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DEPARTMENT OF HEALTH & HUMAN SERVICES

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National Institutes of Health
National Institute of
Environmental Health Sciences
P. O. Box 12233
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March 23, 2000

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Dear Document Control Office:

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 Gavage study on METHACRYLONITRILE (126-98-7) 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 [illegible] reports, and the Report on Carcinogens are available from the Environmental Heal[illegible] [illegible]ion 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,

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
Dr. Bucher
Dr. Ghanayem

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PATHOLOGY WORKING GROUP (PWG) OF THE TWO YEAR CHRONIC STUDY OF METHACRYLONITRILE (C88050B/88050-05) VIA GAVAGE TO F344 RATS PERFORMED AT THE BATTELLE COLUMBUS LABORATORIES

Prepared by:
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Submitted to:
National Toxicology Program
Research Triangle Park, NC 27709

December 10, 1999

CONFLICT OF INTEREST STATEMENT:

Dr. Paul K. Hildebrandt has not been involved in testing or evaluation of Methacrylonitrile for any client other than NTP.

Contain NO CBI

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PATHOLOGY WORKING GROUP (PWG) OF THE TWO YEAR CHRONIC STUDY OF METHACRYLONITRILE (C88050B/88050-05) VIA GAVAGE TO F344 RATS PERFORMED AT THE BATTELLE COLUMBUS LABORATORIES

Date of PWG: November 23, 1999

Site of PWG: National Toxicology Program (NTP/NIEHS)
Research Triangle Park, NC

PWG Participants:	Paul K. Hildebrandt, D.V.M., Chairperson	PATHCO
	Abraham Nyska, D.V.M.	NIEHS
	Ronald Herbert, D.V.M., Ph.D.	NIEHS
	Joel Mahler, D.V.M.	NIEHS
	Bradley Hamilton, D.V.M., Ph.D.	GlaxoWellcome
	Cynthia Shackelford, D.V.M., M.S., Ph.D.	EPL
	Jeff Wolf, D.V.M.	EPL

Study Pathologist: John Yarrington, D.V.M., Ph.D.
Reviewing Pathologist: Deborah Banas, D.V.M., M.S.

I. SUMMARY AND CONCLUSIONS

A. The administration of methacrylonitrile via oral gavage for two years did not result in an increase of neoplastic lesions.

B. Atrophy and respiratory epithelial metaplasia of the olfactory epithelium occurred at a high incidence in the nose of both sexes at the high dose (30 mg/kg).

C. There was an increase in the incidence of pancreatic hyperplasia in male treated rats over that of controls. No increase in hyperplasia of the pancreas occurred in female treated rats.

D. An increase in bone marrow hyperplasia was present in high dose male rats but not in female rats.

E. A slight increase in cytoplasmic vacuolization (glycogen infiltration) of hepatocytes occurred in treated rats of both sexes over that of respective controls.

F. No morphologic differences between the thyroid glands of treated rats and control rats could be detected.

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II. STUDY DESIGN

Fifty rats/sex/dose group were oral gavaged with the test compound at the following doses for up to two years:

Male - Control; 3 mg/kg, 10 mg/kg and 30 mg/kg
Female - Control; 3 mg/kg, 10 mg/kg and 30 mg/kg

III. ANIMAL DISPOSITION SUMMARY

Chronic Toxicity/Carcinogenicity Study

FEMALE RATS

	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Animals Initially in Study	(50)	(50)	(50)	(50)
Early Deaths				
Natural Death	7	6	6	8
Moribund Sacrifice	4	10	9	7
Accidentally Killed				
Other*	1	1	1	
Survivors - Terminal Sacrifice	(38)	(33)	(34)	(35)
Animals Examined Microscopically	50	50	50	50

*Dosing Accident

MALE RATS

	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Animals Initially in Study	(50)	(50)	(50)	(50)
Early Deaths				
Natural Death	12	3	7	6
Moribund Sacrifice	13	13	9	12
Accidentally Killed				
Other*				1
Survivors - Terminal Sacrifice	(25)	(34)	(34)	(31)
Animals Examined Microscopically	50	50	50	50

*Dosing Accident

IV. CONDUCT OF THE PWG

Prior to the PWG, the Chairperson reviewed the pathology incidence tables, the study pathologist's narrative, the report prepared by the reviewing pathologist, and microscopic slides of potential target organs and lesions with discrepancies in diagnoses between the study pathologist (SP) and reviewing pathologist (RP).

Potential target organs in this study were considered to be:

Male Rat	Female Rat
Nose	Nose

The following organs from the sex indicated were reviewed from all animals in all groups, but only for the presence of the following diagnoses:

Male Rats

Bone Marrow - Hyperplasia
Pancreas - Hyperplasia
Thyroid Gland, Follicular Cell - Hyperplasia
Liver - Vacuolization Cytoplasmic
Liver - Basophilic Focus
Liver - Leukemia Mononuclear
Spleen - Leukemia Mononuclear
Adrenal Gland - Angiectasis

Female Rats

Bone Marrow - Hyperplasia
Thyroid Gland, Follicular Cell - Hyperplasia
Pancreas - Hyperplasia
Clitoral Gland - Hyperplasia
Liver - Inflammation, Chronic Active

At [illegible]'G the chairperson led a short discussion in the form of introductory remarks which included the following:

A. Survival: All three male treated groups had a slightly higher survival rate than male controls. In females the survival rate in controls was- 78%, in 3 mg/kg - 67%, in 10 mg/kg - 69% and in 30 mg/kg - 72%.

B. Clinical Signs: No treatment related clinical signs were reported.

C. Body Weights:
Males - The 3 mg/kg and 10 mg/kg dose groups were similar to controls. The 30 mg/kg dose group was 8% less than controls.

Females - The 3 mg/kg and 10 mg/kg dose groups were similar to controls. The 30 mg/kg dose group was slightly less than the controls but not statistically significant.

D. The only gross lesions recorded were a few liver foci that correlated microscopically with basophilic foci.

E. In the 13-week subchronic study, metaplasia and necrosis was observed in the olfactory epithelium of the nose. These lesions occurred in doses of 60 mg/kg and 120 mg/kg which were higher than the doses in this chronic study.

The chairperson had photographed a number of lesions occurring in potential target organs and projected these photomicrographs to the PWG to illustrate the lesions/changes present for discussion and to review respective diagnostic criteria.

Nose

A series of slides with sections of nose from control and high dose (30 mg/kg) male and female rats were examined by the PWG. Atrophy of the olfactory epithelium was recognized by the PWG. The lesion was characterized by loss of sensory cells that occurred in the dorsal meatus in the second level of the nose and segmentally along the ethmoid turbinates and lateral walls of the third level. The epithelium in these areas was thinner with columnar sustentacular cells predominating. In some areas, there was complete loss of sensory and sustentacular cells which was replaced by ciliated and non-ciliated columnar and cuboidal epithelial cells. This finding was diagnosed as respiratory metaplasia. This change was also present along the nasal septum, primarily in level two. The PWG was in agreement with the reviewing pathologist's diagnosis and characterization of nasal lesions and believed that the lesions are related to compound administration.

Thyroid

A very high incidence of thyroid follicular cell hyperplasia had been diagnosed in treated male and female rats of all treated groups. The PWG examined a series of thyroid glands from control and treated rats and was unable to detect any morphologic differences between these thyroid glands.

The PWG recognized that considerable variability in size and shape of follicles existed but no consistent increase in height of epithelial cells or numbers of epithelial cells per unit area was recognized. Some thyroids appeared to be more active with smaller follicles in the center of the gland that had a somewhat basophilic hue, while other follicles at the periphery of the gland were large, contained, abundant colloid and had a flattened epithelium. This variability occurred in the thyroids of both control and treated rats. It was the opinion of the PWG that no compound effect was present in the thyroid gland.

Pancreas

The PWG observed several of the photomicrographs of pancreases with exocrine gland hyperplasia and recognized that this was typical hyperplasia of the pancreas. The PWG accepted the incidence of lesions of the study pathologist, RP and chairperson and agreed that a higher

incidence was present in male rats and appeared to be treatment related. In female rats no treatment effect was present.

Liver

There was some discrepancy between the SP and RP regarding a non-neoplastic change in the liver. The SP had diagnosed a number of livers with cytoplasmic vacuolization in all dose groups but more in the high dose. The RP was of the opinion that the cytoplasmic vacuolization was somewhat different and diagnosed the change as cytologic alteration and had a higher incidence in high dose rats. The livers of control rats had a few small clear vacuoles consistent with lipid, whereas the livers of high dosed rats had hepatocytes with fine vacuoles giving a ground glass appearance. There was also a suggestion of a slight centrilobular distribution to these finely vacuolated hepatocytes.

The PWG examined a series of male control and high dose livers and was of the opinion that the livers of these rats had varying degrees of glycogen deposition. Most was considered to be within normal variation. There were no changes consistent with a lesion of cytologic alteration and the term should not be utilized in this study. Because there was some indication that there may be more livers with increased glycogen in the high dose rats, the PWG chairperson was instructed to review all livers from all groups and evaluate for cytoplasmic vacuolization. This was done in a "blind fashion" and the following results were obtained. Individual animal (liver) diagnoses are presented in Appendix A.

In this re-read the following criteria were utilized. Livers with mononuclear cell leukemia or autolysis were not included in this evaluation.

1) Minimal lesions - These lesions had very few and small vacuoles within hepatocytes. When there were a few clear vacuoles suggestive of containing lipid, the diagnosis of cytoplasmic vacuolization, fat was rendered. If ground glass appearance was the predominate feature, the diagnosis of cytoplasmic vacuolization was rendered.

2) Mild lesions - The same features as the minimal lesions described above but more observable. The difference between minimal and mild is quite subjective.

The livers graded as minimal and mild in this exercise would generally be accepted as normal with normal variation and no diagnosis would have been rendered.

3) Moderate lesions - The grade of moderate was given when the degree of vacuolization was clear-cut and would have been diagnosed as cytoplasmic vacuolization, minimal or mild, by most pathologists reading a routine chronic study.

There was an increase in cytoplasmic vacuolization (glycogen infiltration) in treated rats of both sexes over that of respective controls and a dose response did appear to be present. The degree of severity of this glycogen infiltration in treated rats was only slightly more than that observed in controls. The significance of the increased cytoplasmic vacuolization in a two-year study is unknown. No increase in hepatic proliferative lesions occurred in this study. Basophilic foci actually decreased in the livers of treated rats.

Bone Marrow

The incidence of bone marrow hyperplasia was reported to be higher in high dose rats in both sexes but more in females compared to controls. The PWG examined a series of bone slides from control rats and high dose rats and agreed there was increased bone marrow activity (hyperplasia) in the high dose female rats.

The PWG noted that, in some cases, the bone marrow hyperplasia was primarily a myeloid hyperplasia and correlated with an inflammatory lesion in another organ. In such cases there was also extramedullary hematopoiesis in the spleen and liver.

In a number of rats, with what appeared to be bone marrow hyperplasia (minimal to mild), there was not good morphologic evidence of which cell type predominated. In a few cases, there was a suggestion that the erythroid series predominated. In most rats diagnosed with minimal to mild bone marrow hyperplasia, there generally was no extramedullary hematopoiesis in the spleen or liver and no increase in pigment (hemosiderin) in the spleen, liver or bone marrow; changes that usually accompany bone marrow hyperplasia in an anemic animal. A number of animals with mononuclear leukemia were diagnosed with bone marrow hyperplasia.

The PWG agreed that a higher incidence of bone marrow hyperplasia appeared to be present in high dose female rats over that of controls but was cautious in stating this was due to a compound effect. The numerous variables and lack of additional supporting lesions usually associated with bone marrow hyperplasia negates a clear compound effect.

Schwannomas

The incidence of schwannomas in this study was slightly higher than generally observed in a two-year chronic study. As a result, all lesions diagnosed with schwannoma were presented to the PWG for evaluation. There were a few cases diagnosed with schwannoma in the heart that the PWG diagnosed as fibrosis of the heart. Also, a few lesions were considered to be primary schwannoma of the salivary gland rather than the overlying skin. There is no compound effect regarding the incidence of schwannomas.

Miscellaneous Lesions

Several examples of interesting and unusual lesions and a few discrepancies in diagnoses in non-target organs were presented to the PWG for evaluation. Results are presented in the PWG worksheets (Appendix B).

The PWG was in agreement that no compound effect was present regarding clitoral gland hyperplasia in females, and angiectasis in the adrenal glands of male rats. The decreased incidence of mononuclear cell leukemia in treated males rats was recognized but, other than the weight lose that was reported, no explanation could be offered for this negative trend.

Paul K. Hildebrandt, D.V.M.
Diplomate, American College of
Veterinary Pathologists

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CHAIRPERSON'S REPORT
PATHOLOGY WORKING GROUP (PWG)
OF THE CHRONIC STUDY OF
METHACRYLONITRILE (C88050B/88050-05)
VIA GAVAGE TO B6C3F1 MICE
PERFORMED AT
THE BATTELLE COLUMBUS LABORATORIES

Prepared by:

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Submitted to:

National Toxicology Program
Research Triangle Park, NC 27709

Conflict of Interest Statement:

PATHCO, Inc. employee Dr. Paul K. Hildebrandt served as chairperson for this PWG and had not been involved in the testing or evaluation of Methacrylonitrile (C88050B) for any clients other than NTP.

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PATHOLOGY WORKING GROUP (PWG) OF THE CHRONIC STUDY OF METHACRYLONITRILE (C88050B/88050-05) VIA GAVAGE TO B6C3F1 MICE PERFORMED AT THE BATTELLE COLUMBUS LABORATORIES

Date of PWG: July 01, 1999

Site of PWG: National Toxicology Program (NTP/NIEHS)
Research Triangle Park, NC

PWG Participants:		
	Paul K. Hildebrandt, D.V.M., Chairperson	PATHCO
	Ronald Herbert, D.V.M., Ph.D.	NIEHS
	Abraham Nyska, D.V.M.	NIEHS
	Glen Marrs, D.V.M., M.S.	EPL
	Cynthia Shackelford, D.V.M., M.S., Ph.D.	EPL
	Bradley Hamilton, D.V.M., Ph.D.	Glaxo-Wellcome
	Amy E. Brix, [illegible], Ph.D.	EPL

Study Pathologist: Dr. John Toft
Reviewing Pathologist: Dr. Cynthia Shackelford

I. SUMMARY AND CONCLUSION

It was the PWG opinion that the administration of methacrylonitrile to male and female mice for two years did not increase the incidence of neoplastic lesions or non-neoplastic lesions in any tissue/organ in this study. A number of lesions were evaluated by the PWG including liver proliferative lesions and non-neoplastic lesions in other organs and none was considered to be related to compound administration.

II. STUDY DESIGN

Fifty mice/sex/dose group were oral gavaged with the test compound at the following doses for up to two years:

Male - Control; 1.5 mg/kg; 3.0 mg/kg and 6.0 mg/kg
Female - Control; 1.5 mg/kg; 3.0 mg/kg and 6.0 mg/kg

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III. ANIMAL DISPOSITION SUMMARY

Chronic Toxicity/Carcinogenicity Study

FEMALE MICE

	0 MG/KG	1.5 MG/KG	3.0 MG/KG	6.0 MG/KG
Animals Initially in Study	(50)	(50)	(50)	(50)
Early Deaths				
Natural Death	15	13	4	7
Moribund Sacrifice	1	2	3	3
Accidentally Killed				15
Survivors - Terminal Sacrifice	(34)	(35)	(43)	(25)
Animals Examined Microscopically	50	50	50	50

MALE MICE

	0 MG/KG	1.5 MG/KG	3.0 MG/KG	6.0 MG/KG
Animals Initially in Study	(50)	(50)	(50)	(50)
Early Deaths				
Natural Death	10	5	6	3
Moribund Sacrifice	5	2	3	
Accidentally Killed				24
Other	1**			1**
Survivors - Terminal Sacrifice	(34)	(43)	(41)	(22)
Animals Examined Microscopically	49	50	50	50

* MISSING
**DOSING ACCIDENT

IV. CONDUCT OF THE PWG

Prior to the PWG, the Chairperson reviewed the pathology incidence tables, the study pathologist's narrative, the report prepared by the reviewing pathologist, and microscopic slides of potential target organs and lesions with discrepancies in diagnoses between the study pathologist (SP) and reviewing pathologist (RP).

Potential target organs in this study were considered to be:

Male Mice	Female Mice
Liver	Liver

During the quality assessment review, the RP identified eight possible neoplastic lesions in the intestines of the male mice which had not been previously diagnosed by the study pathologist. This led to a review of wet tissues from all male and female mice. Any suspect intestinal lesion was collected and examined histopathologically. As a result of this special action, the gastrointestinal tract was also considered a potential target organ for review by the PWG.

In addition, the following organs/tissues were examined for all animals in all groups for the lesions listed below:

Male Mice

Salivary Gland - Infiltration Cellular, Mononuclear Cell*
Adrenal Cortex, Zona Fasciculata - Hyperplasia
Adrenal Cortex, Zona Fasciculata - Hypertrophy
Pituitary Gland, Pars Distalis - Cyst
Lung - Inflammation, chronic
Epididymis - Infiltration Cellular, Mononuclear Cell*
Prostate - Infiltration Cellular, Mononuclear Cell*
Preputial Gland - Infiltration Cellular, Mononuclear Cell*
Kidney - Infiltration Cellular, Mononuclear Cell*
Oral Mucosa, Gingival - Foreign Body
Oral Mucosa, Gingival - Inflammation, chronic active

Female Mice

Liver - Hematopoietic Cell Proliferation
Liver - Infiltration Cellular, Mononuclear Cell*
Mesentery - Mineralization
Mesentery - Fat, Necrosis
Pituitary Gland, Pars Distalis - Angiectasis
Lymph Node, Mandibular - Pigmentation
Ovary - Pigmentation
Uterus, Endometrium - Hyperplasia, Cystic
Kidney - Infiltration Cellular, Mononuclear Cell*
Kidney - Inflammation, chronic active

* In addition to the diagnosis of "Infiltration, Cellular, Mononuclear Cell" the diagnosis for these organs were further reviewed for the presence of other inflammatory lesions.

At the PWG the chairperson led a short discussion in the form of introductory remarks which included the following:

1. Survival was essentially equal in all groups including respective controls with one exception. A dosing error occurred at 15 months. Twenty four male high dose mice and 15 female high dose mice died suddenly.

2. Body weights and weight gains had some fluctuation during the test period but were similar in all test groups and controls at terminal sacrifice.

3. No compound related clinical signs were recorded.

4. No compound related gross lesions were observed at necropsy.

5. No compound related lesions were observed in the mouse 90-day subchronic study.

Livers

All livers with a discrepancy in diagnosis between the SP and RP regarding tumor versus non-tumor were examined by the PWG. Discrepancies between hepatocellular adenoma versus hepatocellular carcinoma or single tumor versus multiple tumors were not examined. The results of the liver review are presented in the PWG work sheets. The PWG also examined a number of livers for non-proliferative lesions from control animals and treated mice. These livers were from terminal sacrifice mice that did not have other liver or systemic lesions. The objective of this exercise was to determine if any histologic differences existed between high dose mice and controls (degeneration, cytomegaly, cytoplasmic vacuolization, etc.).

It was the PWG opinion that no difference existed in the histologic appearance of the livers of control mice and high dose mice. Also, there did not appear to be a compound effect regarding the incidence of hepatic proliferation lesions among the respective dose groups compared to control groups.

Gastrointestinal Lesions

All gastrointestinal proliferative lesions were examined by the PWG. During the initial phases of the quality assessment review, additional intestinal proliferative lesions were discovered. As a result of this finding, a wet tissue review was conducted and eight additional intestinal lesions were diagnosed and are included in this PWG review.

A number of duodenums had been diagnosed with epithelial hyperplasia or an adenomatous polyp. It was noted that almost all sections of duodenum were taken from the extreme anterior portion of the duodenum and, in fact, some sections of duodenum included a portion of pyloric epithelium from the stomach.

