0.521N
LOGISTIC REGRESSION	P=0.038 *	P=0.438	P=0.295	P=0.057	P=0.055	P=0.521N
COCH-ARM / FISHERS	P=0.035 *	P=0.471	P=0.259	P=0.058	P=0.060	P=0.467
ORDER RESTRICTED	P=0.098	P=0.454	P=0.260	P=0.057	P=0.054	P=0.532N
	P=0.053	P=0.421	P=0.500	P=0.115	P=0.051	P=0.475
		(e)	(e)	(e)	P=0.090	(e)

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

All Organs
 Malignant Tumors

TUMOR RATES	#		#		#		#	
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	20/50 (40%)	16/50 (32%)	21/50 (42%)	14/50 (28%)	12/50 (24%)	12/49 (24%)	15/49 (31%)	14/50 (28%)
POLY-3 RATE (b)	20/48.77	16/49.00	21/43.75	14/45.00	12/49.71	12/47.74	15/47.45	14/49.36
POLY-3 PERCENT (g)	41.0%	32.7%	48.0%	31.1%	24.1%	25.1%	31.6%	28.4%
TERMINAL (d)	15/43 (35%)	13/46 (28%)	14/36 (39%)	11/40 (28%)	9/46 (20%)	8/43 (19%)	11/43 (26%)	10/45 (22%)
FIRST INCIDENCE	611	657	512	656	402	620	623	604
STATISTICAL TESTS								
LIFE TABLE	P=0.330N	P=0.213N	P=0.263	P=0.227N	P=0.334	P=0.523	P=0.276	P=0.400
POLY 3	P=0.291N	P=0.260N	P=0.322	P=0.218N	P=0.325	P=0.548	P=0.277	P=0.402
POLY 1.5	P=0.280N	P=0.263N	P=0.334	P=0.211N	P=0.326	P=0.554	P=0.281	P=0.405
POLY 6	P=0.306N	P=0.255N	P=0.314	P=0.227N	P=0.326	P=0.543	P=0.276	P=0.402
LOGISTIC REGRESSION	P=0.247N	P=0.260N	P=0.364	P=0.189N	P=0.317	P=0.585	P=0.322	P=0.375
COCH-ARM / FISHERS	P=0.178N	P=0.266N	P=0.500	P=0.146N	P=0.328	P=0.570	P=0.304	P=0.410
ORDER RESTRICTED	P=0.256N	(e)	(e)	(e)	P=0.407	(e)	(e)	(e)

Dose	Males				Females			
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM

All Organs
 Malignant and Benign Tumors

TUMOR RATES	#		#		#		#	
	0PPM	625 PPM	1250 PPM	2500 PPM	0PPM	625 PPM	1250 PPM	2500 PPM
OVERALL (a)	32/50 (64%)	34/50 (68%)	34/50 (68%)	38/50 (76%)	23/50 (46%)	20/49 (41%)	23/49 (47%)	29/50 (58%)
POLY-3 RATE (b)	32/48.77	34/49.00	34/44.17	38/45.61	23/49.71	20/47.74	23/47.45	29/49.36
POLY-3 PERCENT (g)	65.6%	69.4%	77.0%	83.3%	46.3%	41.9%	48.5%	58.8%
TERMINAL (d)	27/43 (63%)	31/46 (67%)	26/36 (72%)	34/40 (85%)	20/46 (44%)	16/43 (37%)	19/43 (44%)	25/45 (56%)
FIRST INCIDENCE	611	657	512	531	402	620	623	604
STATISTICAL TESTS								
LIFE TABLE	P=0.031 *	P=0.562N	P=0.112	P=0.069	P=0.096	P=0.454N	P=0.466	P=0.158
POLY 3	P=0.023 *	P=0.428	P=0.164	P=0.040 *	P=0.078	P=0.409N	P=0.494	P=0.148
POLY 1.5	P=0.025 *	P=0.423	P=0.172	P=0.042 *	P=0.079	P=0.399N	P=0.501	P=0.152
POLY 6	P=0.020 *	P=0.438	P=0.165	P=0.036 *	P=0.079	P=0.416N	P=0.492	P=0.147
LOGISTIC REGRESSION	P=0.027 *	P=0.441	P=0.162	P=0.049 *	P=0.083	P=0.369N	P=0.543	P=0.150
COCH-ARM / FISHERS	P=0.117	P=0.417	P=0.417	P=0.138	P=0.082	P=0.376N	P=0.543	P=0.158
ORDER RESTRICTED	P=0.034 *	(e)	(e)	(e)	P=0.107	(e)	(e)	(e)

(a) Number of tumor-bearing animals / number of animals examined at site.
 (b) Number of tumor-bearing animals / Poly-3 number
 (d) Observed incidence at terminal kill.

(f) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. Logistic regression is an alternative method for analyzing the incidence of non-fatal tumors. The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates and for all tests a negative trend is indicated by N

(e) Value of Statistic cannot be computed.

(g) Poly-3 adjusted lifetime tumor incidence.

(I) Interim sacrifice

(T) Terminal sacrifice

Tumor rates based on number of animals necropsied.

* To the right of any statistical result, indicates significance at ($P \leq 0.05$).

** To the right of any statistical result, indicates significance at ($P \leq 0.01$).

NTP Experiment-Test: 92012-06
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
2-METHYLMIDAZOLE

Report: PEIRPT18
Date: 03/14/03
Time: 11:38:08

FINAL#1: REVISION#1

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25022 Accidentally Killed
25019 Moribund Sacrifice
25026 Other
25023 Missing
25020 Natural Death
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

- a Number of animals examined microscopically at site and number of animals with lesion
- b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLIMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Disposition	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	2	3	4	4
Natural Death	2	3	2	1
Survivors				
Terminal Sacrifice	46	42	42	45
Moribund Sacrifice				
Natural Death		1	1	
Other		1	1	
Animals Examined Microscopically	50	49	49	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(50)	(48)	(48)	(50)
Edema	2 [2.0]		2 [2.0]	2 [2.0]
Intestine Small, Jejunum	(50)	(46)	(48)	(49)
Hyperplasia, Lymphoid		1 [3.0]		1 [3.0]
Peyer's Patch, Infiltration Cellular,				
Polymorphonuclear	(47)	(49)	(47)	1 [3.0]
Intestine Small, Ileum	1 [3.0]			(48)
Hyperplasia, Lymphoid				
Peyer's Patch, Infiltration Cellular,				
Polymorphonuclear	(50)	(49)	(49)	1 [3.0]
Liver				
Angiectasis	1 [3.0]	4	1	1
Basophilic Focus			1	4
Clear Cell Focus	1		1	
Eosinophilic Focus			1	
Hematopoietic Cell Proliferation	3 [3.0]	3 [2.0]	5 [1.8]	3 [3.0]
Hemorrhage		1 [3.0]		
Hepatodiaphragmatic Nodule			1	2
Hyperplasia, Lymphoid	3 [2.0]	3 [2.3]		6 [2.2]
Infarct	1 [3.0]	1 [3.0]		
Infiltration Cellular, Mixed Cell	13 [1.7]	5 [1.6]	12 [1.3]	10 [1.1]
Mixed Cell Focus	4	1	3	
Necrosis, Focal	5 [1.6]	2 [1.0]	3 [2.7]	4 [3.3]
Tension Lipidosis			2	
Bile Duct, Hyperplasia		1 [3.0]		
Hepatocyte, Vacuolization			1 [3.0]	
Kupffer Cell, Pigmentation		2 [4.0]		

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADE(S)^b
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

ALIMENTARY SYSTEM - CONT

Mesentery	(3)	(4)	(6)	(6)
Inflammation, Chronic	1 [4.0]	1 [3.0]	1 [3.0]	1 [3.0]
Fat, Angiectasis	2 [3.0]	3 [2.3]	6 [1.8]	6 [2.8]
Fat, Necrosis	(50)	(49)	(48)	(50)
Pancreas	1 [4.0]	1 [3.0]	1 [3.0]	2 [3.0]
Atrophy	1 [3.0]	1 [3.0]	2 [3.0]	1 [3.0]
Cyst	1 [3.0]	1 [3.0]	2 [3.0]	1 [1.0]
Acinus, Cytoplasmic Alteration	(50)	(49)	(49)	(49)
Salivary Glands	2 [2.0]	5 [2.6]	3 [2.0]	2 [2.0]
Atrophy	(50)	(49)	(49)	(50)
Hyperplasia, Lymphoid	(50)	(49)	(49)	5
Stomach, Forestomach	1	1 [2.0]	2 [2.5]	1 [1.0]
Diverticulum	1 [2.0]	1 [2.0]	4 [2.5]	
Inflammation, Chronic Active	1 [2.0]	1 [2.0]	2 [2.5]	
Epithelium, Hyperplasia	1 [2.0]		4 [2.5]	

CARDIOVASCULAR SYSTEM

Heart	(50)	(49)	(49)	(50)
Cardiomyopathy				2 [1.0]
Thrombosis			1 [2.0]	1 [3.0]
Myocardium, Necrosis				

ENDOCRINE SYSTEM

Adrenal Cortex	(50)	(49)	(49)	(50)
Accessory Adrenal Cortical Nodule	7 [3.0]	5 [3.0]	4 [3.0]	6 [3.0]
Hyperplasia, Focal	3 [2.0]	(49)	2 [1.5]	
Capsule, Hyperplasia	(50)	(49)	(49)	(50)
Adrenal Medulla	(50)	(48)	(48)	(50)
Hyperplasia	1 [2.0]	1 [2.0]	1 [2.0]	1 [2.0]
Islets, Pancreatic	(48)	(46)	(45)	(48)
Hyperplasia	1 [2.0]	1 [3.0]	1 [3.0]	1 [3.0]
Parathyroid Gland	(48)	(47)	(49)	(49)
Cyst	(50)	3 [2.3]	1 [2.0]	1 [2.0]
Pituitary Gland	1 [3.0]	3 [3.0]	1 [2.0]	2 [2.0]
Pars Distalis, Angiectasis	1 [3.0]	2 [1.5]	1 [1.0]	
Pars Distalis, Cyst	(49)	(48)	(48)	(50)
Pars Distalis, Hyperplasia, Focal	15 [2.1]	14 [1.8]	12 [1.7]	9 [1.2]
Thyroid Gland				
Degeneration, Cystic				

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES(b)
 2-METHYLLIMITAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

ENDOCRINE SYSTEM - CONT	0PPM	625 PPM	1250 PPM	2500 PPM
Follicle, Cyst	1 [1.0]	1 [2.0]	1 [3.0]	1 [3.0]
Follicular Cell, Hyperplasia	6 [1.2]	3 [1.0]	1 [1.0]	9 [1.6]
Follicular Cell, Hypertrophy			23 [1.1]	46 [1.7]