Sections diagnosed as duodenal hyperplasia were cross sections of duodenum and consisted of a thickened mucosa with a prominent layer of Brunner's glands. In some specimens the inner surface was irregular and, occasionally, islands of mucosal epithelium were present in the intestinal lumen. This gave the impression that a proliferative lesion was present but not sectioned through the stalk. There were no cellular changes in these types of duodenal sections to suggest a proliferative lesion. There was no change in nucleus to cytoplasmic ratio, no tinctorial changes, no crowding or piling-up of epithelial cells, and mitotic figures were not more numerous than in other areas of the duodenum.

At a later re-review of these duodenums, several slides of mouse stomachs with attached duodenum that had been sectioned longitudinally were presented for examination by the PWG. These slides were from control mice from another study and, because they were sectioned longitudinally, they demonstrated the junction of duodenum and pyloric stomach very clearly. It was noted that the duodenal mucosa bends or invaginates slightly into the lumen of the pyloris. This feature causes a thickening and/or "puckering" effect of the duodenal mucosa such that when a cross section is taken from this area, as many were in this study, the duodenum is seen to have a mucosa with variable thickness and can have islands of mucosa in the lumen.

At this re-review, it was the PWG opinion that many of the duodenums originally diagnosed with hyperplasia or adenoma in this study were, in fact, normal.

There were a few duodenums in all dose groups including controls that, indeed, did have proliferative mucosal lesions (see Pathology Working Group sheets).

Hyperplasia of the duodenum was characterized by increased numbers of intestinal glands unit area that had glandular epithelial cells that were slightly smaller than normal. These glandular epithelial cells were similar to basal cells of normal glands but had scant basophilic cytoplasm. Occasionally, a few glands had epithelial cells with oval nuclei and pale eosinophilic cytoplasm that resembled squamous cells in squamous metaplasia. With one exception, duodenums with this change were not diagnosed as squamous metaplasia. The supporting lamina propria of these hyperplastic foci generally had a minimal increase in chronic inflammatory cells and immature mesenchymal elements.

Adenomas of the duodenum were characterized by proliferating intestinal glands that extended into the intestinal lumen. The glandular epithelial cells were fairly well differentiated but did vary considerably in size. Mitotic figures were slightly more prevalent than normal. Crowding and areas of multi-layers of epithelial cells were present to varying degrees. In some cases, basophilic basilar cells were more prominent than seen in hyperplastic lesions.

Adenocarcinoma of the duodenum consisted of a proliferation of intestinal glands that protruded extensively into the intestinal lumen. The glandular epithelium of these glands was fairly well differentiated in some areas while anaplastic epithelial cells predominated in other areas. The anaplastic cells were large with large nuclei containing prominent nucleoli. Mitotic figures were numerous. In more differentiated areas, the epithelial cells were larger than normal and crowding and multi-layering was evident. Individual cell necrosis was present and aggregates of cellular debris in intestinal glands were frequently observed. The supporting lamina propria in the tumor contained chronic inflammatory cells with a sprinkling of polymorphonuclear cells. Invasion of the underlying muscle was not evident in the adenocarcinoma of the duodenum.

Proliferative lesions occurred in other segments of the small intestine and in the cecum of the large intestine. These adenocarcinomas were solitary lesions and consisted of fairly well-differentiated neoplastic glandular epithelial cells. The glandular architecture was maintained; however, the glandular epithelial cells were slightly larger than normal. The nuclear to cytoplasm ratio was increased and mitotic figures were increased over that of normal intestinal cells. Multiple layers of cells or piling up of cells was a common feature. Villi were somewhat thicker and, occasionally, longer than normal. The neoplastic cells extended through the muscularis mucosa and into the underlying muscle and serosa in the form of glandular nests.

Although several proliferative lesions of the gastrointestinal tract were observed in this study, it was the PWG opinion that the incidence was similar in the respective dose groups and that no compound effect is present.

Adrenal Gland

There were a few differences in terminology of adrenal cortical lesions between the SP and RP. The PWG examined a number of adrenal glands with capsular lesions, subcapsular lesions and cortical lesions. It was the PWG opinion that lesions of the adrenal cortex need not be specified as to which zone was affected i.e., glomerulosa fasciculata or reticularis. The PWG also recognized that lesions diagnosed as hyperplasia and/or adenoma of the glomerulosa were in fact subcapsular (B-Cell) hyperplasia or adenoma. The PWG chairperson was directed to re-examine all male mouse adrenals to diagnose any subcapsular lesions. The SP had diagnosed capsular hyperplasia in almost 100% of males in each dose group including controls. This lesion was characterized by small basophilic cells just beneath the capsule that extended into the cortex to varying degrees. These are the subcapsular (A-cells) that are commonly observed in the adrenals of male mice and are generally not diagnosed unless the hyperplasia is quite prominent. The PWG was of the opinion that no compound related adrenal lesions were present.

The PWG Chairperson re-examined all male adrenals and diagnosed several subcapsular proliferative lesions rather than cortical (glomerular) lesions. No compound related adrenal lesions are present.

Multiple Organ Mononuclear Cell Infiltrate

Mononuclear cell infiltrate was diagnosed in several organs (epididymis, preputial gland, prostate, liver, kidney) by the SP. The RP diagnosed mononuclear cell infiltrate in additional mice of all dose groups. It was noted that most organs diagnosed with mononuclear cell infiltrate also had additional diagnoses of inflammation, chronic or acute. Also, many of the lesions diagnosed as mononuclear cell infiltrate consisted of a single blood vessel with a small aggregate of lymphocytes. The PWG was of the opinion that mononuclear cell infiltrate was such a minor change and was so often associated with an inflammatory lesion, or other lesion, that this separate diagnoses added little to the overall characterization of the changes in the respective organs.

Oral Lesions

Several cases of gingival inflammation and/or foreign body were examined by the PWG. These lesions were located primarily around molar teeth in section three of the nose. The lesions consisted of embedded foreign material around the root of a molar tooth. This foreign material was most often a fragment of plant material, although an occasional hair shaft could be identified. Varying degrees of chronic/active inflammation was usually associated with this foreign material.

The PWG agreed the lesions observed in this study were no different than the commonly encountered gingival lesions observed in most chronic two-year mouse studies. The majority of

lesions were very minimal consisting of a minute fragment of foreign material with no or very little inflammation. No treatment related gingival lesions were considered to be present in this study.

Ovary and Mandibular Lymph Node Pigment

Pigment in the ovary and mandibular lymph node was also evaluated by the PWG. It was the opinion of the PWG that the pigment observed in the series of slides examined that the pigment in the ovary and mandibular gland was well within the normal limits of two-year old mice and no treatment effect was present.

Pituitary Cysts

The PWG noted the slight increase in the incidence of pituitary cysts in treated male mice over that of controls. Because small pituitary cysts are such a common background lesion and the incidence was so low in all dose groups, the PWG was of the opinion that no compound effect was present. Biological variation of such a common background lesion can easily explain the incidences of pituitary cysts in this study.

Miscellaneous Lesions

A number of interesting and unusual lesions were presented to the PWG for interest and/or classification of diagnoses. See Pathology Working Group Worksheets.

Paul K. Hildebrandt, D.V.M.
Diplomate, American College of
Veterinary Pathologists

NATIONAL TOXICOLOGY PROGRAM

TR-497 METHACRYLONITRILE

Pathology Tables - Rats

P03 - Incidence Rates of Non-Neoplastic Lesions

P05 - Incidence Rates of Neoplasms by Anatomic Site (systemic lesions abridged)

P08 - Statistical Analysis of Primary Tumors

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

R 09

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FINAL#1 2 YEAR CHRONIC RATS

Facility: Battelle Columbus Laboratory

Chemical CAS #: 126-98-7

Lock Date: 05/05/99

Cage Range: All

Reasons For Removal: All

Removal Date Range: All

Treatment Groups: Include All

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

210

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	4	10	9	7
Natural Death	7	6	6	7
Dosing Accident	1	1	1	
Survivors				
Terminal Sacrifice	38	33	34	35
Natural Death				1
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Periesophageal Tissue, Hemorrhage		1 (2%)	2 (4%)	
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan	2 (4%)	5 (10%)	5 (10%)	4 (8%)
Intestine Large, Cecum	(50)	(50)	(50)	(50)
Inflammation, Chronic Active				1 (2%)
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Fibrosis				1 (2%)
Liver	(50)	(49)	(48)	(50)
Angiectasis		1 (2%)	2 (4%)	1 (2%)
Basophilic Focus	43 (86%)	43 (88%)	35 (73%)	39 (78%)
Clear Cell Focus	4 (8%)	2 (4%)	1 (2%)	3 (6%)
Degeneration			1 (2%)	
Degeneration, Cystic	1 (2%)		1 (2%)	
Eosinophilic Focus			3 (6%)	
Fatty Change	21 (42%)	13 (27%)	11 (23%)	7 (14%)
Hepatodiaphragmatic Nodule	9 (18%)	7 (14%)	8 (17%)	12 (24%)
Hyperplasia		1 (2%)		
Inflammation, Chronic Active	31 (62%)	27 (55%)	27 (56%)	27 (54%)
Mixed Cell Focus	2 (4%)	7 (14%)	8 (17%)	5 (10%)
Necrosis	2 (4%)	3 (6%)	1 (2%)	
Thrombosis	2 (4%)		3 (6%)	
Vacuolization Cytoplasmic	7 (14%)	14 (29%)	17 (35%)	30 (60%)
Bile Duct, Hyperplasia	14 (28%)	5 (10%)	13 (27%)	9 (18%)
Mesentery	(7)	(2)	(8)	(4)
Fat, Inflammation, Chronic Active	5 (71%)	1 (50%)	2 (25%)	1 (25%)
Fat, Necrosis	1 (14%)	1 (50%)	4 (50%)	2 (50%)
Pancreas	(50)	(50)	(50)	(50)
Cytoplasmic Alteration			1 (2%)	
Hyperplasia	1 (2%)		1 (2%)	1 (2%)
Acinus, Atrophy	8 (16%)	4 (8%)	7 (14%)	10 (20%)
Stomach, Forestomach	(50)	(50)	(50)	(50)

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

B 11

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
ALIMENTARY SYSTEM CONT				
Edema	1 (2%)	1 (2%)		
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Inflammation, Chronic Active	1 (2%)	2 (4%)	1 (2%)	
Ulcer			1 (2%)	
Stomach, Glandular	(50)	(50)	(50)	(50)
Erosion	1 (2%)	1 (2%)	2 (4%)	5 (10%)
Mineralization			1 (2%)	
Ulcer	1 (2%)			1 (2%)
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	24 (48%)	19 (38%)	16 (32%)	21 (42%)
Fibrosis	1 (2%)			
Thrombosis		1 (2%)	2 (4%)	1 (2%)
Epicardium, Inflammation, Chronic Active	1 (2%)			
Pericardium, Inflammation, Chronic Active			1 (2%)	
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Angiectasis	23 (46%)	6 (12%)	12 (24%)	19 (38%)
Degeneration			1 (2%)	
Hemorrhage	1 (2%)			
Hyperplasia	7 (14%)	6 (12%)	10 (20%)	7 (14%)
Hypertrophy		1 (2%)		
Necrosis				2 (4%)
Thrombosis				1 (2%)
Vacuolization Cytoplasmic	4 (8%)	1 (2%)	2 (4%)	6 (12%)
Capsule, Fibrosis	1 (2%)			
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	2 (4%)		3 (6%)	1 (2%)
Pituitary Gland	(50)	(50)	(50)	(50)
Angiectasis	6 (12%)	4 (8%)	3 (6%)	5 (10%)
Cyst	19 (38%)	13 (26%)	14 (28%)	15 (30%)
Hyperplasia	20 (40%)	23 (46%)	16 (32%)	16 (32%)
Craniopharyngeal Duct, Hyperplasia	1 (2%)			
Pars Nervosa, Hyperplasia	1 (2%)			
Thyroid Gland	(50)	(50)	(50)	(50)
C Cell, Hyperplasia	36 (72%)	25 (50%)	37 (74%)	32 (64%)

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

B 12

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral Gland	(49)	(48)	(50)	(49)
Cyst	1 (2%)	4 (8%)	5 (10%)	1 (2%)
Hyperplasia	10 (20%)	7 (15%)	10 (20%)	2 (4%)
Inflammation, Chronic Active	6 (12%)	2 (4%)	5 (10%)	8 (17%)
Ovary	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		
Cyst			1 (2%)	
Mineralization			1 (2%)	
Follicle, Cyst	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Periovarian Tissue, Cyst	4 (8%)	3 (6%)	2 (4%)	3 (6%)
Uterus	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Hydrometra	2 (4%)	2 (4%)	2 (4%)	2 (4%)
Inflammation, Chronic Active		2 (4%)		
Cervix, Fibrosis	1 (2%)		1 (2%)	1 (2%)
Cervix, Inflammation, Chronic Active			3 (6%)	1 (2%)
Endometrium, Hyperplasia, Cystic	4 (8%)	1 (2%)	3 (6%)	3 (6%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Atrophy	1 (2%)	1 (2%)		1 (2%)
Hyperplasia	12 (24%)	11 (22%)	12 (24%)	25 (50%)
Myelofibrosis	1 (2%)			
Lymph Node	(6)	(1)	(5)	(1)
Mediastinal, Hyperplasia			1 (20%)	
Lymph Node, Mandibular	(50)	(49)	(50)	(50)
Ectasia	1 (2%)	1 (2%)		1 (2%)
Hyperplasia			1 (2%)	
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Ectasia		1 (2%)		1 (2%)
Spleen	(50)	(50)	(50)	(50)
Accessory Spleen				1 (2%)
Fibrosis	1 (2%)	1 (2%)	1 (2%)	
Hematopoietic Cell Proliferation	1 (2%)	8 (16%)	7 (14%)	5 (10%)
Capsule, Necrosis				1 (2%)

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

B 13

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANALOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(50)
Galactocele	13 (26%)	9 (18%)	9 (18%)	9 (18%)
Hyperplasia	8 (16%)	11 (22%)	9 (18%)	6 (12%)
Inflammation, Chronic Active		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Parakeratosis		1 (2%)		
Ulcer		1 (2%)		
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteosclerosis	1 (2%)	1 (2%)	1 (2%)	1 (2%)
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)		
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Congestion			1 (2%)	
Hemorrhage		1 (2%)	2 (4%)	
Inflammation, Chronic Active	5 (10%)	4 (8%)	4 (8%)	4 (8%)
Necrosis			1 (2%)	
Pigmentation			1 (2%)	
Alveolar Epithelium, Hyperplasia	6 (12%)	3 (6%)	4 (8%)	6 (12%)
Mediastinum, Inflammation			1 (2%)	
Nose	(50)	(50)	(50)	(50)
Inflammation		1 (2%)		
Inflammation, Chronic Active	1 (2%)		2 (4%)	1 (2%)
Thrombosis		3 (6%)	1 (2%)	2 (4%)
Olfactory Epithelium, Atrophy			1 (2%)	19 (38%)
Olfactory Epithelium, Metaplasia				47 (94%)
SPECIAL SENSES SYSTEM				
Eye	(4)	(1)	(3)	(1)
Cataract	4 (100%)	1 (100%)	3 (100%)	1 (100%)
Lens, Mineralization	3 (75%)		2 (67%)	
Retina, Degeneration	3 (75%)	1 (100%)	3 (100%)	1 (100%)
Zymbal's Gland			(1)	

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

B 14

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
SPECIAL SENSES SYSTEM - CONT				
Inflammation, Chronic Active			1 (100%)	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Accumulation, Hyaline Droplet	2 (4%)		1 (2%)	
Congestion		1 (2%)		
Hydronephrosis				1 (2%)
Inflammation, Chronic Active	3 (6%)	9 (18%)	5 (10%)	3 (6%)
Necrosis	1 (2%)			
Nephropathy	29 (58%)	27 (54%)	29 (58%)	25 (50%)
Pigmentation	3 (6%)	3 (6%)	2 (4%)	
Renal Tubule, Hyperplasia		1 (2%)		
Urinary Bladder	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)		
Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	
Transitional Epithelium, Hyperplasia				1 (2%)

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

C 01

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Natural Death	12	3	6	6
Moribund Sacrifice	13	13	9	12
Dosing Accident				1
Survivors				
Natural Death			1	
Terminal Sacrifice	25	34	34	31
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Intestine Large, Colon	(50)	(50)	(50)	(50)
Inflammation, Chronic Active			1 (2%)	
Parasite Metazoan		1 (2%)	1 (2%)	
Pigmentation			1 (2%)	
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan	10 (20%)	8 (16%)	7 (14%)	5 (10%)
Intestine Large, Cecum	(49)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)			
Epithelium, Atrophy			1 (2%)	
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Inflammation, Chronic Active		1 (2%)	1 (2%)	
Parasite Metazoan		1 (2%)		
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Inflammation, Chronic Active			2 (4%)	
Intestine Small, Ileum	(50)	(50)	(49)	(50)
Inflammation, Chronic Active			2 (4%)	
Parasite Metazoan	1 (2%)			
Liver	(50)	(50)	(50)	(49)
Angiectasis	2 (4%)	4 (8%)	7 (14%)	4 (8%)
Basophilic Focus	26 (52%)	33 (66%)	35 (70%)	13 (27%)
Clear Cell Focus	8 (16%)	16 (32%)	16 (32%)	4 (8%)
Congestion	1 (2%)		1 (2%)	
Cyst				1 (2%)
Degeneration, Cystic	3 (6%)	7 (14%)	5 (10%)	6 (12%)
Eosinophilic Focus	10 (20%)	8 (16%)	9 (18%)	7 (14%)
Fatty Change	23 (46%)	18 (36%)	21 (42%)	9 (18%)
Hematopoietic Cell Proliferation				1 (2%)
Hepatodiaphragmatic Nodule	8 (16%)	5 (10%)	9 (18%)	6 (12%)
Inclusion Body Intracytoplasmic				1 (2%)
Inflammation, Chronic Active	16 (32%)	21 (42%)	29 (58%)	10 (20%)
Mixed Cell Focus	16 (32%)	23 (46%)	22 (44%)	10 (20%)
Necrosis	4 (8%)	1 (2%)		3 (6%)

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

C 02

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
ALIMENTARY SYSTEM - CONT				
Thrombosis		1 (2%)		
Vacuolization Cytoplasmic	14 (28%)	18 (36%)	23 (46%)	28 (57%)
Bile Duct, Fibrosis	1 (2%)			
Bile Duct, Hyperplasia	42 (84%)	48 (96%)	48 (96%)	36 (73%)
Mesentery	(13)	(13)	(11)	(12)
Artery, Inflammation, Chronic Active	1 (8%)			
Fat, Inflammation, Chronic Active	8 (62%)	12 (92%)	11 (100%)	9 (75%)
Fat, Mineralization		1 (8%)		
Fat, Necrosis	1 (8%)	1 (8%)		1 (8%)
Pancreas	(50)	(49)	(50)	(50)
Cytoplasmic Alteration	2 (4%)		3 (6%)	
Fibrosis		1 (2%)		
Hyperplasia	4 (8%)	10 (20%)	11 (22%)	12 (24%)
Acinus, Atrophy	10 (20%)	13 (27%)	12 (24%)	14 (28%)
Artery, Inflammation, Chronic Active	1 (2%)		1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(50)
Erosion	1 (2%)			
Hyperkeratosis	1 (2%)			
Hyperplasia	3 (6%)	3 (6%)		1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)		
Perforation	1 (2%)			
Ulcer	2 (4%)	2 (4%)	2 (4%)	
Epithelium, Hyperplasia			1 (2%)	
Stomach, Glandular	(50)	(50)	(50)	(50)
Erosion	3 (6%)		5 (10%)	2 (4%)
Mineralization	1 (2%)			
Ulcer	4 (8%)			
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(49)	(50)	(50)
Inflammation, Chronic Active	1 (2%)	1 (2%)		
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	43 (86%)	48 (96%)	41 (82%)	46 (92%)
Fibrosis	1 (2%)		1 (2%)	
Thrombosis	3 (6%)	1 (2%)	1 (2%)	3 (6%)
Artery, Inflammation, Chronic Active	1 (2%)			
Endocardium, Hyperplasia				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Angiectasis	5 (10%)	3 (6%)	12 (24%)	9 (18%)
Atrophy	1 (2%)		1 (2%)	
Degeneration, Cystic			1 (2%)	