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Clitoral Gland	(50)	(48)	(48)	(50)
Inflammation, Chronic				1 [4.0]
Ovary	(50)	(49)	(49)	(48)
Angiectasis	12 [2.3]	7 [2.4]	8 [2.8]	8 [2.6]
Cyst	10 [3.0]	11 [3.0]	15 [3.0]	10 [3.0]
Inflammation, Chronic	3 [4.0]		2 [3.0]	
Thrombosis				1 [4.0]
Corpus luteum, Hyperplasia	(50)	(49)	(49)	(50)
Uterus				1 [3.0]
Angiectasis	3 [3.3]	2 [2.5]	2 [3.5]	6 [2.2]
Inflammation, Chronic	6 [2.8]	2 [2.0]	9 [2.7]	4 [3.3]
Metaplasia, Squamous	5 [3.0]		5 [3.0]	1 [3.0]
Cervix, Cyst Epithelial Inclusion		1		
Endometrium, Fibrosis				1 [3.0]
Endometrium, Hyperplasia, Cystic	48 [3.0]	47 [3.1]	46 [3.3]	45 [3.4]

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(49)	(48)	(50)
Hyperplasia	10 [2.7]	5 [2.0]	13 [3.2]	16 [2.4]
Lymph Node	(12)	(6)	(8)	(9)
Bronchial, Hyperplasia, Lymphoid	1 [3.0]			2 [2.5]
Iliac, Ectasia				
Iliac, Hematopoietic Cell Proliferation	2 [2.5]	1 [2.0]	1 [3.0]	
Iliac, Hyperplasia, Lymphoid	5 [2.2]	3 [3.0]	4 [3.0]	2 [4.0]
Iliac, Pigmentation		1 [2.0]		
Inguinal, Hyperplasia, Lymphoid			1 [2.0]	
Lumbar, Hyperplasia, Lymphoid	1 [2.0]	1 [2.0]	2 [3.0]	2 [3.0]
Lumbar, Pigmentation		1 [2.0]		
Mediastinal, Hyperplasia, Lymphoid	1 [4.0]	1 [3.0]		

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES(b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM - CONT

Pancreatic, Hyperplasia, Lymphoid	1 [3.0]		1 [2.0]	1 [2.0]
Renal, Hematopoietic Cell Proliferation	3 [2.7]	1 [4.0]	1 [2.0]	2 [2.5]
Renal, Hyperplasia, Lymphoid	(48)	(48)	(46)	(48)
Lymph Node, Mandibular			2 [2.5]	
Atrophy	3 [2.3]			
Hematopoietic Cell Proliferation				1 [2.0]
Hemorrhage	11 [2.0]	12 [1.8]	10 [2.0]	15 [1.7]
Hyperplasia, Lymphoid	2 [2.0]	1 [3.0]	4 [1.8]	1 [2.0]
Hyperplasia, Plasma Cell	24 [2.2]	20 [2.2]	21 [2.2]	21 [2.1]
Pigmentation	(48)	(48)	(47)	(48)
Lymph Node, Mesenteric				1 [2.0]
Ectasia	5 [2.2]	3 [2.3]	4 [2.5]	6 [2.7]
Hematopoietic Cell Proliferation		1 [2.0]	1 [2.0]	1 [2.0]
Hemorrhage	3 [2.3]	7 [2.9]	1 [3.0]	3 [2.3]
Hyperplasia, Lymphoid	(50)	(49)	(49)	(50)
Hyperplasia, Plasma Cell				
Spleen				
Angiectasis	2 [2.0]	1 [1.0]	1 [2.0]	1 [2.0]
Atrophy	15 [2.1]	20 [3.2]	24 [2.5]	39 [2.4]
Congestion		1 [3.0]	11 [1.5]	34 [1.7]
Hematopoietic Cell Proliferation		4 [1.3]	3 [2.0]	4 [3.3]
Hyperplasia, Plasma Cell		3 [2.0]	13 [2.3]	16 [2.2]
Pigmentation	1 [2.0]	14 [1.8]	(48)	(50)
Lymphoid Follicle, Atrophy	12 [1.8]	2 [2.0]	7 [3.1]	3 [3.0]
Lymphoid Follicle, Hyperplasia	(50)			4 [2.5]
Thymus				
Atrophy				
Hyperplasia, Lymphoid				

INTEGUMENTARY SYSTEM

Mammary Gland	(49)	(49)	(49)	(50)
Hyperplasia	(50)	(49)	(49)	(50)
Skin				
Edema			1 [3.0]	

MUSCULOSKELETAL SYSTEM

Bone	(30)	(49)	(49)	(50)
Hyperostosis	9 [1.9]	13 [2.2]	10 [2.2]	11 [2.1]
Skeletal Muscle	(1)	(1)	(1)	

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

MUSCULOSKELETAL SYSTEM - CONT

1 [4.0]

NERVOUS SYSTEM

Brain (50) (49) (49) (50)
 Hemorrhage 1 [1.0]
 Inflammation, Chronic Active 1 [2.0]
 Vacuolization Cytoplasmic 1 [3.0]

RESPIRATORY SYSTEM

Lung (50) (49) (49) (50)
 Edema 2 [2.0]
 Foreign Body 2
 Hemorrhage 4 [1.3]
 Hyperplasia, Lymphoid 9 [2.2]
 Infiltration Cellular, Histocyte 2 [1.5]
 Thrombosis 1 [2.0]
 Alveolar Epithelium, Hyperplasia 1 [1.0]
 Nose (50) (49)
 Foreign Body 1