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

C 03

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
ENDOCRINE SYSTEM - CONT				
Hematopoietic Cell Proliferation				2 (4%)
Hyperplasia	9 (18%)	10 (20%)	11 (22%)	8 (16%)
Necrosis			1 (2%)	
Pigmentation			1 (2%)	
Thrombosis			1 (2%)	
Vacuolization Cytoplasmic	8 (16%)	3 (6%)	3 (6%)	5 (10%)
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	11 (22%)	5 (10%)	7 (14%)	7 (14%)
Mineralization		1 (2%)		
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Parathyroid Gland	(46)	(46)	(50)	(50)
Fibrosis		1 (2%)		
Hyperplasia, Focal			1 (2%)	
Pituitary Gland	(50)	(50)	(50)	(50)
Angiectasis	2 (4%)		3 (6%)	
Atrophy	1 (2%)		1 (2%)	
Cyst	5 (10%)	5 (10%)	7 (14%)	1 (2%)
Hyperplasia	13 (26%)	17 (34%)	16 (32%)	10 (20%)
Craniopharyngeal Duct, Hyperplasia		1 (2%)		
Thyroid Gland	(50)	(50)	(50)	(50)
C-Cell, Hyperplasia	23 (46%)	29 (58%)	35 (70%)	29 (58%)
Follicle, Cyst	1 (2%)			
Follicular Cell, Hyperplasia	3 (6%)			1 (2%)
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)		1 (2%)	
Preputial Gland	(50)	(50)	(50)	(49)
Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Inflammation, Chronic Active	41 (82%)	45 (90%)	46 (92%)	45 (92%)
Prostate	(50)	(50)	(50)	(50)
Atrophy		1 (2%)	1 (2%)	3 (6%)
Cyst	1 (2%)			
Hyperplasia			5 (10%)	2 (4%)
Inflammation	25 (50%)	25 (50%)	17 (34%)	24 (48%)
Seminal Vesicle	(50)	(50)	(50)	(50)
Atrophy	1 (2%)	2 (4%)	1 (2%)	4 (8%)
Inflammation, Chronic Active	1 (2%)			
Testes	(50)	(50)	(50)	(50)

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

C 04

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
GENITAL SYSTEM - CONT				
Atrophy	6 (12%)	6 (12%)	5 (10%)	2 (4%)
Mineralization	1 (2%)			
Necrosis			1 (2%)	
Interstitial Cell, Hyperplasia	9 (18%)	6 (12%)	4 (8%)	3 (6%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hyperplasia	17 (34%)	14 (28%)	19 (38%)	20 (40%)
Myelofibrosis	1 (2%)			
Lymph Node	(7)	(3)	(3)	(4)
Mediastinal, Congestion	1 (14%)			
Mediastinal, Ectasia			1 (33%)	
Mediastinal, Inflammation, Chronic Active			1 (33%)	
Renal, Congestion			1 (33%)	
Renal, Ectasia		1 (33%)		
Renal, Inflammation, Chronic Active			1 (33%)	
Lymph Node, Mandibular	(49)	(50)	(49)	(49)
Ectasia	1 (2%)	4 (8%)	1 (2%)	4 (8%)
Hyperplasia	1 (2%)			
Hyperplasia, Plasma Cell	2 (4%)	1 (2%)		2 (4%)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Congestion	1 (2%)			
Ectasia	2 (4%)	3 (6%)	1 (2%)	4 (8%)
Inflammation, Chronic Active			2 (4%)	
Spleen	(50)	(50)	(50)	(49)
Accessory Spleen			1 (2%)	
Angiectasis		1 (2%)		
Fibrosis	6 (12%)	4 (8%)	4 (8%)	4 (8%)
Hematopoietic Cell Proliferation	4 (8%)	3 (6%)	3 (6%)	7 (14%)
Hemorrhage	1 (2%)			
Hyperplasia, Histiocytic				1 (2%)
Necrosis	1 (2%)		1 (2%)	1 (2%)
Capsule, Fibrosis		1 (2%)		
Capsule, Inflammation, Chronic Active				1 (2%)
Thymus	(49)	(47)	(45)	(50)
Cyst	1 (2%)			
INTEGUMENTARY SYSTEM				
Mammary Gland	(46)	(50)	(49)	(49)
Galactocele		5 (10%)		1 (2%)
Hyperplasia	2 (4%)	3 (6%)	4 (8%)	4 (8%)
Skin	(49)	(50)	(50)	(50)
Cyst Epithelial Inclusion	1 (2%)			

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

C 05

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
INTEGUMENTARY SYSTEM - CONT				
Hyperkeratosis			2 (4%)	1 (2%)
Hyperplasia			2 (4%)	
Inflammation, Chronic Active			1 (2%)	1 (2%)
Parakeratosis			1 (2%)	
Subcutaneous Tissue, Fibrosis			1 (2%)	
Subcutaneous Tissue, Inflammation, Chronic Active			1 (2%)	
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hydrocephalus				1 (2%)
Necrosis	2 (4%)		1 (2%)	
Artery, Inflammation, Chronic Active	1 (2%)			
Spinal Cord	(1)	(2)	(1)	(1)
Hemorrhage				1 (100%)
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)		
Congestion		2 (4%)	1 (2%)	
Edema		1 (2%)		
Hemorrhage	4 (8%)		2 (4%)	
Inflammation, Chronic Active	3 (6%)	3 (6%)	4 (8%)	6 (12%)
Leukocytosis			1 (2%)	
Alveolar Epithelium, Hyperplasia	3 (6%)	8 (16%)	6 (12%)	4 (8%)
Nose	(50)	(50)	(49)	(50)
Abscess				1 (2%)
Inflammation, Chronic Active	6 (12%)	7 (14%)	6 (12%)	6 (12%)
Thrombosis	2 (4%)	1 (2%)		1 (2%)
Olfactory Epithelium, Atrophy				48 (96%)
Olfactory Epithelium, Metaplasia				47 (94%)

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

C 06

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
SPECIAL SENSES SYSTEM				
Eye	(1)	(1)		
Cataract		1 (100%)		
Degeneration	1 (100%)			
Lens, Mineralization		1 (100%)		
Retina, Atrophy		1 (100%)		
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Cyst		2 (4%)	1 (2%)	
Fibrosis			1 (2%)	
Infarct	1 (2%)		1 (2%)	
Inflammation, Chronic Active	13 (26%)	25 (50%)	22 (44%)	18 (36%)
Mineralization				1 (2%)
Nephropathy	44 (88%)	48 (96%)	46 (92%)	47 (94%)
Pigmentation		2 (4%)	3 (6%)	1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)		
Inflammation, Chronic Active		1 (2%)		

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

C 07

END OF REPORT

FINAL#1 2 YEAR CHRONIC RATS

Facility: Battelle Columbus Laboratory

Chemical CAS #: 126-98-7

Lock Date: 05/05/99

Cage Range: All

Reasons For Removal: All

Removal Date Range: All

Treatment Groups: Include All

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

C 09

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	4	10	9	7
Natural Death	7	6	6	7
Dosing Accident	1	1	1	
Survivors				
Terminal Sacrifice	38	33	34	35
Natural Death				1
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Periesophageal Tissue, Lipoma				1 (2%)
Intestine Large, Colon	(50)	(50)	(50)	(50)
Polyp Adenomatous		1 (2%)		1 (2%)
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Intestine Small, Ileum	(50)	(50)	(50)	(50)
Liver	(50)	(49)	(48)	(50)
Hepatocellular Adenoma	1 (2%)			
Histiocytic Sarcoma			1 (2%)	
Mesentery	(7)	(2)	(8)	(4)
Lipoma				1 (25%)
Fat, Histiocytic Sarcoma			1 (13%)	
Pancreas	(50)	(50)	(50)	(50)
Histiocytic Sarcoma			1 (2%)	
Salivary Glands	(50)	(50)	(50)	[illegible]
Stomach, Glandular	(50)	(50)	(50)	(50)
Adenoma		1 (2%)		
Tongue				(1)
Squamous Cell Papilloma				1 (100%)
CARDIOVASCULAR SYSTEM				
Blood Vessel	(49)	(50)	(50)	(50)
Heart	(50)	(50)	(50)	(50)

C 10

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			
Adrenal Medulla	(50)	(50)	(50)	(50)
Pheochromocytoma Benign	1 (2%)	3 (6%)	2 (4%)	1 (2%)
Islets, Pancreatic	(50)	(50)	(50)	(50)
Adenoma		1 (2%)	1 (2%)	
Parathyroid Gland	(48)	(47)	(46)	(47)
Adenoma	1 (2%)			
Pituitary Gland	(50)	(50)	(50)	(50)
Adenoma	12 (24%)	14 (28%)	19 (38%)	14 (28%)
Carcinoma	1 (2%)			
Pars Intermedia, Adenoma				1 (2%)
Thyroid Gland	(50)	(50)	(50)	(50)
Bilateral, C-Cell, Adenoma				1 (2%)
C-Cell, Adenoma	3 (6%)	8 (16%)	5 (10%)	7 (14%)
C Cell, Carcinoma	2 (4%)	1 (2%)	1 (2%)	
Follicular Cell, Carcinoma	1 (2%)			
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral Gland	(49)	(48)	(50)	(48)
Adenoma	2 (4%)			
Carcinoma	1 (2%)	2 (4%)	1 (2%)	
Hemangiosarcoma	1 (2%)			
Ovary	(50)	(50)	(50)	(50)
Granulosa Cell Tumor Malignant	1 (2%)			
Histiocytic Sarcoma			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Adenoma				1 (2%)
Carcinoma		1 (2%)		
Deciduoma Benign				1 (2%)
Leiomyosarcoma				1 (2%)
Polyp Stromal	6 (12%)	8 (16%)	9 (18%)	8 (16%)
Polyp Stromal, Multiple				3 (6%)
Sarcoma Stromal			1 (2%)	2 (4%)
Cervix, Polyp Stromal	1 (2%)			
Cervix, Sarcoma Stromal		1 (2%)		
Vagina				(2)
Leiomyoma				1 (50%)
Sarcoma Stromal				1 (50%)

C 11

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Histiocytic Sarcoma			1 (2%)	
Lymph Node	(0)	(0)	(0)	(0)
Lymph Node, Mandibular	(50)	(49)	(50)	(50)
Carcinoma, Metastatic, Mammary Gland	1 (2%)			
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(50)
Thymus	(48)	(49)	(47)	(47)
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			
Carcinoma	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Fibroadenoma	16 (32%)	17 (34%)	10 (20%)	16 (32%)
Fibroadenoma, Multiple	5 (10%)	9 (18%)	9 (18%)	7 (14%)
Skin	(50)	(50)	(50)	(50)
Basal Cell Adenoma	1 (2%)	1 (2%)		
Squamous Cell Papilloma	1 (2%)			
Subcutaneous Tissue, Fibroma				2 (4%)
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Carcinoma, Metastatic, Pituitary Gland	1 (2%)			
Glioma Malignant			1 (2%)	
Oligodendroglioma Benign	1 (2%)			
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma				2 (4%)
Carcinoma, Metastatic, Mammary Gland	1 (2%)		1 (2%)	
Carcinoma, Metastatic, Thyroid Gland	2 (4%)			
Histiocytic Sarcoma			1 (2%)	
Nephroblastoma, Metastatic, Kidney				1 (2%)

C 12

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
SPECIAL SENSES SYSTEM				
Zymbal's Gland			(1)	
Adenoma			1 (100%)	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Nephroblastoma				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
Transitional Epithelium, Papilloma			1 (2%)	
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Histiocytic Sarcoma			1 (2%)	
Leukemia Mononuclear	21 (42%)	19 (38%)	16 (32%)	19 (38%)

* Number of animals with any tissue examined microscopically

C 13

FISCHER 344 RATS FEMALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	45	45	42	44
Total Primary Neoplasms	84	88	79	84
Total Animals with Benign Neoplasms	35	38	34	37
Total Benign Neoplasms	53	63	57	64
Total Animals with Malignant Neoplasms	26	21	21	24
Total Malignant Neoplasms	31	25	22	25
Total Animals with Metastatic Neoplasms	5		1	1
Total Metastatic Neoplasm	5		1	1
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

C 14

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Natural Death	12	3	6	6
Moribund Sacrifice	13	13	9	12
Dosing Accident				1
Survivors				
Natural Death			1	
Terminal Sacrifice	25	34	34	31
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Intestine Large, Colon	(50)	(50)	(50)	(50)
Polyp Adenomatous	1 (2%)		1 (2%)	
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Polyp Adenomatous		1 (2%)		1 (2%)
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Polyp Adenomatous		1 (2%)		
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Polyp Adenomatous			1 (2%)	
Liver	(50)	(50)	(50)	(49)
Hepatocellular Adenoma	1 (2%)	2 (4%)		
Histiocytic Sarcoma				1 (2%)
Mesentery	(13)	(13)	(11)	(12)
Fat, Sarcoma	1 (8%)			
Fat, Schwannoma Malignant				1 (8%)
Pancreas	(50)	(49)	(50)	(50)
Adenoma	2 (4%)		1 (2%)	2 (4%)
Mixed Tumor Benign			1 (2%)	
Salivary Glands	(50)	(50)	(50)	(50)
Neural Crest Tumor				1 (2%)
Schwannoma Malignant	2 (4%)		1 (2%)	1 (2%)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma				1 (2%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Carcinoma	1 (2%)			
Tongue				(1)
Squamous Cell Papilloma				1 (100%)

D 01

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Histiocytic Sarcoma				1 (2%)
Osteosarcoma, Metastatic, Bone		1 (2%)		
Schwannoma Malignant				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)	2 (4%)		
Osteosarcoma, Metastatic, Bone		1 (2%)		
Adrenal Medulla	(50)	(50)	(50)	(50)
Osteosarcoma, Metastatic, Bone		1 (2%)		
Pheochromocytoma Malignant	1 (2%)	1 (2%)	2 (4%)	
Pheochromocytoma Benign	2 (4%)	6 (12%)	6 (12%)	2 (4%)
Bilateral, Pheochromocytoma Benign	1 (2%)	1 (2%)		
Islets, Pancreatic	(50)	(50)	(50)	(50)
Adenoma		2 (4%)	1 (2%)	1 (2%)
Carcinoma		2 (4%)		
Parathyroid Gland	(46)	(46)	(50)	(50)
Adenoma			1 (2%)	1 (2%)
Pituitary Gland	(50)	(50)	(50)	(50)
Adenoma	17 (24%)	18 (36%)	11 (22%)	20 (40%)
Craniopharyngioma				1 (2%)
Osteosarcoma, Metastatic, Bone		1 (2%)		
Thyroid Gland	(50)	(50)	(50)	(50)
Schwannoma Malignant, Metastatic, Skin	1 (2%)			
Bilateral, C Cell, Adenoma	1 (2%)	2 (4%)	1 (2%)	
C-Cell, Adenoma	8 (16%)	10 (20%)	7 (14%)	6 (12%)
C-Cell, Carcinoma	1 (2%)	1 (2%)	1 (2%)	
Follicular Cell, Adenoma	1 (2%)		2 (4%)	
Follicular Cell, Carcinoma		1 (2%)	1 (2%)	2 (4%)
GENERAL BODY SYSTEM				
Tissue NOS		(1)	(1)	
Chemodectoma Benign			1 (100%)	
Osteosarcoma, Metastatic, Bone		1 (100%)		

D.02

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Preputial Gland	(50)	(50)	(50)	(49)
Adenoma	2 (4%)	1 (2%)	4 (8%)	4 (8%)
Carcinoma	1 (2%)	1 (2%)	3 (6%)	2 (4%)
Prostate	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			1 (2%)
Seminal Vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Hemangiosarcoma				1 (2%)
Bilateral, Interstitial Cell, Adenoma	34 (68%)	40 (80%)	43 (86%)	45 (90%)
Interstitial Cell, Adenoma	6 (12%)	5 (10%)	4 (8%)	1 (2%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Histiocytic Sarcoma				1 (2%)
Lymph Node	(7)	(3)	(3)	(4)
Osteosarcoma, Metastatic, Bone		1 (33%)		
Inguinal, Fibrosarcoma, Metastatic, Skin				1 (25%)
Mediastinal, Histiocytic Sarcoma				1 (25%)
Lymph Node, Mandibular	(49)	(50)	(49)	(49)
Neural Crest Tumor, Metastatic, Lymph Node, Mandibular				1 (2%)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Carcinoma	1 (2%)			
Histiocytic Sarcoma				1 (2%)
Spleen	(50)	(50)	(50)	(49)
Hemangiosarcoma		1 (2%)	1 (2%)	
Histiocytic Sarcoma				1 (2%)
Leiomyoma		1 (2%)		
Thymus	(49)	(47)	(45)	(50)
INTEGUMENTARY SYSTEM				
Mammary Gland	(46)	(50)	(49)	(49)
Fibroadenoma	2 (4%)	6 (12%)	2 (4%)	8 (16%)
Fibroadenoma, Multiple		1 (2%)		
Skin	(49)	(50)	(50)	(50)
Basal Cell Adenoma			1 (2%)	
Basal Cell Carcinoma			1 (2%)	
Carcinoma, Metastatic, Nose				1 (2%)
Hemangiosarcoma		1 (2%)		
Keratoacanthoma		4 (8%)	3 (6%)	2 (4%)
Keratoacanthoma, Multiple	1 (2%)	1 (2%)		

D 03

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
INTEGUMENTARY SYSTEM - cont				
Sarcoma		1 (2%)		
Squamous Cell Carcinoma	1 (2%)			
Subcutaneous Tissue, Fibroma	3 (6%)	3 (6%)	2 (4%)	5 (10%)
Subcutaneous Tissue, Fibroma, Multiple		1 (2%)		
Subcutaneous Tissue, Fibrosarcoma			1 (2%)	2 (4%)
Subcutaneous Tissue, Fibrous Histiocytoma				1 (2%)
Subcutaneous Tissue, Lipoma	1 (2%)		1 (2%)	
Subcutaneous Tissue, Neural Crest Tumor, Metastatic, Skin				1 (2%)
Subcutaneous Tissue, Schwannoma Malignant, Metastatic, Salivary Glands	2 (4%)			1 (2%)
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteoma		1 (2%)		
Cranium, Osteosarcoma	1 (2%)			
Vertebra, Osteosarcoma		1 (2%)		
Skeletal Muscle	(1)	(1)		
Rhabdomyosarcoma	1 (100%)			
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Astrocytoma Malignant			1 (2%)	
Carcinoma, Metastatic, Zymbal's Gland		1 (2%)		
Oligodendroglioma Malignant		1 (2%)		
Meninges, Osteosarcoma, Metastatic, Bone	1 (2%)			
Spinal Cord	(1)	(2)	(1)	(1)
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma		3 (6%)	1 (2%)	1 (2%)
Alveolar/Bronchiolar Carcinoma			1 (2%)	
Histiocytic Sarcoma				1 (2%)
Osteosarcoma, Metastatic, Bone		1 (2%)		
Pheochromocytoma Malignant, Metastatic, Adrenal Medulla			1 (2%)	
Schwannoma Malignant, Metastatic, Skin	1 (2%)			
Mediastinum, Osteosarcoma, Metastatic, Bone		1 (2%)		
Nose	(50)	(50)	(49)	(50)
Osteosarcoma, Metastatic, Bone		1 (2%)		
Respiratory Epithelium, Squamous Cell				

D 04

FISCHER 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	49	50	49	49
Total Primary Neoplasms	116	146	124	133
Total Animals with Benign Neoplasms	47	49	49	47
Total Benign Neoplasms	85	114	95	104
Total Animals with Malignant Neoplasms	29	30	24	26
Total Malignant Neoplasms	31	32	29	28
Total Animals with Metastatic Neoplasms	3	2	1	4
Total Metastatic Neoplasm	5	10	1	5
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				1
Total Uncertain Neoplasms				1

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

F/CHEP 344 RATS MALE	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
RESPIRATORY SYSTEM - cont				
Carcinoma				1 (2%)
SPECIAL SENSES SYSTEM				
Zymbal's Gland		(2)		(1)
Adenoma		1 (50%)		
Carcinoma		1 (50%)		1 (100%)
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Histiocytic Sarcoma				1 (2%)
Renal Tubule, Adenoma		1 (2%)		1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Histiocytic Sarcoma				1 (2%)
Leukemia Mononuclear	20 (40%)	20 (40%)	14 (28%)	12 (24%)
Mesothelioma Malignant			2 (4%)	2 (4%)

* Number of animals with any tissue examined microscopically

D 06

END OF REPORT

D 07

D.08

FINAL#1 2 YEAR CHRONIC RATS

REASONS FOR REMOVAL: ALL

REMOVAL DATE RANGE: ALL

TREATMENT GROUPS: INCLUDE ALL

D 09

NTP
LAB: Battelle Columbus

STATISTICAL ANALYSIS OF PRIMARY TUMORS
METHACRYLONITRILE

REPORT: PEIRPTOP
DATE: 02/24/00

EXPERIMENT: 88050 TEST: 05
TEST TYPE: CHRONIC
CONT: N01-ES-55388
PATHOLOGIST: YARRINGTON, JOHN

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

TIME: 14:19:04

NTP C#: 88050B
CAS: 126-98-7

Rats(FISCHER 344)

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
Heart
Islets, Pancreatic
Kidney
Liver
Lung
Nose
Ovary
Pancreas
Parathyroid Gland
Pituitary Gland
Prostate
Salivary Glands
Spleen
Testes
Thyroid Gland
Urinary Bladder

D 10

NTP
LAB: Battelle Columbus
EXPERIMENT: 88050 TEST: 05
TEST TYPE: CHRONIC
CONT: NO1-ES-55388
PATHOLOGIST: YARRINGTON, JOHN

STATISTICAL ANALYSIS OF PRIMARY TUMORS
METHACRYLONITRILE

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

REPORT: PLIRPT08
DATE: 02/24/06
TIME: 14 19 06

NTP C#: 880508
CAS: 126-98-7

SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS
IN THE ANALYSIS OF METHACRYLONITRILE

Male Rats

Organ	Morphology
Mammary Gland	Fibroadenoma
	Fibroma, Fibroadenoma or Adenoma
	Fibroma, Fibroadenoma, Carcinoma, or Adenoma
Testes	Adenoma
All Organs	Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated
	Malignant and Benign Tumors

Female Rats

Organ	Morphology
Lung	Alveolar/Bronchiolar Adenoma
	Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma
Pituitary Gland: Pars Distalis or Unspecified Site	Adenoma
Skin	Fibroma
	Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma

D 11

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Adrenal Cortex Adenoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	4.4%	0.0%	0.0%	2.1%	0.0%	0.0%	0.0%
TERMINAL (d)	1/25 (4%)	1/34 (3%)	0/35 (0%)	0/31 (0%)	1/38 (3%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	729 (T)	592	---	---	731 (T)	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.199N	P=0.584	P=0.433N	P=0.457N	P=0.474N	P=0.528N	P=0.522N	P=0.511N
POLY 3	P=0.203N	P=0.537	P=0.483N	P=0.490N	P=0.463N	P=0.513N	P=0.516N	P=0.511N
POLY 1.5	P=0.205N	P=0.524	P=0.490N	P=0.493N	P=0.467N	P=0.508N	P=0.511N	P=0.507N
POLY 6	P=0.200N	P=0.555	P=0.473N	P=0.484N	P=0.459N	P=0.519N	P=0.520N	P=0.515N
LOGISTIC REGRESSION	P=0.209N	P=0.502	(e)	(e)	P=0.474N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.209N	P=0.500	P=0.500N	P=0.500N	P=0.474N	P=0.500N	P=0.500N	P=0.500N

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Adrenal Medulla Pheochromocytoma Benign								
TUMOR RATES								
OVERALL (a)	3/50 (6%)	7/50 (14%)	6/50 (12%)	2/50 (4%)	1/50 (2%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
POLY-3 ADJUSTED (b)	7.3%	15.5%	13.5%	4.6%	2.1%	6.8%	4.7%	2.3%
TERMINAL (d)	2/25 (8%)	6/34 (18%)	6/35 (17%)	1/31 (3%)	0/38 (0%)	2/33 (6%)	2/34 (6%)	1/36 (3%)
FIRST INCIDENCE	716	697	729 (T)	680	718	441	731 (T)	731 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.152N	P=0.299	P=0.425	P=0.415N	P=0.421N	P=0.270	P=0.456	P=0.743
POLY 3	P=0.167N	P=0.199	P=0.283	P=0.475N	P=0.440N	P=0.288	P=0.473	P=0.749
POLY 1.5	P=0.172N	P=0.185	P=0.266	P=0.483N	P=0.433N	P=0.295	P=0.480	P=0.752
POLY 6	P=0.158N	P=0.221	P=0.310	P=0.461N	P=0.447N	P=0.279	P=0.464	P=0.743
LOGISTIC REGRESSION	P=0.164N	P=0.249	P=0.387	P=0.458N	P=0.416N	P=0.363	P=0.463	P=0.746
COCH-ARM / FISHERS	P=0.185N	P=0.159	P=0.243	P=0.500N	P=0.419N	P=0.309	P=0.500	P=0.753N

D 12

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Adrenal Medulla								
Pheochromocytoma Malignant								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	2.2%	4.5%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/25 (4%)	0/34 (0%)	2/35 (6%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	729 (T)	536	729 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.320N	P=0.719N	P=0.617	P=0.457N	(e)	(e)	(e)	(e)
POLY 3	P=0.333N	P=0.736N	P=0.529	P=0.490N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.332N	P=0.744N	P=0.517	P=0.493N	(e)	(e)	(e)	(e)
POLY 6	P=0.332N	P=0.724N	P=0.547	P=0.484N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.334N	P=0.735	P=0.617	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.333N	P=0.753N	P=0.500	P=0.500N	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Adrenal Medulla								
Pheochromocytoma: Benign, Complex, Malignant, NOS								
TUMOR RATES								
OVERALL (a)	4/50 (8%)	8/50 (16%)	8/50 (16%)	2/50 (4%)	1/50 (2%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
POLY-3 ADJUSTED (b)	9.8%	17.5%	18.0%	4.6%	2.1%	6.8%	4.7%	2.3%
TERMINAL (d)	3/25 (12%)	6/34 (18%)	8/35 (23%)	1/31 (3%)	0/38 (0%)	2/33 (6%)	2/34 (6%)	1/36 (3%)
FIRST INCIDENCE	716	536	729 (T)	680	718	441	731 (T)	731 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.089N	P=0.335	P=0.372	P=0.254N	P=0.421N	P=0.270	P=0.456	P=0.743
POLY 3	P=0.101N	P=0.235	P=0.217	P=0.311N	P=0.440N	P=0.288	P=0.471	P=0.748
POLY 1.5	P=0.104N	P=0.213	P=0.201	P=0.320N	P=0.433N	P=0.295	P=0.480	P=0.752
POLY 6	P=0.095N	P=0.264	P=0.245	P=0.297N	P=0.447N	P=0.279	P=0.464	P=0.743
LOGISTIC REGRESSION	P=0.104N	P=0.232	P=0.333	P=0.290N	P=0.416N	P=0.363	P=0.461	P=0.746
COCH-ARM / FISHERS	P=0.114N	P=0.178	P=0.178	P=0.339N	P=0.419N	P=0.309	P=0.500	P=0.753N

D13

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Bone								
Osteosarcoma or Osteoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	4.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	1/34 (3%)	0/35 (0%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	474	716	---	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.201N	P=0.566	P=0.500N	P=0.500N	(e)	(e)	(e)	(e)
POLY 3	P=0.205N	P=0.528	P=0.497N	P=0.493N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.206N	P=0.519	P=0.492N	P=0.495N	(e)	(e)	(e)	(e)
POLY 6	P=0.202N	P=0.541	P=0.478N	P=0.489N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.218N	P=0.451	P=0.591N	P=0.605N	(e)	(e)	(e)	(e)
COCH ARM / FISHERS	P=0.209N	P=0.500	P=0.500N	P=0.500N	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Clitoral/Preputial Gland								
Adenoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	1/50 (2%)	4/50 (8%)	4/49 (8%)	2/49 (4%)	0/48 (0%)	0/50 (0%)	0/48 (0%)
POLY-3 ADJUSTED (b)	4.9%	2.2%	9.0%	9.5%	4.4%	0.0%	0.0%	0.0%
TERMINAL (d)	2/25 (8%)	1/34 (3%)	4/35 (11%)	3/30 (10%)	2/37 (5%)	0/31 (0%)	0/34 (0%)	0/34 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	681	731 (T)	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.181	P=0.393N	P=0.500	P=0.418	P=0.246N	P=0.278N	P=0.257N	P=0.252N
POLY 3	P=0.169	P=0.466N	P=0.376	P=0.352	P=0.231N	P=0.258N	P=0.251N	P=0.255N
POLY 1.5	P=0.170	P=0.478N	P=0.360	P=0.344	P=0.235N	P=0.252N	P=0.249N	P=0.253N
POLY 6	P=0.170	P=0.451N	P=0.401	P=0.365	P=0.227N	P=0.265N	P=0.255N	P=0.260N
LOGISTIC REGRESSION	P=0.173	P=0.393N	P=0.500	P=0.375	P=0.246N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.170	P=0.500N	P=0.339	P=0.329	P=0.243N	P=0.253N	P=0.249N	P=0.253N

D 14

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Clitoral/Preputial Gland Carcinoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	1/50 (2%)	3/50 (6%)	2/49 (4%)	1/49 (2%)	2/48 (4%)	1/50 (2%)	[illegible]
POLY-3 ADJUSTED (b)	2.4%	2.2%	6.6%	4.[illegible]%	2.2%	4.8%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	1/34 (3%)	1/35 (3%)	0/30 (0%)	0/37 (0%)	2/31 (7%)	[illegible]	[illegible]
FIRST INCIDENCE	579	729 (T)	464	466	438	731 (T)	[illegible]	
STATISTICAL TESTS								
LIFE TABLE	P=0.403	P=0.716N	P=0.366	P=0.514	P=0.237N	P=0.457	[illegible]	[illegible]
POLY 3	P=0.402	P=0.741N	P=0.338	P=0.514	P=0.249N	P=0.402	[illegible]	[illegible]
POLY 1.5	P=0.399	P=0.748N	P=0.325	P=0.507	P=0.244N	P=0.474	[illegible]	[illegible]
POLY 6	P=0.408	P=0.733N	P=0.358	P=0.524	P=0.255N	P=0.400	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.360	P=0.748	P=0.258	P=0.415	P=0.219N	P=0.586	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.390	P=0.753N	P=0.309	P=0.492	P=0.232N	P=0.492	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Clitoral/Preputial Gland Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	3/50 (6%)	2/50 (4%)	7/50 (14%)	6/49 (12%)	3/49 (6%)	2/48 (4%)	6/50 (12%)	[illegible]
POLY-3 ADJUSTED (b)	7.2%	4.4%	15.4%	13.9%	6.5%	4.8%	9.3%	[illegible]
TERMINAL (d)	2/25 (8%)	2/34 (6%)	5/35 (14%)	3/30 (10%)	2/37 (5%)	2/31 (7%)	6/34 (18%)	[illegible]
FIRST INCIDENCE	579	729 (T)	464	466	438	731 (T)	731 (T)	
STATISTICAL TESTS								
LIFE TABLE	P=0.141	P=0.381N	P=0.289	P=0.313	P=0.090N	P=0.566N	P=0.335N	P=0.134N
POLY 3	P=0.132	P=0.461N	P=0.196	P=0.263	P=0.090N	P=0.549N	P=0.323N	P=0.137N
POLY 1.5	P=0.129	P=0.474N	P=0.181	P=0.253	P=0.089N	P=0.536N	P=0.322N	P=0.132N
POLY 6	P=0.137	P=0.445N	P=0.221	P=0.279	P=0.091N	P=0.565N	P=0.342N	P=0.142N
LOGISTIC REGRESSION	P=0.125	P=0.470N	P=0.163	P=0.229	P=0.084N	P=0.461N	P=0.240N	P=0.076N
COCH-ARM / FISHERS	P=0.125	P=0.500N	P=0.159	P=0.233	P=0.087N	P=0.510N	P=0.301N	P=0.125N

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Islets, Pancreatic Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	4.4%	2.3%	2.3%	0.0%	2.3%	2.3%	[illegible]
TERMINAL (d)	0/25 (0%)	2/34 (6%)	1/35 (3%)	0/31 (0%)	0/18 (0%)	1/33 (3%)	1/34 (3%)	[illegible]
FIRST INCIDENCE	---	729 (T)	729 (T)	680	---	731 (T)	[illegible] (T)	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.638	P=0.308	P=0.567	P=0.528	P=0.535N	P=[illegible]	P=[illegible]	(e)
POLY 3	P=0.638	P=0.259	P=0.519	P=0.511	P=0.[illegible]N	P=[illegible]	P=[illegible]	(e)
POLY 1.5	P=0.531	P=0.252	P=0.510	P=0.507	P=0.[illegible]N	P=0.492	P=[illegible]	(e)
POLY 6	P=0.648	P=0.270	P=0.527	P=0.517	P=0.[illegible]N	P=[illegible]	P=[illegible]	(e)
LOGISTIC REGRESSION	P=0.625	P=0.308	P=0.567	P=0.502	(e)	P=[illegible]	P=[illegible]	(e)
COCH-ARM / FISHERS	P=0.619	P=0.247	P=0.500	P=0.500	P=0.[illegible]N	P=[illegible]	P=[illegible]	(e)

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Islets, Pancreatic Carcinoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	[illegible]	[illegible] (6%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	4.4%	0.0%	0.0%	0.0%	[illegible]	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	2/34 (6%)	0/35 (0%)	0/31 (0%)	0/18 (0%)	[illegible]	[illegible] (6%)	[illegible]
FIRST INCIDENCE	---	729 (T)	---	---	---			
STATISTICAL TESTS								
LIFE TABLE	P=0.[illegible]N	P=0.308	(e)	(e)	(e)	(e)	(e)	(e)
POLY 3	P=0.348N	P=0.259	(e)	(e)	(e)	(e)	(e)	(e)
POLY 1.5	P=0.355N	P=0.252	(e)	(e)	(e)	(e)	(e)	(e)
POLY 6	P=0.340N	P=0.270	(e)	(e)	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	(e)	P=0.308	(e)	(e)	(e)	(e)	(e)	(e)
COCH ARM / FISHERS	P=0.369N	P=0.247	(e)	(e)	(e)	(e)	(e)	(e)

E 02

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Islets, Pancreatic Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	4/50 (8%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	0.0%	8.9%	2.3%	2.3%	0.0%	2.3%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	4/34 (12%)	1/35 (3%)	0/31 (0%)	0/38 (0%)	1/33 (3%)	[illegible]	[illegible]
FIRST INCIDENCE	---	729 (T)	729 (T)	680	---	731 (T)	[illegible]	
STATISTICAL TESTS								
LIFE TABLE	P=0.440N	P=0.107	P=0.567	P=0.528	P=0.535N	P=0.472	[illegible]	[illegible]
POLY 3	P=0.436N	P=0.073	P=0.516	P=0.511	P=0.550N	P=0.487	[illegible]	[illegible]
POLY 1.5	P=0.445N	P=0.069	P=0.510	P=0.507	P=0.546N	P=0.492	[illegible]	[illegible]
POLY 6	P=0.422N	P=0.080	P=0.527	P=0.517	P=0.555N	[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.455N	P=0.107	P=0.567	P=0.502	(e)	P=0.472	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.465N	P=0.059	P=0.500	P=0.500	P=0.536N	P=0.500	[illegible]	[illegible]

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Liver Hepatocellular Adenoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/49 (0%)	1/50 (2%)	0/49 (0%)	0/48 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	4.4%	0.0%	0.0%	2.3%	0.0%	0.0%	0.0%
TERMINAL (d)	1/25 (4%)	2/34 (6%)	0/35 (0%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/36 (0%)	0/30 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	---	---	589	---		
STATISTICAL TESTS								
LIFE TABLE	P=0.192N	P=0.607	P=0.4[illegible]	P=0.457N	P=0.482N	P=0.517N	P=0.522N	P=0.51[illegible]
POLY 3	P=0.206N	P=0.534	P=0.4[illegible]	P=0.4[illegible]3N	P=0.463N	P=0.516N	P=0.521N	P=0.51[illegible]
POLY 1.5	P=0.208N	P=0.522	P=0.490N	P=0.497N	P=0.469N	P=0.511N	P=0.517N	P=0.509N
POLY 6	P=0.203N	P=0.549	P=0.473N	P=0.488N	P=0.458N	P=0.522N	P=0.524N	P=0.51[illegible]
LOGISTIC REGRESSION	P=0.192N	P=0.607	(e)	(e)	P=0.437N	P=0.424N	P=0.417N	P=0.41[illegible]
COCH-ARM / FISHERS	P=0.213N	P=0.500	P=0.500N	P=0.505N	P=0.473N	P=0.505N	P=0.510N	P=0.500N

E 03

Date: 02/24/00 EXPERIMENT: 8965 TEST: 05

Statistical Analysis of Primary Tumors in Rats/FISCHER 344 METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
	Males				Females			
Lung Alveola /Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	6.6%	2.3%	2.3%	0.0%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	2/34 (6%)	1/33 (3%)	1/31 (3%)	0/38 (0%)	0/31 (0%)	0/31 (0%)	[illegible]
FIRST INCIDENCE	---	674	729 (T)	729 (T)	---		-	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.564N	P=0.175	P=0.567	P=0.542	P=0.044 *	(e)	[illegible]	[illegible]
POLY 3	P=0.559N	P=0.138	P=0.516	P=0.510	P=0.040 *	(e)	[illegible]	[illegible]
POLY 1.5	P=0.566N	P=0.141	P=0.519	P=0.507	P=0.040 *	(e)	[illegible]	[illegible]
POLY 6	P=0.549N	P=0.148	P=0.527	P=0.516	P=0.040 *	(e)	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.575N	P=0.140	P=0.567	P=0.543	P=0.044 *	(e)	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.581N	P=0.121	P=0.500	P=0.500	P=0.042 *	(e)	[illegible]	[illegible]
	Males				Females			
Dose	0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	0 MG/KG	3 MG/KG	[illegible]	[illegible]
Lung Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	6.6%	2.3%	2.3%	0.0%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	2/34 (6%)	1/33 (3%)	1/31 (3%)	0/38 (0%)	0/31 (0%)	0/31 (0%)	[illegible]
FIRST INCIDENCE	-	674	729 (T)	729 (T)	---			[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.564N	P=0.175	P=0.567	P=0.542	P=0.044 *	(e)	[illegible]	[illegible]
POLY 3	P=0.559N	P=0.138	P=0.516	P=0.510	P=0.040 *	(e)	[illegible]	[illegible]
POLY 1.5	P=0.566N	P=0.141	P=0.519	P=0.507	P=0.040 *	(e)	[illegible]	[illegible]
POLY 6	P=0.549N	P=0.148	P=0.527	P=0.516	P=0.040 *	(e)	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.575N	P=0.140	P=0.567	P=0.543	P=0.044 *	(e)	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.581N	P=0.121	P=0.500	P=0.500	P=0.042 *	(e)	[illegible]	[illegible]