SPECIAL SENSES SYSTEM

Eye (50) (49) (49) (50)
 Atrophy
 Cataract 1 [2.0]
 Inflammation, Chronic 2 [2.5]
 Harderian Gland (50) (49) (49) (50)
 Hyperplasia 1 [2.0]
 Hyperplasia, Focal 3 [3.0] 2 [2.0] 1 [2.0]

URINARY SYSTEM

Kidney (50) (49) (49) (50)
 Cyst 1 [3.0]
 Hyperplasia, Lymphoid 8 [2.0] 16 [2.1] 8 [2.1] 4 [2.3]
 Infarct 2 [1.5] 2 [1.5]
 Inflammation, Chronic 1 [2.0]

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE FEMALE	0PPM	625 PPM	1250 PPM	2500 PPM
URINARY SYSTEM - CONT				
Metaplasia, Osseous		1 [2.0]		2 [2.5]
Nephropathy	27 [1.1]	17 [1.1]	21 [1.1]	19 [1.0]
Papilla, Necrosis		1 [2.0]		1 [3.0]
Renal Tubule, Accumulation, Hyaline Droplet			1 [2.0]	1 [4.0]
Renal Tubule, Dilatation				
Renal Tubule, Necrosis		2 [2.5]		1 [2.0]
Urinary Bladder	(50)	(49)	(49)	(50)
Hyperplasia, Lymphoid	16 [2.3]	16 [2.1]	6 [2.0]	11 [2.3]
Inflammation, Chronic	1 [1.0]	1 [2.0]		
Transitional Epithelium, Hyperplasia		1 [1.0]		

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES^(b)
 2-METHYLMIDAZOLE

Report: PETRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Early Deaths				
Moribund Sacrifice	4	1	5	5
Natural Death	3	3	9	5
Survivors				
Terminal Sacrifice	43	46	36	40
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Intestine Large, Cecum	(49)	(49)	(47)	(50)
Edema	2 [2.0]	1 [2.0]	1 [2.0]	1 [2.0]
Intestine Small, Duodenum	(49)	(49)	(45)	(50)
Epithelium, Hyperplasia				1 [3.0]
Intestine Small, Jejunum	(50)	(49)	(46)	(50)
Hyperplasia, Lymphoid		1 [2.0]	1 [3.0]	1 [3.0]
Infiltration Cellular, Polymorphonuclear	(49)	(50)	(45)	(49)
Intestine Small, Ileum		1 [2.0]		1 [2.0]
Hyperplasia, Lymphoid				1 [2.0]
Infiltration Cellular, Polymorphonuclear	(50)	(50)	(50)	(50)
Liver				
Angiectasis	2 [3.0]	3	1 [4.0]	3
Basophilic Focus	2	9	1	8
Clear Cell Focus	6	1 [3.0]		
Cyst		3	2	6
Eosinophilic Focus			2 [1.5]	2 [2.0]
Hematopoietic Cell Proliferation	1 [3.0]			1
Hepatodysplastic Nodule				
Infarct	1	7 [1.1]	7 [1.3]	7 [1.4]
Infiltration Cellular, Mixed Cell	5 [1.4]	3	4	4
Mixed Cell Focus	4			1 [3.0]
Necrosis, Diffuse		6 [1.5]	2 [2.5]	6 [2.2]
Necrosis, Focal	2 [2.0]	2	1	37 [1.8]
Tension Lipidosis				29 [1.3]
Hepatocyte, Cytoplasmic Alteration				10 [1.0]
Hepatocyte, Karyomegaly		1 [3.0]		1 [2.0]
Hepatocyte, Vacuolization Cytoplasmic		1 [3.0]		19 [1.5]
Kupffer Cell, Pigmentation		(2)	1 [2.0]	(2)
Mesenterly	(6)	1 [2.0]		
Angiectasis				

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NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES(b)
 2-METHYLMIMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
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B6C3F1 MICE MALE	0PPM	625 PPM	1250 PPM	2500 PPM
ALIMENTARY SYSTEM - CONT				
Inflammation, Chronic		1 [1.0]		2 [2.5]
Fat, Necrosis	4 [2.3]	1 [2.0]	3 [2.3]	(50)
Pancreas	(50)	(50)	(49)	(50)
Atrophy	1 [2.0]	1 [4.0]	1 [4.0]	2 [3.0]
Cyst	2 [3.0]	3 [3.0]	2 [2.0]	1 [3.0]
Acinus, Cytoplasmic Alteration	(50)	(50)	(50)	(50)
Salivary Glands	2 [2.0]	2 [2.0]	(50)	(50)
Hyperplasia, Lymphoid	(50)	(49)	(50)	(50)
Stomach, Forestomach		2		
Diverticulum	1 [2.0]	1 [1.0]	1 [2.0]	1 [3.0]
Inflammation, Chronic Active		1 [3.0]	2 [1.5]	1 [3.0]
Ulcer	2 [2.0]	2 [1.5]	(49)	(50)
Epithelium, Hyperplasia	(50)	(49)	1 [2.0]	(50)
Stomach, Glandular				
Glands, Dysplasia	1 [3.0]			(1)
Tooth				1 [4.0]
Inflammation, Chronic				

CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	1 [1.0]			1 [1.0]
Perivascular, Inflammation, Chronic	3 [1.7]			

ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule	2 [3.0]	6 [3.0]	8 [3.0]	6 [3.0]
Hyperplasia, Focal	2 [1.5]	4 [1.5]	3 [1.3]	1 [1.0]
Hypertrrophy, Focal	13 [1.3]	18 [1.6]	10 [1.2]	10 [1.7]
Capsule, Hyperplasia	1 [1.0]	2 [1.5]	3 [1.3]	2 [1.5]
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia			2 [1.5]	
Islets, Pancreatic	(50)	(50)	(49)	(50)
Hyperplasia		2 [2.0]		1 [2.0]
Parathyroid Gland	(49)	(47)	(45)	(48)
Cyst	3 [3.0]	1 [3.0]	2 [3.0]	1 [3.0]
Pituitary Gland	(49)	(48)	(48)	(50)
Pars Distalis, Cyst	2 [3.0]	1 [3.0]	2 [3.0]	2 [3.0]
Pars Distalis, Hyperplasia, Focal		1 [4.0]		
Thyroid Gland	(50)	(50)	(50)	(50)

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NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES^(b)
 2-METHYLMIDAZOLE

Report: PE1RPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE MALE	0PPM	625 PPM	1250 PPM	2500 PPM
ENDOCRINE SYSTEM - CONT				
Degeneration, Cystic	10 [2.0]	2 [1.0]	3 [2.0]	4 [1.5]
Follicular Cell, Hyperplasia		2 [1.5]	3 [1.7]	33 [1.9]
Follicular Cell, Hypertrophy	1 [1.0]		6 [1.2]	25 [1.3]

GENERAL BODY SYSTEM
 None

GENITAL SYSTEM	(50)	(50)	(50)	(50)
Epididymis				
Fibrosis	1 [2.0]			
Granuloma Sperm			2 [3.0]	5 [2.6]
Hyperplasia, Lymphoid			2 [2.5]	1 [3.0]
Hypospermia			1 [4.0]	
Inflammation, Chronic Active	1 [1.0]	3 [1.3]	7 [2.0]	8 [2.9]
Penis	(1)		(1)	(1)
Angiectasis			1 [3.0]	1 [3.0]
Preputial Gland	(50)	(50)	(50)	(50)
Cyst	18 [3.0]	23 [3.0]	16 [3.0]	21 [3.0]
Inflammation, Chronic	14 [2.4]	10 [2.2]	14 [2.1]	7 [2.4]
Prostate	(49)	(50)	(49)	(50)
Inflammation, Chronic				2 [2.5]
Seminal Vesicle	(50)	(50)	(50)	(50)
Atrophy	1 [2.0]			
Testes	(50)	(50)	(50)	(50)
Germinal Epithelium, Atrophy	1 [2.0]	4 [2.0]	8 [2.3]	14 [2.0]

HEMATOPOIETIC SYSTEM	(50)	(50)	(50)	(50)
Bone Marrow				
Hyperplasia	4 [3.0]	10 [2.8]	20 [2.1]	42 [2.5]
Lymph Node	(2)	(3)	(1)	(1)
Bronchial, Hyperplasia, Lymphoid		1 [2.0]		
Lymph Node, Mandibular	(48)	(46)	(45)	(50)
Atrophy	1 [3.0]		2 [2.0]	4 [2.8]
Ectasia			1 [2.0]	
Hyperplasia, Lymphoid	10 [2.1]	14 [2.3]	9 [2.6]	13 [2.2]
Pigmentation	8 [2.1]	6 [2.2]	9 [2.0]	6 [2.0]
Lymph Node, Mesenteric	(47)	(47)	(46)	(48)

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 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLIMIDAZOLE

Report: PEIRPT18
 Date: 03/14/03
 Time: 11:38:08

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM - CONT

Angiectasis	1 [2.0]	1 [3.0]	2 [2.5]	1 [3.0]
Atrophy	4 [1.8]	2 [1.5]	2 [2.0]	2 [3.0]
Hemorrhage	7 [2.4]	7 [2.1]	15 [2.4]	10 [2.3]
Hyperplasia, Lymphoid	1 [4.0]			1 [3.0]
Necrosis				(50)
Spleen	(50)	(50)	(49)	(50)
Angiectasis				1 [2.0]
Atrophy		1 [3.0]	4 [3.0]	3 [2.7]
Hematopoietic Cell Proliferation	10 [2.2]	21 [2.3]	38 [2.5]	45 [2.9]
Pigmentation	1 [2.0]	16 [1.1]	33 [1.6]	43 [2.2]
Lymphoid Follicle, Atrophy		4 [3.3]	14 [1.6]	30 [1.8]
Lymphoid Follicle, Hyperplasia	5 [2.0]	2 [1.5]	2 [2.0]	
Thymus	(47)	(46)	(46)	(47)
Atrophy	7 [2.6]	5 [2.2]	9 [3.4]	8 [3.1]
Cyst	1 [3.0]		1 [3.0]	1 [3.0]
Hyperplasia, Lymphoid		1 [3.0]		

INTEGUMENTARY SYSTEM

Skin	(50)	(50)	(50)	(50)
Inflammation, Chronic		1 [4.0]		

MUSCULOSKELETAL SYSTEM

Skeletal Muscle	(1)	(1)		(2)
Atrophy				1 [2.0]