E 04

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Mammary Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	6.4%	2.3%	2.3%	2.3%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	0/35 (0%)	0/31 (0%)	3/38 (8%)	0/33 (0%)	1/34 (3%)	1/36 (3%)
FIRST INCIDENCE	--	--	---	---	731 (T)	609	731 (T)	731 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.347N	P=0.353N	P=0.345N	P=0.324N
POLY 3	(e)	(e)	(e)	(e)	P=0.344N	P=0.326N	P=0.335N	P=0.326N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.344N	P=0.318N	P=0.326N	P=0.319N
POLY 6	(e)	(e)	(e)	(e)	P=0.344N	P=0.334N	P=0.342N	P=0.332N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.350N	P=0.305N	P=0.345N	P=0.324N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.342N	P=0.309N	P=0.309N	P=0.309N

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Mammary Gland Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	6.4%	2.3%	2.3%	2.3%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	0/35 (0%)	0/31 (0%)	3/38 (8%)	0/33 (0%)	1/34 (3%)	1/36 (3%)
FIRST INCIDENCE	---	---	---	---	731 (T)	609	731 (T)	731 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.347N	P=0.353N	P=0.345N	P=0.324N
POLY 3	(e)	(e)	(e)	(e)	P=0.344N	P=0.326N	P=0.335N	P=0.326N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.344N	P=0.318N	P=0.326N	P=0.319N
POLY 6	(e)	(e)	(e)	(e)	P=0.344N	P=0.334N	P=0.342N	P=0.332N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.350N	P=0.305N	P=0.345N	P=0.324N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.342N	P=0.309N	P=0.309N	P=0.309N

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - MEHACR/CONTROLS

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Mammary Gland Fibroadenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	7/50 (14%)	2/50 (4%)	8/50 (16%)	21/50 (42%)	26/50 (52%)	19/50 (38%)	[illegible]
POLY-3 ADJUSTED (b)	4.9%	15.4%	4.5%	18.5%	44.9%	57.0%	41.5%	[illegible]
TERMINAL (d)	0/25 (0%)	5/24 (15%)	2/31 (6%)	7/31 (23%)	19/38 (50%)	20/33 (61%)	15/34 (44%)	[illegible]
FIRST INCIDENCE	724	696	729 (1)	680	679	527	651	499
STATISTICAL TESTS								
LIFE TABLE	P=0.100	P=0.168	P=0.583N	P=0.092	P=0.161N	P=0.085	P=0.566	P=0.121N
POLY 3	P=0.089	P=0.105	P=0.664N	P=0.053	P=0.155N	P=0.135	P=0.533N	[illegible]
POLY 1.5	P=0.087	P=0.095	P=0.670N	P=0.051	P=0.134N	P=0.179	P=0.560N	[illegible]
POLY 6	P=0.092	P=0.119	P=0.645N	P=0.058	P=0.153N	P=0.135	P=0.547N	[illegible]
LOGISTIC REGRESSION	P=0.086	P=0.127	P=0.603N	P=0.067	P=0.177N	P=0.121	P=0.579	[illegible]
COCH-ARM / FISHERS	P=0.084	P=0.080	P=0.691N	P=0.046 *	P=0.149N	P=0.212	P=0.419N	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Mammary Gland Fibroma, Fibroadenoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	7/50 (14%)	2/50 (4%)	8/50 (16%)	21/50 (42%)	26/50 (52%)	19/50 (38%)	[illegible]
POLY-3 ADJUSTED (b)	4.9%	15.4%	4.5%	18.5%	44.9%	57.0%	41.5%	39.5%
TERMINAL (d)	0/25 (0%)	5/24 (15%)	2/31 (6%)	7/31 (23%)	19/38 (50%)	20/33 (61%)	15/34 (44%)	[illegible]
FIRST INCIDENCE	724	696	729 (1)	680	679	527	651	499
STATISTICAL TESTS								
LIFE TABLE	P=0.100	P=0.168	P=0.583N	P=0.092	P=0.161N	P=0.085	P=0.566	P=0.140
POLY 3	P=0.089	P=0.105	P=0.664N	P=0.053	P=0.155N	P=0.135	P=0.533N	[illegible]
POLY 1.5	P=0.087	P=0.095	P=0.670N	P=0.051	P=0.134N	P=0.179	P=0.560N	[illegible]
POLY 6	P=0.092	P=0.119	P=0.645N	P=0.058	P=0.153N	P=0.135	P=0.547N	[illegible]
LOGISTIC REGRESSION	P=0.086	P=0.127	P=0.603N	P=0.067	P=0.177N	P=0.121	P=0.579	[illegible]
COCH-ARM / FISHERS	P=0.084	P=0.080	P=0.691N	P=0.046 *	P=0.149N	P=0.212	P=0.419N	[illegible]

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Mammary Gland								
Fibroma, Fibroadenoma, Carcinoma, or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	7/50 (14%)	2/50 (4%)	8/50 (16%)	23/50 (46%)	26/50 (52%)	20/50 (40%)	[illegible]
POLY-3 ADJUSTED (b)	4.9%	15.4%	4.5%	18.5%	48.1%	57.9%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	5/34 (15%)	2/35 (6%)	7/31 (23%)	21/38 (55%)	20/33 (61%)	16/34 (47%)	[illegible]
FIRST INCIDENCE	724	696	729 (T)	680	679	527	651	494
STATISTICAL TESTS								
LIFE TABLE	P=0.100	P=0.166	P=0.583N	P=0.092	P=0.153N	P=0.149	P=0.529N	[illegible]
POLY 3	P=0.089	P=0.105	P=0.664N	P=0.053	P=0.147N	P=0.289	P=0.455N	[illegible]
POLY 1.5	P=0.087	P=0.095	P=0.676N	P=0.051	P=0.147N	P=0.306	P=0.424N	[illegible]
POLY 6	P=0.092	P=0.119	P=0.645N	P=0.058	P=0.144N	P=0.278	P=0.473N	[illegible]
LOGISTIC REGRESSION	P=0.086	P=0.127	P=0.603N	P=0.067	P=0.171N	P=0.217	P=0.[illegible]N	[illegible]
COCH-ARM / FISHERS	P=0.084	P=0.080	P=0.691N	P=0.046 *	P=0.142N	P=0.345	P=0.343N	P=0.[illegible]N

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Pancreas								
Adenoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	0/49 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.9%	0.0%	2.3%	4.6%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	2/25 (8%)	0/34 (0%)	1/35 (3%)	2/31 (7%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	729 (T)	---	729 (T)	729 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.426	P=0.173N	P=0.383N	P=0.616N	(e)	(e)	(e)	(e)
POLY 3	P=0.391	P=0.217N	P=0.471N	P=0.676N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.398	P=0.225N	P=0.483N	P=0.681N	(e)	(e)	(e)	(e)
POLY 6	P=0.385	P=0.207N	P=0.453N	P=0.666N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.426	(e)	P=0.383N	P=0.616N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.407	P=0.253N	P=0.500N	P=0.691N	(e)	(e)	(e)	(e)

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Pituitary Gland: Pars Distalis or Unspecified Site Adenoma								
TUMOR RATES								
OVERALL (a)	17/50 (34%)	18/50 (36%)	11/50 (22%)	20/50 (40%)	12/50 (24%)	14/50 (28%)	19/50 (38%)	14/50 (28%)
POLY-3 ADJUSTED (b)	38.0%	39.1%	23.6%	45.4%	25.7%	31.6%	43.9%	[illegible]
TERMINAL (d)	8/25 (32%)	13/34 (38%)	7/35 (20%)	14/31 (45%)	10/38 (26%)	10/33 (30%)	16/34 (47%)	13/25 (52%)
FIRST INCIDENCE	453	592	464	624	718	609	690	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.359	P=0.337N	P=0.050N	P=0.574N	P=0.458	P=0.269	P=0.042 *	P=0.347
POLY 3	P=0.242	P=0.547	P=0.100N	P=0.312	P=0.418	P=0.341	P=0.052	[illegible]
POLY 1.5	P=0.260	P=0.537	P=0.111N	P=0.330	P=0.431	P=0.369	P=0.064	[illegible]
POLY 6	P=0.229	P=0.565	P=0.085N	P=0.305	P=0.405	P=0.329	P=0.042 *	[illegible]
LOGISTIC REGRESSION	P=0.288	P=0.527	P=0.155N	P=0.374	P=0.405	P=0.298	P=0.033 *	[illegible]
COCH-ARM / FISHERS	P=0.284	P=0.500	P=0.133N	P=0.339	P=0.459	P=0.4[illegible]	P=0.09[illegible]	[illegible]

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Pituitary Gland: Pars Distalis or Unspecified Site Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	17/50 (34%)	18/50 (36%)	11/50 (22%)	20/50 (40%)	13/50 (26%)	14/50 (28%)	19/50 (38%)	[illegible]
POLY-3 ADJUSTED (b)	38.0%	39.1%	23.6%	45.4%	27.8%	31.6%	43.9%	[illegible]
TERMINAL (d)	8/25 (32%)	13/34 (38%)	7/35 (20%)	14/31 (45%)	11/38 (29%)	10/33 (30%)	16/34 (47%)	[illegible]
FIRST INCIDENCE	453	592	464	624	718	609	690	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.359	P=0.337N	P=0.050N	P=0.574N	P=0.514	P=0.342	P=0.07[illegible]	[illegible]
POLY 3	P=0.242	P=0.547	P=0.100N	P=0.312	P=0.478	P=0.434	P=0.082	[illegible]
POLY 1.5	P=0.260	P=0.537	P=0.111N	P=0.330	P=0.490	P=0.458	P=0.098	[illegible]
POLY 6	P=0.229	P=0.565	P=0.085N	P=0.305	P=0.465	P=0.412	P=0.071	[illegible]
LOGISTIC REGRESSION	P=0.288	P=0.527	P=0.155N	P=0.374	P=0.462	P=0.379	P=0.061	[illegible]
COCH-ARM / FISHERS	P=0.284	P=0.500	P=0.133N	P=0.339	P=0.516	P=0.500	P=0.142	[illegible]

E 08

Date: 02/24/00 EXPERIMENT: 88050 TEST: 05

Statistical Analysis of Primary Tumors in Rats(CD BER 344)

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Salivary Glands								
Schwannoma Malignant								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.8%	0.0%	2.3%	2.3%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	1/35 (3%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/31 (0%)
FIRST INCIDENCE	563	---	729 (T)	618	---	---		
STATISTICAL TESTS								
LIFE TABLE	P=0.614N	P=0.214N	P=0.442N	P=0.480N	(e)	(e)	(e)	(e)
POLY 3	P=0.629N	P=0.220N	P=0.478N	P=0.486N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.625N	P=0.226N	P=0.487N	P=0.490N	(e)	(e)	(e)	(e)
POLY 6	P=0.634N	P=0.214N	P=0.465N	P=0.479N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.634N	P=0.285N	P=0.524N	P=0.549N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.619N	P=0.247N	P=0.500N	P=0.500N	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin								
Basal Cell Carcinoma, Basal Cell Adenoma, Basosquamous Tumor (benign, malignant or NOS), or Trichoepithelioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	4.5%	0.0%	2.3%	2.3%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	1/35 (3%)	0/31 (0%)	1/38 (3%)	0/33 (0%)	0/34 (0%)	0/30 (0%)
FIRST INCIDENCE	---	---	722	---	731 (T)	609	---	
STATISTICAL TESTS								
LIFE TABLE	P=0.684N	(e)	P=0.314	(e)	P=0.311N	P=0.735	P=0.522N	P=0.511N
POLY 3	P=0.696N	(e)	P=0.256	(e)	P=0.306N	P=0.748	P=0.516N	P=0.513N
POLY 1.5	P=0.696N	(e)	P=0.248	(e)	P=0.305N	P=0.752	P=0.511N	P=0.507N
POLY 6	P=0.694N	(e)	P=0.269	(e)	P=0.307N	P=0.743	P=0.520N	P=0.515N
LOGISTIC REGRESSION	P=0.692N	(e)	P=0.289	(e)	P=0.295N	P=0.742N	(e)	(e)
COCH-ARM / FISHERS	P=0.697N	(e)	P=0.247	(e)	P=0.303N	P=0.753N	P=0.500N	P=0.500N

E 09

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin: Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthoma, Trichoepithelioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	5/50 (10%)	5/50 (10%)	2/50 (4%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.8%	11.0%	11.2%	4.6%	4.3%	2.3%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	3/34 (9%)	4/35 (11%)	2/31 (7%)	2/38 (5%)	0/33 (0%)	0/33 (0%)	0/36 (0%)
FIRST INCIDENCE	579	674	722	729 (T)	731 (T)	809	-	-
STATISTICAL TESTS								
LIFE TABLE	P=0.330N	P=0.326	P=0.340	P=0.644N	P=0.175N	P=0.543N	P=0.263N	P=0.253N
POLY 3	P=0.349N	P=0.253	P=0.243	P=0.682N	P=0.168N	P=0.320N	P=0.256N	P=0.254N
POLY 1.5	P=0.349N	P=0.241	P=0.233	P=0.685N	P=0.168N	P=0.513N	P=0.256N	P=0.246N
POLY 6	P=0.347N	P=0.279	P=0.261	P=0.677N	P=0.168N	P=0.327N	P=0.260N	P=0.243N
LOGISTIC REGRESSION	P=0.351N	P=0.218	P=0.237	P=0.694N	P=0.148N	P=0.427N	(e)	(e)
COCH-ARM / FISHERS	P=0.357N	P=0.218	P=0.218	P=0.691N	P=0.169N	P=0.560N	P=0.247N	P=0.247N

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin: Fibroma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	4/50 (8%)	2/50 (4%)	5/50 (10%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	7.3%	8.8%	4.5%	11.6%	0.0%	0.0%	0.0%	4.3%
TERMINAL (d)	2/25 (8%)	2/34 (6%)	2/35 (6%)	5/31 (16%)	0/38 (0%)	0/33 (0%)	0/36 (0%)	2/36 (6%)
FIRST INCIDENCE	701	641	729 (T)	729 (T)	-	-	-	729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.334	P=0.537	P=0.361N	P=0.472	P=0.004 *	(e)	-	P=0.222
POLY 3	P=0.308	P=0.557	P=0.464N	P=0.382	P=0.019 *	(e)	-	P=0.325
POLY 1.5	P=0.309	P=0.537	P=0.478N	P=0.375	P=0.040 *	(e)	(e)	P=0.224
POLY 6	P=0.307	P=0.585	P=0.441N	P=0.396	P=0.039 *	(e)	(e)	P=0.[illegible]
LOGISTIC REGRESSION	P=0.311	P=0.552	P=0.402N	P=0.435	(e)	(e)	(e)	P=0.224
COCH-ARM / FISHERS	P=0.305	P=0.500	P=0.500N	P=0.357	P=0.042 *	(e)	(e)	P=0.247

E 10

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	5/50 (10%)	3/50 (6%)	8/50 (16%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	7.3%	11.0%	6.8%	18.2%	0.0%	0.0%	0.0%	4.5%
TERMINAL (d)	2/25 (8%)	3/34 (9%)	3/35 (9%)	5/31 (16%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	2/16 (13%)
FIRST INCIDENCE	701	641	729 (T)	603	---			603 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.085	P=0.508	P=0.511N	P=0.168	P=0.044 *	(e)	(e)	P=0.224
POLY 3	P=0.078	P=0.416	P=0.625N	P=0.121	P=0.039 *	(e)	(e)	P=0.221
POLY 1.5	P=0.076	P=0.394	P=0.640N	P=0.113	P=0.040 *	(e)	(e)	P=0.229
POLY 6	P=0.082	P=0.445	P=0.601N	P=0.135	P=0.039 *	(e)	(e)	P=0.221
LOGISTIC REGRESSION	P=0.073	P=0.416	P=0.560N	P=0.117	(e)	(e)	(e)	P=0.226
COCH-ARM / FISHERS	P=0.072	P=0.357	P=0.661N	P=0.100	P=0.042 *	(e)	(e)	P=0.236

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin Fibrosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	2.3%	4.6%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	1/35 (3%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/16 (0%)
FIRST INCIDENCE	---		729 (T)	603	---		---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.085	(e)	P=0.567	P=0.260	(e)	(e)	(e)	(e)
POLY 3	P=0.086	(e)	P=0.516	P=0.252	(e)	(e)	(e)	(e)
POLY 1.5	P=0.085	(e)	P=0.510	P=0.247	(e)	(e)	(e)	(e)
POLY 6	P=0.089	(e)	P=0.527	P=0.261	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.083	(e)	P=0.567	P=0.221	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.084	(e)	P=0.500	P=0.247	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin								
Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	3/50 (6%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	2.2%	2.3%	6.8%	0.0%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	1/34 (3%)	1/35 (3%)	3/41 (8%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/[illegible] (0%)
FIRST INCIDENCE	---	729 (T)	729 (T)	604	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.067	P=0.561	P=0.567	P=0.140	(e)	(e)	(e)	(e)
POLY 3	P=0.070	P=0.519	P=0.516	P=0.132	(e)	(e)	(e)	(e)
POLY 1.5	P=0.068	P=0.513	P=0.510	P=0.127	(e)	(e)	(e)	(e)
POLY 6	P=0.073	P=0.528	P=0.527	P=0.141	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.063	P=0.561	P=0.567	P=0.105	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.064	P=0.500	P=0.500	P=0.121	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Skin								
Keratoacanthoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	5/50 (10%)	3/50 (6%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	11.0%	6.8%	4.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	3/34 (9%)	3/35 (9%)	2/41 (5%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/38 (0%)
FIRST INCIDENCE	579	674	729 (T)	729 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.441N	P=0.172	P=0.464	P=0.522	(e)	(e)	(e)	(e)
POLY 3	P=0.490N	P=0.124	P=0.331	P=0.514	(e)	(e)	(e)	(e)
POLY 1.5	P=0.453N	P=0.116	P=0.321	P=0.5[illegible]	(e)	(e)	(e)	(e)
POLY 6	P=0.443N	P=0.136	P=0.347	P=0.521	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.461N	P=0.105	P=0.316	P=0.503	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.466N	P=0.102	P=0.309	P=0.500	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Skin								
Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	5/50 (10%)	3/50 (6%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	[illegible]
POLY-3 ADJUSTED (b)	4.8%	11.0%	6.8%	4.6%	2.1%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	3/34 (9%)	3/35 (9%)	2/31 (7%)	1/38 (3%)	0/33 (0%)	0/34 (0%)	[illegible]
FIRST INCIDENCE	579	674	729 (T)	729 (T)	731 (T)	---		
STATISTICAL TESTS								
LIFE TABLE	P=0.338N	P=0.326	P=0.610	P=0.644N	P=0.474N	P=0.528N	P=0.522N	[illegible]
POLY 3	P=0.352N	P=0.253	P=0.530	P=0.682N	P=0.463N	P=0.513N	[illegible]	[illegible]
POLY 1.5	P=0.353N	P=0.241	P=0.518	P=0.685N	P=0.467N	P=0.508N	[illegible]	[illegible]
POLY 6	P=0.350N	P=0.270	P=0.548	P=0.677N	P=0.459N	P=0.519N	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.356N	P=0.218	P=0.511	P=0.694N	P=0.474N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.361N	P=0.218	P=0.500	P=0.691N	P=0.474N	P=0.500N	[illegible]	[illegible]

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
Skin								
Squamous Cell Papilloma, Papilloma, or Keratoacanthoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	5/50 (10%)	3/50 (6%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	[illegible]
POLY-3 ADJUSTED (b)	2.4%	11.0%	6.8%	4.6%	2.1%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	3/34 (9%)	3/35 (9%)	2/31 (7%)	1/38 (3%)	0/33 (0%)	0/34 (0%)	[illegible]
FIRST INCIDENCE	579	674	729 (T)	729 (T)	731 (T)	---		
STATISTICAL TESTS								
LIFE TABLE	P=0.441N	P=0.172	P=0.404	P=0.552	P=0.474N	P=0.528N	P=0.522N	P=0.511N
POLY 3	P=0.450N	P=0.124	P=0.331	P=0.514	P=0.463N	P=0.513N	P=0.510N	P=0.511N
POLY 1.5	P=0.453N	P=0.116	P=0.321	P=0.510	P=0.467N	P=0.508N	[illegible]	[illegible]
POLY 6	P=0.443N	P=0.136	P=0.347	P=0.521	P=0.459N	P=0.519N	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.461N	P=0.105	P=0.316	P=0.503	P=0.474N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.466N	P=0.102	P=0.309	P=0.500	P=0.474N	P=0.500N	P=0.500N	[illegible]

E 13

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Testes Adenoma								
TUMOR RATES								
OVERALL (a)	40/50 (80%)	45/50 (90%)	47/50 (94%)	46/50 (92%)				
POLY-3 ADJUSTED (b)	89.7%	97.6%	96.7%	95.4%				
TERMINAL (d)	25/25 (100%)	32/34 (94%)	35/35 (100%)	33/35 (94%)				
FIRST INCIDENCE	439	474	474	456				
STATISTICAL TESTS								
LIFE TABLE	P=0.418	P=0.179N	P=0.202N	P=0.466N				
POLY 3	P=0.112	P=0.394	P=0.024 *	P=0.185				
POLY 1.5	P=0.132	P=0.27[illegible]	P=0.125 *	P=0.1[illegible]				
POLY 6	P=0.242	P=0.62[illegible]	P=0.046 *	P=0.2[illegible]				
LOGISTIC REGRESSION	P=0.186	P=0.359	P=0.039 *	P=0.534				
COCH ARM / FISHERS	P=0.117	P=0.331	P=0.036 *	P=0.6[illegible]				

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland (C Cell) Adenoma								
TUMOR RATES								
OVERALL (a)	9/50 (18%)	12/50 (24%)	8/50 (16%)	6/50 (12%)	3/50 (6%)	[illegible]	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	21.6%	26.4%	17.6%	13.6%	6.4%	[illegible]	11.6%	[illegible]
TERMINAL (d)	6/25 (24%)	9/34 (27%)	5/35 (14%)	4/33 (12%)	3/38 (8%)	[illegible]	[illegible]	[illegible]
FIRST INCIDENCE	579	674	474	416	731 (T)	[illegible]	[illegible]	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.109N	P=0.307	P=0.278N	P=0.180N	P=0.299	P=0.581	P=0.29[illegible]	P=[illegible]
POLY 3	P=0.116N	P=0.391	P=0.429N	P=0.247N	P=0.184	[illegible]	P=[illegible]	P=[illegible]
POLY 1.5	P=0.120N	P=0.364	P=0.451N	P=0.253N	P=0.187	[illegible]	P=[illegible]	[illegible]
POLY 6	P=0.112N	P=0.428	P=0.275N	P=0.230N	P=0.184	[illegible]	P=[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.127N	P=0.432	P=0.467N	P=0.267N	P=0.186	P=0.[illegible]	P=[illegible]	[illegible]
COCH ARM / FISHERS	P=0.132N	P=0.312	P=0.500N	P=0.288N	P=0.196	P=0.[illegible]	P=[illegible]	[illegible]

E 14

Date: 02/24/00 EXPERIMENT BROSE TEST 95

Statistical Analysis of Primary Tumors in Rats(FISCHER 344)

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland: (C-Cell) Carcinoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	2/50 (4%)	1/50 (2%	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	2.4%	2.2%	2.3%	0.6%	4.7%	2.3%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	1/34 (3%)	1/35 (3%)	0/31 (0%)	2/38 (5%)	1/33 (3%)	[illegible]	[illegible]
FIRST INCIDENCE	697	729 (T)	729 (T)	-	711 (T)	711 (T)	[illegible]	
STATISTICAL TESTS								
LIFE TABLE	P=0.308N	P=0.703N	P=0.703N	P=0.477N	P=0.196N	P=0.549N	[illegible]	[illegible]
POLY 3	P=0.323N	P=0.739N	P=0.743N	P=0.490N	P=0.196N	[illegible]	[illegible]	[illegible]
POLY 1.5	P=0.322N	P=0.747N	P=0.750N	P=0.493N	P=0.196N	[illegible]	[illegible]	[illegible]
POLY 6	P=0.322N	P=0.730N	P=0.731N	P=0.486N	P=0.197N	[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.316N	P=0.735N	P=0.738N	P=0.492N	P=0.200N	[illegible]	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.323N	P=0.753N	P=0.753N	P=0.500N	P=0.194N	[illegible]	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland: C-Cell Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	10/50 (20%)	13/50 (26%)	9/50 (18%)	6/50 (12%)	5/50 (10%)	9/50 (18%)	6/50 (12%)	[illegible]
POLY-3 ADJUSTED (b)	23.9%	28.6%	19.8%	13.6%	10.7%	20.3%	[illegible]	[illegible]
TERMINAL (d)	6/25 (24%)	10/34 (29%)	6/35 (17%)	4/31 (13%)	5/38 (13%)	8/33 (24%)	5/36 (15%)	[illegible]
FIRST INCIDENCE	579	674	464	456	731 (T)	505	724	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.068N	P=0.587N	P=0.267N	P=0.126N	P=0.392	P=0.126	P=0.[illegible]	P=0.244
POLY 3	P=0.072N	P=0.399	P=0.417N	P=0.171N	P=0.377	P=0.164	P=0.444	P=0.257
POLY 1.5	P=0.075N	P=0.372	P=0.449N	P=0.182N	P=0.379	P=0.175	P=0.463	P=0.261
POLY 6	P=0.069N	P=0.435	P=0.372N	P=0.158N	P=0.379	P=0.152	P=0.[illegible]	P=0.234
LOGISTIC REGRESSION	P=0.080N	P=0.447	P=0.459N	P=0.188N	P=0.372	P=0.159	P=0.465	P=0.249
COCH-ARM / FISHERS	P=0.084N	P=0.318	P=0.500N	P=0.207N	P=0.390	P=0.194	P=0.500	P=0.[illegible]

F 01

Date. 02/21/00 EXPERIMENT 98050 TEST: 06

Statistical Analysis of Primary Tumors in Rats(FISCHER 344)

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland: Follicular Cell Adenoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	2.4%	0.0%	4.5%	0.0%	2.0%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	0/24 (0%)	2/25 (8%)	0/21 (0%)	0/22 (0%)	0/23 (0%)	0/24 (0%)	1/22 (5%)
FIRST INCIDENCE	629	---	729 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.444N	P=0.471N	P=0.591	P=0.490N	n/a	n/a	n/a	n/a
POLY 3	P=0.462N	P=0.482N	P=0.525	P=0.491N	n/a	n/a	n/a	n/a
POLY 1.5	P=0.439N	P=0.488N	P=0.516	P=0.493N	n/a	n/a	n/a	n/a
POLY 6	P=0.465N	P=0.475N	P=0.542	P=0.487N	n/a	n/a	n/a	n/a
LOGISTIC REGRESSION	P=0.434N	P=0.535N	P=0.518	P=0.518N	n/a	n/a	n/a	n/a
COCH ARM / FISHERS	P=0.495N	P=0.500N	P=0.500	P=0.500N	n/a	n/a	n/a	n/a

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland: Follicular Cell Carcinoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	2.2%	2.2%	4.6%	2.1%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	0/24 (0%)	0/25 (0%)	2/21 (7%)	1/22 (5%)	0/23 (0%)	0/24 (0%)	0/22 (0%)
FIRST INCIDENCE	---	696	642	729 (T)	731 (T)			
STATISTICAL TESTS								
LIFE TABLE	P=0.201	P=0.565	P=0.535	P=0.286	P=0.474N	P=0.528N	P=0.524N	P=0.500N
POLY 3	P=0.201	P=0.520	P=0.218	P=0.249	P=0.463N	P=0.510N	P=0.490N	P=0.500N
POLY 1.5	P=0.199	P=0.513	P=0.511	P=0.247	P=0.460N	P=0.508N	P=0.500N	P=0.500N
POLY 6	P=0.204	P=0.529	P=0.529	P=0.255	P=0.494N	P=0.519N	P=0.524N	P=0.500N
LOGISTIC REGRESSION	P=0.194	P=0.511	P=0.488	P=0.286	P=0.474N	n/a	n/a	n/a
COCH-ARM / FISHERS	P=0.194	P=0.500	P=0.500	P=0.247	P=0.474N	P=0.500	P=0.500	P=0.500

F 02

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Thyroid Gland: Follicular Cell Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	1/50 (2%)	3/50 (6%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	[illegible]	[illegible]
POLY-3 ADJUSTED (r)	2.4%	2.2%	6.7%	4.6%	2.[illegible]%	6.[illegible]%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	0/34 (0%)	2/35 (6%)	2/31 (7%)	1/38 (3%)	0/33 (0%)	[illegible]	[illegible]
FIRST INCIDENCE	629	696	642	729 (T)	731 (T)	-	-	-
STATISTICAL TESTS								
LIFE TABLE	P=0.416	P=0.719N	P=0.396	P=0.555	P=0.474N	P=0.528N	P=0.524N	[illegible]
POLY 3	P=0.401	P=0.740N	P=0.335	P=0.515	P=0.463N	P=0.512N	[illegible]	[illegible]
POLY 1.5	P=0.402	P=0.747N	P=0.323	P=0.511	P=0.467N	P=0.508N	[illegible]	[illegible]
POLY 6	P=0.401	P=0.731N	P=0.354	P=0.529	P=0.459N	P=0.519N	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.401	P=0.753	P=0.308	P=0.513	P=0.474N	(d)	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.399	P=0.752N	P=0.309	P=0.500	P=0.474N	P=0.500N	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Uterus Polyp Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					7/50 (14%)	8/50 (16%)	9/50 (18%)	[illegible]
POLY-3 ADJUSTED (b)					14.9%	18.3%	[illegible]	26.8%
TERMINAL (d)					5/38 (13%)	8/33 (24%)	8/34 (24%)	[illegible]
FIRST INCIDENCE					616	731 (T)	497	693
STATISTICAL TESTS								
LIFE TABLE					P=0.185	P=0.184	P=0.[illegible]	P=0.166
POLY 3					P=0.155	P=0.437	P=0.332	P=0.[illegible]
POLY 1.5					P=0.163	P=0.461	P=0.[illegible]	P=0.[illegible]
POLY 6					P=0.149	P=0.409	P=0.310	P=0.[illegible]
LOGISTIC REGRESSION					P=0.157	P=0.417	P=0.353	P=0.[illegible]
COCH-ARM / FISHERS					P=0.179	P=0.500	P=0.393	P=0.216

Statistical Analysis of Primary Tumors in Rats/FISCHER 344. [illegible]

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Uterus								
Sarcoma Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					[illegible]	[illegible]	[illegible]	[illegible]
POLY-3 ADJUSTED (b)					[illegible]	[illegible]	[illegible]	[illegible]
TERMINAL (d)					[illegible]	[illegible]	[illegible]	[illegible]
FIRST INCIDENCE					[illegible]	441	[illegible]	560
STATISTICAL TESTS								
LIFE TABLE					P=[illegible]	P=[illegible]	P=[illegible]	[illegible]
POLY 3					P=[illegible]	P=[illegible]	P=[illegible]	[illegible]
POLY 1.5					P=[illegible]	P=[illegible]	P=[illegible]	[illegible]
POLY 6					P=[illegible]	P=[illegible]	P=[illegible]	[illegible]
LOGISTIC REGRESSION					P=[illegible]	P=[illegible]	P=[illegible]	[illegible]
COCH-ARM / FISHERS					P=[illegible]	[illegible]	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Uterus								
Sarcoma Stromal or Polyp Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					7/50 (14%)	9/[illegible] (18%)	[illegible]	[illegible]
POLY-3 ADJUSTED (b)					14.3%	20.3%	[illegible]	[illegible]
TERMINAL (d)					7/38 (18%)	8/33 (24%)	[illegible]	[illegible]
FIRST INCIDENCE					546	441	477	540
STATISTICAL TESTS								
LIFE TABLE					P=[illegible]	P=[illegible]	[illegible]	[illegible]
POLY 3					P=[illegible]	P=[illegible]	[illegible]	[illegible]
POLY 1.5					P=[illegible]	P=[illegible]	[illegible]	[illegible]
POLY 6					P=[illegible]	P=[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION					P=[illegible]	P=[illegible]	[illegible]	[illegible]
COCH-ARM / FISHERS					P=[illegible]	P=[illegible]	[illegible]	[illegible]

Date 02/24/00 EXPERIMENT [illegible]

Statistical Analysis of Primary Tumors in Male(F)B6C3F1 (441)

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
Zymbal's Gland								
Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	0.0%	4.4%	0.0%	2.3%	0.0%	0.0%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	1/34 (3%)	0/35 (0%)	1/31 (3%)	0/38 (0%)	0/33 (0%)	[illegible]	[illegible]
FIRST INCIDENCE	---	697	-	729 (T)	---	--	[illegible]	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.638	P=0.297	(e)	P=0.543	P=0.782N	(e)	[illegible]	[illegible]
POLY 3	P=0.641	P=0.260	(e)	P=0.510	P=0.790N	(e)	[illegible]	[illegible]
POLY 1.5	P=0.635	P=0.252	(e)	P=0.507	P=0.789N	(e)	[illegible]	[illegible]
POLY 6	P=0.649	P=0.271	(e)	P=0.516	P=0.792N	(e)	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.628	P=0.265	(e)	P=0.543	(e)	(e)	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.622	P=0.247	(e)	P=0.500	P=0.786N	(e)	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs								
Hemangiosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	0.0%	4.4%	2.3%	2.3%	2.1%	0.0%	[illegible]	[illegible]
TERMINAL (d)	0/25 (0%)	2/34 (6%)	1/35 (3%)	1/31 (3%)	1/38 (3%)	0/33 (0%)	[illegible]	[illegible]
FIRST INCIDENCE	---	729 (T)	729 (T)	729 (T)	731 (T)	---		---
STATISTICAL TESTS								
LIFE TABLE	P=0.642	P=0.308	P=0.567	P=0.543	P=0.474N	P=0.528N	P=0.522N	[illegible]
POLY 3	P=0.636	P=0.259	P=0.516	P=0.510	P=0.463N	P=0.513N	[illegible]	[illegible]
POLY 1.5	P=0.631	P=0.252	P=0.510	P=0.507	P=0.467N	P=0.508N	[illegible]	[illegible]
POLY 6	P=0.645	P=0.270	P=0.527	P=0.516	P=0.459N	P=0.519N	P=0.520N	[illegible]
LOGISTIC REGRESSION	(e)	P=0.308	P=0.567	P=0.543	P=0.474N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.619	P=0.247	P=0.500	P=0.500	P=0.474N	P=0.500N	P=0.500N	P=0.500N

F05

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
All Organs								
Leukemia Lymphocytic, Monocytic, Mononuclear, or Undifferentiated								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	20/50 (40%)	20/50 (40%)	14/50 (28%)	12/50 (24%)	21/50 (42%)	19/50 (38%)	16/50 (32%)	19/50 (38%)
POLY-3 ADJUSTED (b)	46.4%	42.9%	30.9%	26.9%	42.2%	40.3%	35.3%	[illegible]
TERMINAL (d)	9/25 (36%)	13/34 (38%)	7/35 (20%)	7/31 (23%)	12/38 (32%)	9/33 (27%)	8/34 (24%)	[illegible]
FIRST INCIDENCE	584	589	642	351	638	527	562	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.036N*	P=0.238N	P=0.039N*	P=0.033N*	P=0.481N	P=0.545	P=0.361N	[illegible]
POLY 3	P=0.030N*	P=0.450N	P=0.096N	P=0.043N*	P=0.579N	P=0.505N	P=0.312N	[illegible]
POLY 1.5	P=0.030N*	P=0.492N	P=0.112N	P=0.047N*	P=0.508N	P=0.470N	P=0.281N	[illegible]
POLY 6	P=0.033N*	P=0.400N	P=0.075N	P=0.040N*	P=0.525	P=0.559N	P=0.345N	[illegible]
LOGISTIC REGRESSION	P=0.033N*	P=0.448N	P=0.090N	P=0.052N	P=0.442N	P=0.298N	P=0.[illegible]N	[illegible]
COCH-ARM / FISHERS	P=0.036N*	P=0.581N	P=0.140N	P=0.066N	P=0.454N	P=0.419N	P=0.243N	[illegible]

Dose	Males 0 MG/KG	Males 3 MG/KG	Males 10 MG/KG	Males 30 MG/KG	Females 0 MG/KG	Females 3 MG/KG	Females 10 MG/KG	Females 30 MG/KG
All Organs								
Mesothelioma: Benign, Malignant, NOS								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	[illegible]	[illegible]
POLY-3 ADJUSTED (b)	0.0%	0.0%	4.5%	4.6%	0.0%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/25 (0%)	0/34 (0%)	2/35 (6%)	2/31 (7%)	0/38 (0%)	0/33 (0%)	[illegible]	[illegible]
FIRST INCIDENCE	---		729 (T)	729 (T)		---	---	
STATISTICAL TESTS								
LIFE TABLE	P=0.128	(e)	P=0.317	P=0.[illegible]	(e)	(e)	(e)	(e)
POLY 3	P=0.123	(e)	P=0.255	P=0.2[illegible]	(e)	(e)	(e)	(e)
POLY 1.5	P=0.123	(e)	P=0.248	P=0.245	(e)	(e)	(e)	(e)
POLY 6	P=0.124	(e)	P=0.268	P=0.255	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	(e)	(e)	P=0.315	P=0.286	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.122	(e)	P=0.247	P=0.247	(e)	(e)	(e)	(e)

Date: 02/24/00 EXPERIMENT: 68050 TEST: 05

Statistical Analysis of Primary Tumors in Rats(Crl:CD 344)

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs								
Mesothelioma: Malignant								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	4.5%	4.6%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	0/34 (0%)	2/35 (6%)	2/31 (7%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	---	---	729 (T)	729 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.128	(e)	P=0.315	P=0.286	(e)	(e)	(e)	(e)
POLY 3	P=0.123	(e)	P=0.256	P=0.249	(e)	(e)	(e)	(e)
POLY 1.5	P=0.123	(e)	P=0.248	P=0.245	(e)	(e)	(e)	(e)
POLY 6	P=0.124	(e)	P=0.268	P=0.255	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	(e)	(e)	P=0.315	P=0.286	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.122	(e)	P=0.247	P=0.247	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs								
Osteosarcoma or Osteoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.4%	4.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/25 (0%)	1/34 (3%)	0/35 (0%)	0/31 (0%)	0/38 (0%)	0/33 (0%)	0/34 (0%)	0/36 (0%)
FIRST INCIDENCE	474	716	---	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.201N	P=0.566	P=0.500N	P=0.500N	(e)	(e)	(e)	(e)
POLY 3	P=0.205N	P=0.528	P=0.487N	P=0.493N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.206N	P=0.519	P=0.492N	P=0.495N	(e)	(e)	(e)	(e)
POLY 6	P=0.202N	P=0.541	P=0.478N	P=0.489N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.218N	P=0.451	P=0.591N	P=0.605N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.209N	P=0.500	P=0.500N	P=0.500N	(e)	(e)	(e)	(e)

F 07

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) [illegible]