NERVOUS SYSTEM

Brain	(50)	(50)	(50)	(50)
Compression		1 [3.0]		
Peripheral Nerve	(1)			(1)
Atrophy				1 [2.0]

RESPIRATORY SYSTEM

Lung	(50)	(50)	(50)	(50)
Edema	1 [2.0]	3 [2.0]	1 [2.0]	3 [2.0]
Hemorrhage	4 [2.0]	8 [1.5]	4 [1.8]	2 [3.0]

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 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES^(b)
 2-METHYLMIDAZOLE

Report: PETRPT18
 Date: 03/14/03
 Time: 11:38:08

	0PPM	625 PPM	1250 PPM	2500 PPM
RESPIRATORY SYSTEM - CONT				
Hyperplasia, Lymphoid	1 [2.0]	2 [2.0]	2 [2.0]	4 [2.0]
Infiltration Cellular, Histiocyte	4 [2.8]	4 [3.0]	4 [2.0]	2 [3.0]
Inflammation, Chronic			1 [1.0]	2 [1.5]
Metaplasia, Osseous			2 [1.0]	
Thrombosis	1 [1.0]	3 [2.0]	1 [1.0]	1 [2.0]
Alveolar Epithelium, Hyperplasia	5 [3.2]		1 [3.0]	3 [2.3]
Alveolar Epithelium, Multifocal	1 [3.0]		(50)	(50)
Nose	(50)			
Foreign Body	1	3	3	2
Inflammation, Chronic	1 [1.0]	4 [2.5]	3 [1.7]	2 [2.0]

	(50)	(50)	(50)	(50)
SPECIAL SENSES SYSTEM				
Eye				
Cataract	(50)	(50)	(50)	(50)
Inflammation, Chronic	1 [3.0]	2 [3.0]	1 [3.0]	1 [2.0]
Cornea, Hyperplasia	1 [2.0]	(50)	1 [2.0]	2 [3.0]
Harderian Gland	(50)		(48)	(50)
Hyperplasia, Focal	1 [2.0]	4 [1.8]	2 [2.5]	
Inflammation, Chronic	3 [1.7]			2 [2.0]

	(50)	(50)	(50)	(50)
URINARY SYSTEM				
Kidney				
Cyst	13 [3.0]	11 [3.0]	12 [3.0]	19 [3.0]
Hydronephrosis	1 [2.0]	3 [2.0]	3 [2.0]	3 [2.0]
Hyperplasia, Lymphoid	1 [2.0]	6 [1.8]	6 [2.2]	1 [2.0]
Infarct	6 [1.8]			1 [4.0]
Inflammation, Suppurative	5 [1.8]	3 [1.3]	2 [1.0]	3 [1.7]
Metaplasia, Osseous	34 [1.2]	43 [1.5]	32 [1.5]	31 [1.1]
Nephropathy				1 [2.0]
Papilla, Necrosis				3 [1.7]
Renal Tubule, Hyperplasia	1 [1.0]	1 [1.0]	2 [1.0]	3 [1.7]
Renal Tubule, Pigmentation	1 [2.0]			45 [2.5]
Urethra				(1)
Angiectasis				1 [4.0]
Inflammation, Suppurative				1 [3.0]
Urinary Bladder	(50)	(50)	(50)	(50)
Transitional Epithelium, Hyperplasia				1 [2.0]

^a Number of animals examined microscopically at site and number of animals with lesion
^b Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

END OF REPORT

NTP Experiment-Test: 92012-06
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
2-METHYLLIMIDAZOLE

Report: PEIRPT03
Date: 02/24/03
Time: 14:41:02

27 WEEK SSAC/PTNA#1 MICE

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25017 Scheduled Sacrifice
Removal Date Range: All
Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:41:02

B6C3F1 MICE FEMALE

0PPM

625 PPM

1250 PPM

2500 PPM

DISPOSITION SUMMARY

	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation	1 (10%)	7 (70%)	3 (30%)	5 (50%)
Infiltration Cellular, Mixed Cell	6 (60%)	1 (10%)	2 (20%)	4 (40%)
Necrosis, Focal		1 (10%)		
Hepatocyte, Vacuolization Cytoplasmic		1 (10%)		

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule	2 (20%)	(10)	(10)	1 (10%)
Thyroid Gland	(8)	(10)	(10)	(10)
Follicular Cell, Hypertrophy		8 (80%)	10 (100%)	10 (100%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)
Cyst	1 (10%)	1 (10%)	(10)	(10)
Uterus	(10)	(10)	(10)	(10)
Hyperplasia, Cystic	3 (30%)	1 (10%)	4 (40%)	1 (10%)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:41:02

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM	0PPM	625 PPM	1250 PPM	2500 PPM
Lymph Node, Mandibular	(10)	(10)	(10)	(10)
Pigmentation	2 (20%)	1 (10%)	(10)	2 (20%)
Spleen	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation	2 (20%)	5 (50%)	6 (60%)	10 (100%)
Pigmentation	1 (10%)	3 (30%)	7 (70%)	10 (100%)
Lymphoid Follicle, Atrophy	(10)	(10)	(10)	4 (40%)

INTEGUMENTARY SYSTEM

Skin	(10)	(10)	(10)	(10)
Inflammation, Chronic	1 (10%)	(10)	(10)	(10)

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)
Hyperplasia, Lymphoid	(10)	(10)	(10)	1 (10%)

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

Kidney	(10)	(10)	(10)	(10)
Nephropathy	1 (10%)	1 (10%)	(10)	(10)