Terminal Sacrifice at [illegible] weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs								
Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	47/50 (94%)	49/50 (98%)	49/50 (98%)	47/50 (94%)	[illegible]	[illegible]	[illegible]	[illegible]
POLY 3 ADJUSTED (b)	97.8%	99.7%	99.9%	97.2%	73.2%	[illegible]	[illegible]	[illegible]
TERMINAL (d)	27/25 (100%)	34/34 (100%)	35/35 (100%)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
FIRST INCIDENCE	439	474	464	458	588	441	470	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.298N	P=0.072N	P=0.053N	P=0.146N	[illegible]	[illegible]	[illegible]	[illegible]
POLY 3	P=0.405N	P=0.541	P=0.489	P=0.700N	[illegible]	[illegible]	[illegible]	[illegible]
POLY 1.5	P=0.357N	P=0.487	P=0.423	P=0.642N	[illegible]	[illegible]	[illegible]	[illegible]
POLY 6	P=0.409N	P=0.692	P=0.679	P=0.790N	[illegible]	[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.352N	P=0.627	P=0.373	P=0.606N	[illegible]	[illegible]	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.414N	P=0.309	P=0.309	P=0.669N	[illegible]	[illegible]	[illegible]	[illegible]

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs								
Malignant Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	29/50 (58%)	30/50 (60%)	24/50 (48%)	26/50 (52%)	[illegible]	[illegible]	[illegible]	[illegible]
POLY 3 ADJUSTED (b)	62.4%	62.0%	51.9%	56.7%	52.[illegible]%	43.8%	[illegible]	[illegible]
TERMINAL (d)	11/25 (44%)	18/34 (53%)	15/35 (43%)	14/35 (40%)	17/38 (45%)	10/[illegible]	[illegible]	[illegible]
FIRST INCIDENCE	474	400	464	351	438	441	464	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.239N	P=0.235N	P=0.050N	P=0.182N	P=0.553	P=0.429N	P=0.[illegible]	P=[illegible]
POLY 3	P=0.242N	P=0.569N	P=0.206N	P=0.291N	P=0.526	P=0.[illegible]	P=[illegible]	P=[illegible]
POLY 1.5	P=0.239N	P=0.582	P=0.200N	P=0.292N	P=0.53[illegible]	P=0.2[illegible]	P=0.[illegible]	[illegible]
POLY 6	P=0.254N	P=0.558N	P=0.208N	P=0.278N	P=0.517	P=0.[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.262N	P=0.516	P=0.177N	P=0.352N	P=0.539N	P=0.329N	P=0.[illegible]	P=[illegible]
COCH-ARM / FISHERS	P=0.265N	P=0.500	P=0.212N	P=0.344N	P=0.529	P=0.[illegible]	P=[illegible]	[illegible]

F 08

Date: 02/24/00 EXPERIMENT 88050 [illegible]

Statistical Analysis of Primary Tumors in Rats [illegible] (64)

Terminal Sacrifice at 104 weeks

Dose	Males 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG	Females 0 MG/KG	3 MG/KG	10 MG/KG	30 MG/KG
All Organs Malignant and Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	49/50 (98%)	50/50 (100%)	49/50 (98%)	49/50 (98%)	45/50 (90%)	[illegible]	[illegible]	[illegible]
POLY 3 ADJUSTED (b)	100.0%	100.0%	99.9%	98.0%	90.0%	92.0%	[illegible]	[illegible]
TERMINAL (d)	25/25 (100%)	34/34 (100%)	35/35 (100%)	30/31 (97%)	33/38 (87%)	[illegible]	[illegible]	[illegible]
FIRST INCIDENCE	439	400	464	351	438	66	[illegible]	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.338N	P=0.056N	P=0.028N*	P=0.156N	P=0.436	[illegible]	[illegible]	[illegible]
POLY 3	P=0.218N	P=1.000	P=1.000N	P=0.504N	P=0.487	P=0.699	[illegible]	[illegible]
POLY 1.5	P=0.231N	P=1.000	P=1.000N	P=0.509N	P=0.464	[illegible]	[illegible]	[illegible]
POLY 6	P=0.210N	P=1.000	P=1.000N	P=0.504N	P=0.565	[illegible]	[illegible]	[illegible]
LOGISTIC REGRESSION	P=0.373N	(e)	(e)	P=0.612N	P=0.363	P=0.598	[illegible]	[illegible]
COCH-ARM / FISHERS	P=0.545N	P=0.500	P=0.753N	P=0.753N	P=0.412	P=0.630N	[illegible]	[illegible]

(a) Number of tumor-bearing animals / number of animals examined at site.
(b) Poly-3 adjusted lifetime tumor incidence.
(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
For all tests a negative trend is indicated by N
(e) Value of Statistic cannot be computed.
(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).

FINAL#1, CORE STUDY MICE

Facility: Battelle Columbus Laboratory

Chemical CAS #: 126-98-7

Lock Date: 06/26/98

Cage Range: All

Reasons For Removal: All

Removal Date Range: All

Treatment Groups: Include All

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

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Natural Death	14	13	4	9
Moribund Sacrifice	1	2	4	1
Accidently Killed				15
Survivors				
Natural Death	1			
Terminal Sacrifice	34	35	43	25
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Periesophageal Tissue, Inflammation, Chronic Active	1 (2%)			
Gallbladder	(50)	(50)	(50)	(46)
Cyst	1 (2%)			
Infiltration Cellular, Mononuclear Cell			1 (2%)	
Intestine Small, Duodenum	(49)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)			
Metaplasia, Squamous			1 (2%)	
Epithelium, Ulcer	1 (2%)			
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Ulcer		1 (2%)		
Epithelium, Inflammation, Suppurative		1 (2%)		
Peyer's Patch, Hyperplasia, Lymphoid				2 (4%)
Liver	(50)	(50)	(49)	(50)
Angiectasis		1 (2%)	1 (2%)	
Basophilic Focus	1 (2%)	7 (14%)	2 (4%)	2 (4%)
Clear Cell Focus	3 (6%)	6 (12%)	6 (12%)	1 (2%)
Eosinophilic Focus	9 (18%)	3 (6%)	11 (22%)	3 (6%)
Hematopoietic Cell Proliferation	2 (4%)	2 (4%)	6 (12%)	2 (4%)
Hepatodiaphragmatic Nodule		1 (2%)		
Infiltration Cellular, Mononuclear Cell	30 (60%)	36 (72%)	40 (82%)	30 (60%)
Inflammation, Chronic Active	32 (64%)	36 (72%)	41 (84%)	38 (76%)
Mineralization			1 (2%)	1 (2%)
Mixed Cell Focus	3 (6%)	1 (2%)	3 (6%)	
Necrosis	3 (6%)	2 (4%)	2 (4%)	1 (2%)
Pigmentation	18 (36%)	12 (24%)	17 (35%)	7 (14%)
Tension Lipidosis	2 (4%)	3 (6%)		
Hepatocyte, Vacuolization Cytoplasmic	7 (14%)	9 (18%)	3 (6%)	18 (36%)
Mesentery	(16)	(11)	(15)	(4)
Fibrosis	8 (50%)	7 (64%)	10 (67%)	2 (50%)
Hemorrhage		1 (9%)		

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

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
ALIMENTARY SYSTEM - CONT				
Inflammation, Chronic Active	5 (31%)	6 (55%)	8 (57%)	
Mineralization	5 (31%)	7 (64%)	12 (86%)	1 (25%)
Pigmentation			1 (7%)	
Thrombosis			1 (7%)	
Fat, Necrosis	8 (50%)	7 (64%)	11 (79%)	3 (75%)
Oral Mucosa	(3)	(5)	(2)	(1)
Gingival, Foreign Body	2 (67%)	5 (100%)	1 (50%)	
Gingival, Inflammation, Chronic Active	2 (67%)	5 (100%)	2 (100%)	
Pharyngeal, Foreign Body	1 (33%)			
Pancreas	(50)	(50)	(50)	(49)
Cyst			1 (2%)	
Infiltration Cellular, Mononuclear Cell				2 (4%)
Acinus, Atrophy	1 (2%)			
Acinus, Hyperplasia				1 (2%)
Salivary Glands	(48)	(50)	(50)	(49)
Infiltration Cellular, Mononuclear Cell	27 (56%)	29 (58%)	32 (64%)	27 (55%)
Inflammation, Chronic Active			2 (4%)	1 (2%)
Mineralization			1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(50)
Diverticulum	1 (2%)			
Hyperkeratosis		1 (2%)		
Epithelium, Hyperplasia	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Epithelium, Inflammation, Chronic Active	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Epithelium, Ulcer	1 (2%)	1 (2%)	1 (2%)	
Stomach, Glandular	(50)	(50)	(50)	(50)
Ectopic Tissue		1 (2%)		
Mineralization	1 (2%)	1 (2%)		1 (2%)
Epithelium, Dysplasia		1 (2%)		
Epithelium, Erosion	1 (2%)			
Glands, Ectasia	16 (32%)	9 (18%)	10 (20%)	3 (6%)
CARDIOVASCULAR SYSTEM				
Blood Vessel	(49)	(50)	(50)	(50)
Aorta, Mineralization	1 (2%)			
Heart	(50)	(50)	(50)	(50)
Inflammation, Suppurative				1 (2%)
Mineralization	1 (2%)			
Artery, Mineralization	1 (2%)			
Valve, Inflammation, Chronic Active		1 (2%)		
Valve, Inflammation, Suppurative	1 (2%)			

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

F 12

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
ENDOCRINE SYSTEM				
Adrenal Cortex	(49)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule				2 (4%)
Hematopoietic Cell Proliferation		1 (2%)		1 (2%)
Hypertrophy	1 (2%)		1 (2%)	
Infiltration Cellular, Mononuclear Cell		1 (2%)		
Capsule, Hyperplasia	48 (98%)	48 (96%)	50 (100%)	50 (100%)
Zona Reticularis, Hyperplasia			1 (2%)	
Adrenal Medulla	(49)	(50)	(50)	(50)
Hyperplasia	1 (2%)			1 (2%)
Islets, Pancreatic	(50)	(50)	(50)	(49)
Hyperplasia	41 (82%)	37 (74%)	40 (80%)	33 (67%)
Pituitary Gland	(49)	(49)	(49)	(49)
Pars Distalis, Angiectasis	2 (4%)	3 (6%)	6 (12%)	2 (4%)
Pars Distalis, Cyst	1 (2%)		2 (4%)	2 (4%)
Pars Distalis, Hemorrhage		1 (2%)		
Pars Distalis, Hyperplasia	9 (18%)	12 (24%)	10 (20%)	11 (22%)
Pars Distalis, Pigmentation			1 (2%)	
Thyroid Gland	(49)	(50)	(50)	(50)
Ectopic Thymus			1 (2%)	
Infiltration Cellular, Mononuclear Cell	1 (2%)			1 (2%)
Inflammation, Chronic Active	1 (2%)			
C-Cell, Hyperplasia		1 (2%)		
Follicle, Cyst	5 (10%)	3 (6%)	3 (6%)	4 (8%)
Follicular Cell, Hyperplasia	1 (2%)			
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral Gland	(50)	(50)	(50)	(49)
Infiltration Cellular, Mononuclear Cell	4 (8%)	2 (4%)	3 (6%)	1 (2%)
Inflammation, Chronic Active	2 (4%)	1 (2%)		1 (2%)
Pigmentation		1 (2%)		
Duct, Cyst			2 (4%)	2 (4%)
Ovary	(50)	(50)	(50)	(49)
Angiectasis		1 (2%)		
Cyst	17 (34%)	14 (28%)	18 (36%)	10 (20%)
Hemorrhage		1 (2%)	4 (8%)	1 (2%)
Inflammation, Suppurative				1 (2%)
Mineralization	2 (4%)	3 (6%)	2 (4%)	1 (2%)
Pigmentation	7 (14%)	16 (32%)	11 (22%)	6 (12%)
Thrombosis		1 (2%)	3 (6%)	

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

F 13

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
GENITAL SYSTEM - CONT				
Uterus	(50)	(50)	(50)	(50)
Angiectasis				1 (2%)
Hemorrhage				1 (2%)
Hydrometra	23 (46%)	28 (56%)	31 (62%)	20 (40%)
Inflammation, Chronic Active	1 (2%)			
Inflammation, Suppurative		1 (2%)		
Pigmentation		1 (2%)		
Thrombosis	1 (2%)			
Endometrium, Hyperplasia	1 (2%)			
Endometrium, Hyperplasia, Cystic	27 (54%)	24 (48%)	24 (48%)	32 (64%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hyperplasia	2 (4%)	2 (4%)	4 (8%)	1 (2%)
Myelofibrosis	2 (4%)	3 (6%)		
Lymph Node	(2)	(5)	(8)	(5)
Lumbar, Ectasia		1 (17%)		1 (20%)
Lumbar, Hyperplasia, Lymphoid			1 (13%)	
Mediastinal, Hyperplasia, Lymphoid	1 (33%)		2 (25%)	
Mediastinal, Infiltration Cellular, Histiocyte	1 (33%)			
Mediastinal, Inflammation				1 (20%)
Pancreatic, Fibrosis	1 (33%)			
Pancreatic, Hyperplasia, Lymphoid	1 (33%)			
Pancreatic, Pigmentation	1 (33%)			
Lymph Node, Mandibular	(46)	(47)	(48)	(47)
Hyperplasia, Lymphoid	5 (10%)	6 (13%)	3 (7%)	1 (2%)
Infiltration Cellular: Plasma Cell	1 (2%)			
Pigmentation	3 (6%)	16 (33%)	9 (20%)	4 (9%)
Lymph Node, Mesenteric	(47)	(48)	(47)	(46)
Ectasia	2 (4%)			
Hemorrhage	2 (4%)	1 (2%)		
Hyperplasia, Lymphoid	2 (4%)		1 (2%)	1 (2%)
Inflammation, Chronic Active		1 (2%)		
Pigmentation	1 (2%)			
Spleen	(50)	(50)	(49)	(49)
Hematopoietic Cell Proliferation	18 (36%)	22 (44%)	15 (31%)	10 (20%)
Hyperplasia, Lymphoid	1 (2%)	3 (6%)	3 (6%)	
Mineralization			1 (2%)	
Necrosis		1 (2%)		
Pigmentation			1 (2%)	
Thymus	(47)	(48)	(48)	(48)
Cyst	20 (43%)	17 (40%)	27 (56%)	19 (40%)
Ectopic Parathyroid Gland	1 (2%)	1 (2%)	1 (2%)	
Hyperplasia, Lymphoid			2 (4%)	

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

F14

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
MESHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
HEMATOPOIETIC SYSTEM (CONT)				
Thymocyte, Necrosis		1 (2%)		1 (2%)
INTEGUMENTARY SYSTEM				
Mammary Gland	(49)	(50)	(49)	(49)
Hyperplasia, Cystic	3 (6%)	1 (2%)		
Skin	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)			
Epidermis, Ulcer	1 (2%)			
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteosclerosis	1 (2%)			
Skeletal Muscle	(4)	(1)	(2)	
Infiltration Cellular, Mononuclear Cell	1 (25%)			
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)		
Infiltration Cellular, Mononuclear Cell	2 (4%)			
Inflammation, Chronic Active		1 (2%)		
Meninges, Hemorrhage		1 (2%)		
Peripheral Nerve	(1)		(1)	
Sciatic, Axon, Degeneration	1 (100%)			
Spinal Cord	(1)		(2)	
Demyelination	1 (100%)		1 (50%)	
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)		
Inflammation, Chronic Active	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Mineralization	5 (10%)	1 (2%)	2 (4%)	2 (4%)
Necrosis				1 (2%)
Pigmentation	1 (2%)			
Thrombosis		1 (2%)	1 (2%)	
Alveolar Epithelium, Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Alveolus, Infiltration Cellular, Histiocyte	1 (2%)			2 (4%)
Artery, Mediastinum, Mineralization	1 (2%)			
Mediastinum, Mineralization		1 (2%)		
Nose	(50)	(50)	(50)	(50)

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

G 01

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
RESPIRATORY SYSTEM - CONT				
Inflammation, Suppurative	1 (2%)			
SPECIAL SENSES SYSTEM				
Eye	(2)	(1)		(4)
Atrophy	1 (50%)	1 (100%)		1 (25%)
Anterior Chamber, Infiltration Cellular, Polymorphonuclear				1 (25%)
Cornea, Inflammation, Chronic Active				1 (25%)
URINARY SYSTEM				
Kidney	(50)	(50)	(49)	(50)
Accumulation, Hyaline Droplet	2 (4%)	1 (2%)		
Hydronephrosis			1 (2%)	
Infarct, Multiple	1 (2%)			
Infiltration Cellular, Mononuclear Cell	25 (50%)	42 (84%)	45 (92%)	[illegible]
Inflammation, Chronic Active	1 (2%)	1 (2%)		
Mineralization	6 (12%)	8 (16%)	5 (10%)	6 (12%)
Nephropathy	35 (70%)	39 (78%)	22 (45%)	9 (18%)
Pigmentation			1 (2%)	
Capsule, Mineralization	1 (2%)			
Cortex, Cyst	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Papilla, Inflammation, Acute	1 (2%)			
Renal Tubule, Casts Protein			1 (2%)	
Urinary Bladder	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	28 (56%)	31 (62%)	29 (58%)	22 (44%)
Inflammation, Chronic Active	1 (2%)			
Pigmentation	1 (2%)			

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

G 02

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Natural Death	9	5	4	1
Moribund Sacrifice	5	2	1	
Dosing Accident				1
Accidently Killed				26
Survivors				
Terminal Sacrifice	34	41	41	22
Natural Death	1		2	
Missing	1			
Animals Examined Microscopically	49	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(49)	(50)	(50)	(50)
Inflammation, Chronic Active				1 (2%)
Periesophageal Tissue, Inflammation, Chronic Active		1 (2%)		
Intestine Small, Duodenum	(49)	(49)	(50)	(50)
Ectasia			1 (2%)	
Hyperplasia		3 (6%)	1 (2%)	1 (2%)
Intestine Small, Jejunum	(49)	(50)	(50)	(50)
Inflammation, Chronic Active		1 (2%)		
Peyer's Patch, Hyperplasia, Lymphoid			1 (2%)	1 (2%)
Intestine Small, Ileum	(49)	(50)	(50)	(49)
Inflammation, Chronic Active	1 (2%)	1 (2%)		
Liver	(49)	(50)	(50)	(50)
Angiectasis	1 (2%)		1 (2%)	
Basophilic Focus		4 (8%)	6 (12%)	2 (4%)
Clear Cell Focus	7 (14%)	10 (20%)	10 (20%)	4 (8%)
Eosinophilic Focus	16 (33%)	10 (20%)	12 (24%)	3 (6%)
Fibrosis			1 (2%)	
Hematopoietic Cell Proliferation			3 (6%)	1 (2%)
Hepatodiaphragmatic Nodule	1 (2%)			
Infiltration Cellular, Mast Cell	1 (2%)			
Infiltration Cellular, Mononuclear Cell	9 (18%)	11 (22%)	7 (14%)	6 (12%)
Inflammation, Chronic Active	22 (45%)	21 (42%)	19 (38%)	21 (42%)
Inflammation, Granulomatous			1 (2%)	
Malformation	1 (2%)			
Mineralization			1 (2%)	
Mixed Cell Focus		11 (22%)	11 (22%)	2 (4%)
Necrosis	6 (12%)	5 (10%)	1 (2%)	
Pigmentation	3 (6%)		2 (4%)	3 (6%)
Tension Lipidosis	1 (2%)		1 (2%)	