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:41:02

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Disposition	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation			1 (10%)	
Infiltration Cellular, Mixed Cell	2 (20%)	3 (30%)	6 (60%)	2 (20%)
Necrosis, Focal		1 (10%)		
Hepatocyte, Karyomegaly				5 (50%)
Hepatocyte, Vacuolization				4 (40%)
Cytoplasmic				1 (10%)
Mesentery				1 (100%)
Fat, Necrosis				

CARDIOVASCULAR SYSTEM

Heart	(10)	(10)	(10)	(10)
Valve, Hypertrophy		1 (10%)		

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule	2 (20%)			1 (10%)
Hyperplasia, Focal				1 (10%)
Hypertrophy, Focal		1 (10%)	(10)	1 (10%)
Thyroid Gland	(10)	(10)	(10)	(10)
Follicle, Cyst		5 (50%)	9 (90%)	1 (10%)
Follicular Cell, Hypertrophy				10 (100%)

GENERAL BODY SYSTEM

None

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:41:02

B6C3F1 MICE MALE 0PPM 625 PPM 1250 PPM 2500 PPM

GENITAL SYSTEM

Preputial Gland	(10)	(10)	(10)	(10)
Cyst			1 (10%)	1 (10%)
Inflammation, Chronic				

HEMATOPOIETIC SYSTEM

Bone Marrow	(10)	(10)	(10)	(10)
Hyperplasia	1 (10%)		2 (20%)	5 (50%)
Spleen	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation		5 (50%)	10 (100%)	10 (100%)
Pigmentation		1 (10%)	10 (100%)	10 (100%)
Lymphoid Follicle, Atrophy			5 (50%)	10 (100%)
Lymphoid Follicle, Hyperplasia	1 (10%)			
Thymus		(10)	(10)	(10)
Atrophy		1 (10%)		

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)
Hemorrhage			1 (10%)	1 (10%)

SPECIAL SENSES SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 2-METHYLMIDAZOLE

Report: PEIRPT03
 Date: 02/24/03
 Time: 14:41:02

B6C3F1 MICE MALE

0PPM

625 PPM

1250 PPM

2500 PPM

None

URINARY SYSTEM

Lesion	0PPM	625 PPM	1250 PPM	2500 PPM
Kidney	(10)	(10)	(10)	(10)
Cyst		1 (10%)		
Hydronephrosis		1 (10%)		
Nephropathy	1 (10%)		1 (10%)	2 (20%)
Renal Tubule, Pigmentation			1 (10%)	10 (100%)
Urinary Bladder	(10)	(10)	(10)	(10)
Transitional Epithelium, Hyperplasia	1 (10%)			

a Number of animals examined microscopically at site and number of animals with lesion

END OF REPORT

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC 2-METHYLMIDAZOLE
Route: DOSED FEED

27 WEEK SSAC/FINAL#1 MICE

Report: PEIRPT05
Date: 02/24/03
Time: 14:52:39

Facility: Southern Research Institute

Chemical CAS #: 693-98-1

Lock Date: 10/16/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: All

Treatment Groups: Include All

a Number of animals examined microscopically at site and number of animals with lesion

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC 2-METHYLMIDAZOLE
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:52:39

B6C3F1 MICE FEMALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

	0PPM	625 PPM	1250 PPM	2500 PPM
Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC
Route: DOSED FEED

2-METHYLMIDAZOLE

Report: PEIRPT05
Date: 02/24/03
Time: 14:52:39

B6C3F1 MICE FEMALE 0PPM 625 PPM 1250 PPM 2500 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:52:39

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Animals Initially in Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:52:39

B6C3F1 MICE MALE 0PPM 625 PPM 1250 PPM 2500 PPM

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung (10) (10) (10) (10)
 Alveolar/Bronchiolar Adenoma 1 (10%) (10)

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 92012-06 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC
 Route: DOSED FEED
 2-METHYLIMIDAZOLE

Report: PEIRPT05
 Date: 02/24/03
 Time: 14:52:39

B6C3F1 MICE MALE

0PPM

625 PPM

1250 PPM

2500 PPM

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	1
Total Primary Neoplasms	1
Total Animals with Benign Neoplasms	1
Total Benign Neoplasms	1
Total Animals with Malignant Neoplasms	
Total Malignant Neoplasms	
Total Animals with Metastatic Neoplasms	
Total Metastatic Neoplasms	
Total Animals with Malignant Neoplasms Uncertain Primary Site	
Total Animals with Neoplasms Uncertain- Benign or Malignant	
Total Uncertain Neoplasms	

a Number of animals examined microscopically at site and number of animals with lesion
 b Primary tumors: all tumors except metastatic tumors

END OF REPORT

NTP Experiment-Test: 92012-06
Study Type: CHRONIC
Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES (b)
2-METHYLMIDAZOLE

27 WEEK SSAC/FINAL#1 MICE

Report: PEIRPT18
Date: 02/24/03
Time: 15:09:13

Facility: Southern Research Institute
Chemical CAS #: 693-98-1
Lock Date: 10/16/01
Cage Range: All
Reasons For Removal: 25017 Scheduled Sacrifice
Removal Date Range: All
Treatment Groups: Include All

- a Number of animals examined microscopically at site and number of animals with lesion
- b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 15:09:13

B6C3F1 MICE FEMALE 0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation	1 [1.0]	7 [1.0]	3 [1.0]	5 [1.0]
Infiltration Cellular, Mixed Cell	6 [1.0]	1 [1.0]		
Necrosis, Focal		1 [2.0]	2 [2.0]	4 [2.0]
Hepatocyte, Vacuolization Cytoplasmic				

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule	2 [3.0]	(10)	(10)	1 [3.0]
Thyroid Gland	(8)	(10)	(10)	(10)
Follicular Cell, Hypertrophy		8 [1.0]	10 [1.1]	10 [1.7]

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)
Cyst	1 [3.0]	1 [3.0]	(10)	(10)
Uterus	(10)	(10)	(10)	(10)
Hyperplasia, Cystic	3 [1.7]	1 [2.0]	4 [2.3]	1 [2.0]

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 15:09:13

B6C3F1 MICE FEMALE 0PPM 625 PPM 1250 PPM 2500 PPM

HEMATOPOIETIC SYSTEM		0PPM	625 PPM	1250 PPM	2500 PPM
Lymph Node, Mandibular	(10)	(10)	(10)	(10)	(10)
Pigmentation	2 [2.0]	1 [2.0]	(10)	2 [2.0]	(10)
Spleen	(10)	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation	2 [1.0]	5 [1.2]	6 [1.5]	10 [2.6]	10 [1.9]
Pigmentation	1 [1.0]	3 [1.0]	7 [1.3]	10 [1.9]	4 [1.5]
Lymphoid Follicle, Atrophy					

INTEGUMENTARY SYSTEM		0PPM	625 PPM	1250 PPM	2500 PPM
Skin	(10)	(10)	(10)	(10)	(10)
Inflammation, Chronic	1 [2.0]				

MUSCULOSKELETAL SYSTEM
 None

NERVOUS SYSTEM
 None

RESPIRATORY SYSTEM		0PPM	625 PPM	1250 PPM	2500 PPM
Lung	(10)	(10)	(10)	(10)	(10)
Hyperplasia, Lymphoid					1 [2.0]

SPECIAL SENSES SYSTEM
 None

URINARY SYSTEM		0PPM	625 PPM	1250 PPM	2500 PPM
Kidney	(10)	(10)	(10)	(10)	(10)
Nephropathy	1 [1.0]	1 [1.0]			

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 15:09:13

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

DISPOSITION SUMMARY

Animals Initially In Study	60	60	60	60
Scheduled Sacrifice	10	10	10	10
Early Deaths				
Survivors				
Animals Examined Microscopically	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)
Hematopoietic Cell Proliferation			1 [1.0]	
Infiltration Cellular, Mixed Cell	2 [1.0]	3 [1.0]	6 [1.0]	2 [1.0]
Necrosis, Focal		1 [1.0]		
Hepatocyte, Karyomegaly				5 [1.2]
Hepatocyte, Vacuolization				4 [2.0]
Mesentery				1 [1.0]
Fat, Necrosis				1 [2.0]

CARDIOVASCULAR SYSTEM

Heart	(10)	(10)	(10)	(10)
Valve, Hypertrophy		1 [2.0]		

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)
Accessory Adrenal Cortical Nodule	2 [3.0]			1 [3.0]
Hyperplasia, Focal				1 [2.0]
Hypertrophy, Focal		1 [2.0]	(10)	
Thyroid Gland	(10)	(10)	(10)	(10)
Follicle, Cyst				1 [3.0]
Follicular Cell, Hypertrophy		5 [1.0]	9 [1.2]	10 [1.8]

GENERAL BODY SYSTEM

None

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 15:09:13

B6C3F1 MICE MALE

OPPM 625 PPM 1250 PPM 2500 PPM

GENITAL SYSTEM

Preputial Gland (10) (10) (10) (10)
 Cyst (10) (10) (10) (10)
 Inflammation, Chronic 1 [2.0] 1 [3.0]

HEMATOPOIETIC SYSTEM

Bone Marrow (10) (10) (10) (10)
 Hyperplasia 1 [3.0] 2 [2.0] 5 [1.8]
 Spleen (10) (10) (10) (10)
 Hematopoietic Cell Proliferation 5 [1.0] 10 [2.1] 10 [3.0]
 Pigmentation 1 [1.0] 10 [1.1] 10 [2.2]
 Lymphoid Follicle, Atrophy 5 [1.2] 10 [1.0]
 Thymus 1 [1.0] (10) (10) (10)
 Atrophy 1 [2.0] (10)

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung (10) (10) (10) (10)
 Hemorrhage 1 [2.0] 1 [1.0]

SPECIAL SENSES SYSTEM

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

NTP Experiment-Test: 92012-06
 Study Type: CHRONIC
 Route: DOSED FEED

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 2-METHYLMIDAZOLE

Report: PEIRPT18
 Date: 02/24/03
 Time: 15:09:13

B6C3F1 MICE MALE

0PPM 625 PPM 1250 PPM 2500 PPM

None

URINARY SYSTEM

Kidney	(10)	(10)	(10)	(10)
Cyst		1 [4.0]		
Hydronephrosis	1 [2.0]	1 [2.0]		
Nephropathy	1 [1.0]			
Renal Tubule, pigmentation			1 [1.0]	2 [1.0]
Urinary Bladder			1 [1.0]	10 [2.2]
Transitional Epithelium, Hyperplasia	(10)	(10)	(10)	(10)

a Number of animals examined microscopically at site and number of animals with lesion
 b Average severity grade (1-minimal;2-mild;3-moderate;4-marked)

END OF REPORT