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

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
ALIMENTARY SYSTEM - CONT				
Bile Duct, Cyst			1 (2%)	1 (2%)
Bile Duct, Hyperplasia				1 (2%)
Hepatocyte, Vacuolization Cytoplasmic	6 (12%)	10 (20%)	9 (18%)	16 (32%)
Hepatocyte, Portal, Hypertrophy			1 (2%)	
Hepatocyte, Centrilobular, Degeneration			1 (2%)	
Mesentery	(3)	(6)	(6)	(1)
Fibrosis	1 (33%)	1 (17%)		
Inflammation, Chronic Active	1 (33%)	1 (17%)	1 (17%)	1 (100%)
Inflammation, Granulomatous			2 (33%)	
Mineralization		1 (17%)	1 (17%)	
Thrombosis	1 (33%)			
Fat, Necrosis	1 (33%)	2 (33%)	1 (17%)	
Oral Mucosa	(31)	(30)	(27)	(10)
Gingival, Foreign Body	27 (87%)	29 (97%)	26 (96%)	10 (100%)
Gingival, Inflammation, Acute	9 (29%)	3 (10%)	10 (37%)	6 (60%)
Gingival, Inflammation, Chronic		1 (3%)		
Gingival, Inflammation, Chronic Active	19 (61%)	26 (87%)	16 (59%)	2 (20%)
Pancreas	(49)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	1 (2%)	1 (2%)		1 (2%)
Artery, Mineralization				1 (2%)
Salivary Glands	(49)	(50)	(50)	(50)
Granuloma	1 (2%)			
Infiltration Cellular, Mononuclear Cell	22 (45%)	35 (70%)	36 (72%)	29 (58%)
Inflammation, Chronic	1 (2%)			
Inflammation, Chronic Active			1 (2%)	
Mineralization	1 (2%)	1 (2%)	1 (2%)	
Stomach, Forestomach	(49)	(50)	(50)	(50)
Cyst, Squamous			1 (2%)	
Epithelium, Hyperplasia	2 (4%)	3 (6%)	1 (2%)	1 (2%)
Epithelium, Inflammation, Chronic Active	2 (4%)	1 (2%)	2 (4%)	
Epithelium, Ulcer	1 (2%)	1 (2%)		
Stomach, Glandular	(49)	(50)	(50)	(50)
Hyperplasia		1 (2%)		
Mineralization		1 (2%)		2 (4%)
Ulcer	1 (2%)			
Epithelium, Erosion	1 (2%)			
Epithelium, Hyperplasia		1 (2%)	1 (2%)	
Epithelium, Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	
Glands, Ectasia	17 (35%)	10 (20%)	20 (40%)	5 (10%)
Serosa, Inflammation, Granulomatous			1 (2%)	
Tooth	(6)		(1)	(2)
Malformation	6 (100%)		1 (100%)	2 (100%)

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

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
CARDIOVASCULAR SYSTEM				
Heart	(48)	(50)	(50)	(50)
Inflammation, Chronic Active	2 (4%)	1 (2%)		1 (2%)
Mineralization	2 (4%)		1 (2%)	1 (2%)
Artery, Inflammation, Chronic Active		1 (2%)		
ENDOCRINE SYSTEM				
Adrenal Cortex	(49)	(50)	(50)	(50)
Degeneration, Fatty	1 (2%)			
Hematopoietic Cell Proliferation			1 (2%)	
Hyperplasia	14 (29%)	12 (24%)	16 (32%)	7 (14%)
Hypertrophy	26 (53%)	34 (68%)	28 (56%)	15 (30%)
Inflammation, Suppurative		1 (2%)		
Metaplasia, Osseous	1 (2%)			
Capsule, Hyperplasia	41 (84%)	41 (82%)	40 (80%)	45 (90%)
Adrenal Medulla	(49)	(50)	(50)	(50)
Hematopoietic Cell Proliferation			1 (2%)	
Hyperplasia	1 (2%)			
Islets, Pancreatic	(49)	(50)	(50)	(50)
Hyperplasia	47 (96%)	43 (86%)	48 (96%)	46 (92%)
Parathyroid Gland	(42)	(35)	(39)	(38)
Cyst	1 (2%)	2 (6%)	1 (3%)	1 (3%)
Pituitary Gland	(48)	(49)	(49)	(46)
Atypia Cellular				1 (2%)
Pars Distalis, Cyst	1 (2%)	2 (4%)	5 (10%)	3 (7%)
Pars Distalis, Hyperplasia	2 (4%)	2 (4%)		
Thyroid Gland	(49)	(50)	(50)	(50)
Follicle, Cyst	2 (4%)	2 (4%)	2 (4%)	
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Coagulating Gland			(1)	(2)
Inflammation, Suppurative			1 (100%)	
Epididymis	(49)	(50)	(50)	(50)
Atrophy	1 (2%)			
Granuloma Sperm	2 (4%)		1 (2%)	
Infiltration Cellular, Mononuclear Cell	17 (35%)	26 (52%)	30 (60%)	21 (42%)
Inflammation, Chronic Active	1 (2%)	1 (2%)		1 (2%)
Mineralization	2 (4%)		1 (2%)	

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

G 05

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
GENITAL SYSTEM - CONT				
Penis	(1)			
Hemorrhage	1 (100%)			
Preputial Gland	(49)	(50)	(50)	(49)
Atrophy	1 (2%)			
Infiltration Cellular, Mononuclear Cell	21 (43%)	25 (50%)	27 (54%)	26 (53%)
Inflammation, Chronic Active	13 (27%)	6 (12%)	7 (14%)	3 (6%)
Duct, Cyst	18 (37%)	20 (40%)	18 (36%)	16 (33%)
Prostate	(49)	(50)	(50)	(50)
Atrophy	1 (2%)			
Infiltration Cellular, Mononuclear Cell	25 (51%)	31 (62%)	34 (68%)	32 (64%)
Inflammation, Suppurative			1 (2%)	
Artery, Inflammation, Chronic Active		1 (2%)		
Seminal Vesicle	(49)	(50)	(50)	(50)
Atrophy	1 (2%)			
Dilatation		1 (2%)		
Infiltration Cellular, Mononuclear Cell		2 (4%)	2 (4%)	
Testes	(49)	(50)	(50)	(50)
Atrophy			1 (2%)	
Inflammation, Chronic Active		1 (2%)		
Mineralization	2 (4%)	2 (4%)	1 (2%)	
Germinal Epithelium, Atrophy	1 (2%)	2 (4%)	2 (4%)	
HEMATOPOIETIC SYSTEM				
Bone Marrow	(49)	(50)	(50)	(50)
Hyperplasia			4 (8%)	
Lymph Node	(3)	(2)	(2)	(1)
Inguinal, Hyperplasia, Plasma Cell		1 (25%)		
Lumbar, Hyperplasia, Plasma Cell		1 (25%)		
Mediastinal, Hyperplasia, Plasma Cell		1 (25%)		
Pancreatic, Hyperplasia, Lymphoid		1 (25%)		
Renal, Hyperplasia, Plasma Cell		1 (25%)		
Renal, Inflammation, Suppurative		1 (25%)		
Lymph Node, Mandibular	(46)	(48)	(50)	(47)
Hyperplasia, Lymphoid	1 (2%)	1 (2%)		
Hyperplasia, Plasma Cell		1 (2%)	1 (2%)	
Infiltration Cellular, Polymorphonuclear			1 (2%)	
Lymph Node, Mesenteric	(46)	(43)	(49)	(47)
Hematopoietic Cell Proliferation	1 (2%)			
Hemorrhage	1 (2%)			
Hyperplasia, Lymphoid	1 (2%)	1 (2%)	1 (2%)	
Hyperplasia, Plasma Cell	1 (2%)	1 (2%)		
Inflammation, Chronic Active			1 (2%)	1 (2%)
Inflammation, Granulomatous	1 (2%)			
Inflammation, Suppurative		1 (2%)		
Spleen	(49)	(50)	(50)	(50)

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

G 06

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
HEMATOPOIETIC SYSTEM - CONT				
Hematopoietic Cell Proliferation	12 (24%)	13 (26%)	14 (28%)	4 (8%)
Hyperplasia, Lymphoid	1 (2%)	4 (8%)	1 (2%)	
Thymus	(40)	(48)	(40)	(49)
Atypia Cellular			1 (2%)	
Cyst	16 (40%)	19 (40%)	18 (39%)	19 (39%)
Ectopic Parathyroid Gland	3 (8%)	1 (2%)	3 (7%)	1 (2%)
Ectopic Thyroid	1 (3%)			
Mineralization		1 (2%)		
Thymocyte, Necrosis			1 (2%)	
INTEGUMENTARY SYSTEM				
Skin	(49)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell			1 (2%)	
Inflammation, Chronic Active		2 (4%)	3 (6%)	
Epidermis, Hyperkeratosis			1 (2%)	
Epidermis, Hyperplasia		2 (4%)	2 (4%)	
Epidermis, Ulcer		2 (4%)	2 (4%)	
Epidermis, Pinna, Hyperplasia			1 (2%)	
Epidermis, Pinna, Ulcer			1 (2%)	
Pinna, Inflammation, Chronic Active			1 (2%)	
Subcutaneous Tissue, Fibrosis		1 (2%)		
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
None				
RESPIRATORY SYSTEM				
Lung	(49)	(50)	(50)	(50)
Hemorrhage		1 (2%)	1 (2%)	
Infiltration Cellular, Mononuclear Cell	1 (2%)	1 (2%)		
Inflammation, Chronic		1 (2%)		
Inflammation, Chronic Active	2 (4%)	2 (4%)		4 (8%)
Mineralization	3 (6%)	1 (2%)		2 (4%)
Thrombosis	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Alveolar Epithelium, Hyperplasia	3 (6%)	6 (12%)	5 (10%)	4 (8%)
Alveolus, Infiltration Cellular, Histiocyte	4 (8%)	8 (16%)	3 (6%)	3 (6%)
Bronchiole, Foreign Body	1 (2%)			

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

G 07

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
METHACRYLONITRILE

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
RESPIRATORY SYSTEM - CONT				
Mediastinum, Inflammation, Chronic Active				1 (2%)
Mediastinum, Inflammation, Suppurative		1 (2%)		
Pleura, Inflammation, Chronic Active				1 (2%)
Nose	(49)	(50)	(50)	(50)
Foreign Body	3 (6%)	3 (6%)	4 (8%)	1 (2%)
Inflammation, Chronic Active	2 (4%)		3 (6%)	
Nasolacrimal Duct, Inflammation, Suppurative	4 (8%)		1 (2%)	
SPECIAL SENSES SYSTEM				
Eye	(1)	(1)		(1)
Cornea, Inflammation, Chronic Active		1 (100%)		
Cornea, Inflammation, Suppurative	1 (100%)			
Cornea, Metaplasia, Squamous		1 (100%)		
Harderian Gland	(3)	(2)	(7)	(1)
Infiltration Cellular, Mononuclear Cell	1 (33%)			
URINARY SYSTEM				
Kidney	(49)	(50)	(50)	(50)
Infarct	2 (4%)	2 (4%)	1 (2%)	
Infiltration Cellular, Mononuclear Cell	27 (55%)	37 (74%)	39 (78%)	22 (44%)
Inflammation, Chronic Active	1 (2%)		1 (2%)	
Inflammation, Suppurative			1 (2%)	
Metaplasia, Osseous	2 (4%)	1 (2%)		
Mineralization	43 (88%)	49 (98%)	47 (94%)	36 (72%)
Nephropathy	43 (88%)	48 (96%)	47 (94%)	39 (78%)
Artery, Inflammation, Chronic Active		1 (2%)		
Cortex, Cyst	11 (22%)	12 (24%)	8 (16%)	9 (18%)
Renal Tubule, Hyperplasia	9 (18%)	8 (16%)	9 (18%)	2 (4%)
Renal Tubule, Necrosis	1 (2%)			
Urinary Bladder	(49)	(50)	(50)	(50)
Hemorrhage			1 (2%)	
Infiltration Cellular, Mononuclear Cell	12 (24%)	17 (34%)	9 (18%)	10 (20%)
Inflammation, Suppurative			1 (2%)	

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

G 08

G 09

CORE STUDY MICE FINAL #1

Facility: Battelle Columbus Laboratory

Chemical CAS #: 126-98-7

Lock Date: 06/26/98

Cage Range: All

Reasons For Removal All

Removal Date Range: All

Treatment Groups: Include All

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

G 10

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Natural Death	14	13	6	7
Moribund Sacrifice	1	2	1	1
Accidently Killed				15
Survivors				
Natural Death	1			
Terminal Sacrifice	34	35	43	25
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Periesophageal Tissue, Fibrous Histiocytoma, Metastatic, Mesentery			1 (2%)	
Periesophageal Tissue, Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Intestine Large, Cecum	(50)	(50)	(50)	(50)
Adenocarcinoma		1 (2%)		
Leiomyoma	3 (6%)	1 (2%)		
Intestine Small, Duodenum	(49)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)		
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Sarcoma NOS, Metastatic, Uncertain Primary Site	1 (2%)			
Intestine Small, Ileum	(50)	(50)	(50)	(50)
Adenocarcinoma			1 (2%)	
Leiomyosarcoma				1 (2%)
Liver	(50)	(50)	(49)	(50)
Hemangiosarcoma		1 (2%)		1 (2%)
Hepatocellular Carcinoma	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Hepatocellular Carcinoma, Multiple		1 (2%)	1 (2%)	
Hepatocellular Adenoma	6 (12%)	9 (18%)	11 (22%)	4 (8%)
Hepatocellular Adenoma, Multiple	3 (6%)		1 (2%)	1 (2%)
Histiocytic Sarcoma		1 (2%)		1 (2%)
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Mesentery	(16)	(11)	(15)	(4)
Fibrosarcoma, Metastatic, Skin			1 (7%)	
Fibrous Histiocytoma			1 (7%)	
Hepatocellular Carcinoma, Metastatic, Liver			1 (7%)	
Leiomyosarcoma, Metastatic, Uterus	1 (6%)			
Leiomyosarcoma, Metastatic, Intestine Small,				

BEC3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
ALIMENTARY SYSTEM (CONT.)				
Ileum				1 (25%)
Lipoma			1 (2%)	
Sarcoma NOS	1 (6%)			
Sarcoma NOS, Metastatic, Uncertain Primary Site	1 (6%)			
Schwannoma Malignant, Metastatic, Skin	1 (6%)			
Oral Mucosa	(3)	(5)	(1)	(1)
Squamous Cell Carcinoma				1 (100%)
Pharyngeal, Squamous Cell Papilloma	1 (33%)			
Pancreas	(50)	(50)	(50)	(48)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Fibrous Histiocytoma, Metastatic, Mesentery			1 (2%)	
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Salivary Glands	(48)	(50)	(50)	(49)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma			1 (2%)	
Stomach, Glandular	(50)	(50)	(50)	(50)
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung			1 (2%)	
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(49)	(50)	(50)	(50)
Adrenal Medulla	(49)	(50)	(50)	(50)
Pheochromocytoma Benign			1 (2%)	
Pituitary Gland	(49)	(49)	(49)	(49)
Pars Distalis, Adenoma	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Pars Intermedia, Adenoma	2 (4%)			1 (2%)
Thyroid Gland	(49)	(50)	(50)	(50)
Follicular Cell, Adenoma			1 (2%)	
Follicular Cell, Carcinoma		2 (4%)		

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
GENERAL BODY SYSTEM				
Peritoneum				(1)
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (100%)
GENITAL SYSTEM				
Clitoral Gland	(50)	(50)	(50)	(49)
Ovary	(50)	(50)	(50)	(49)
Adenocarcinoma				1 (2%)
Cystadenoma	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Fibrous Histiocytoma, Metastatic, Mesentery			1 (2%)	
Hemangioma	2 (4%)			
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Luteoma			1 (2%)	
Teratoma Benign	1 (2%)			
Thecoma Malignant			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Fibrous Histiocytoma, Metastatic, Mesentery			1 (2%)	
Hemangiosarcoma		1 (2%)		
Leiomyoma	1 (2%)			
Leiomyosarcoma	1 (2%)			
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Polyp Stromal		1 (2%)	1 (2%)	1 (2%)
Cervix, Hemangiosarcoma		1 (2%)		
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Hemangiosarcoma				1 (2%)
Lymph Node	(9)	(6)	(8)	(5)
Mediastinal, Alveolar/Bronchiolar Carcinoma, Metastatic, Lung			1 (13%)	
Mediastinal, Fibrosarcoma, Metastatic, Skin			1 (13%)	
Mediastinal, Sarcoma, Metastatic, Bone				1 (20%)
Renal, Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (20%)
Lymph Node, Mandibular	(48)	(49)	(46)	(47)
Carcinoma, Metastatic, Harderian Gland	1 (2%)			
Lymph Node, Mesenteric	(47)	(48)	(47)	(46)
Histiocytic Sarcoma		1 (2%)		1 (2%)
Sarcoma NOS, Metastatic, Uncertain Primary				

G 13

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
HEMATOPOIETIC SYSTEM - cont				
Site	1 (2%)			
Spleen	(50)	(50)	(49)	(49)
Hemangiosarcoma	1 (2%)			1 (2%)
Hemangiosarcoma, Metastatic, Bone Marrow				1 (2%)
Histiocytic Sarcoma		1 (2%)		
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Thymus	(47)	(43)	(46)	(46)
Sarcoma, Metastatic, Bone				1 (2%)
INTEGUMENTARY SYSTEM				
Mammary Gland	(49)	(50)	(49)	(49)
Adenoacanthoma			1 (2%)	
Carcinoma				2 (4%)
Schwannoma Malignant, Metastatic, Skin	1 (2%)			
Duct, Adenoma		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Subcutaneous Tissue, Fibrosarcoma	2 (4%)	1 (2%)	5 (10%)	1 (2%)
Subcutaneous Tissue, Liposarcoma		1 (2%)		
Subcutaneous Tissue, Sarcoma		1 (2%)		
Subcutaneous Tissue, Sarcoma NOS, Metastatic, Uncertain Primary Site	1 (2%)			
Subcutaneous Tissue, Schwannoma Malignant	2 (4%)			
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Fibrosarcoma Metastatic, Skin			2 (4%)	
Cranium, Carcinoma, Metastatic, Harderian Gland	1 (2%)			
Rib, Periosteum, Sarcoma				1 (2%)
Vertebra, Schwannoma Malignant, Metastatic, Skin	1 (2%)			
Skeletal Muscle	(4)	(1)	(2)	
Fibrosarcoma, Metastatic, Skin			2 (100%)	
Leiomyosarcoma, Metastatic, Uterus	1 (25%)			
Liposarcoma, Metastatic, Skin		1 (100%)		
Schwannoma Malignant, Metastatic, Skin	2 (50%)			

A 01

[illegible] DENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED (a)
METHACRYLONITRILE

[illegible]	0 MG/KG	1.5 MG/KG	[illegible] MG/KG	6 MG/KG
[illegible]				
[illegible]	(50)	(50)	(50)	(50)
[illegible]			1 (2%)	
[illegible]	(1)		(2)	
[illegible] Sarcoma [illegible] Metastatic, Skin			2 (100%)	
[illegible]				
[illegible]	(50)	(50)	(50)	(50)
[illegible] Adenoma	6 (12%)	3 (6%)	1 (2%)	2 (4%)
[illegible] Carcinoma	1 (2%)		1 (2%)	3 (6%)
Alv. Carcinoma, Metastatic, [illegible]				1 (2%)
Car[illegible] [illegible], Harderian Gland	2 (4%)			
[illegible], Thyroid Gland		1 (2%)		
[illegible] Metastatic, Skin			3 (6%)	
[illegible] Carcinoma, Metastatic, Liver	2 (4%)		3 (6%)	
[illegible] Sarcoma, Metastatic, Intestine Small, [illegible]				1 (2%)
[illegible] Metastatic, Skin		1 (2%)		
[illegible] Bone				1 (2%)
[illegible] Malignant, Metastatic, [illegible]	1 (2%)			
[illegible] Alveolar/Bronchiolar Carcinoma, Metastatic, Lung			1 (2%)	
[illegible], Fibrosarcoma, Metastatic, Skin			1 (2%)	
Mediastinum, Leiomyosarcoma, Metastatic, Uterus	1 (2%)			
Mediastinum, Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Mediastinum, Sarcoma, Metastatic, Bone				1 (2%)
[illegible]	(50)	(50)	(50)	(50)
[illegible] Metastatic, Harderian Gland	1 (2%)			
SYSTEM				
[illegible]	(2)	(1)		(4)
Carcinoma, Metastatic, Harderian Gland	1 (50%)			
Harderian Gland	(4)	(2)	(2)	(2)
Adenoma	2 (50%)	1 (50%)	2 (100%)	2 (100%)
Carcinoma	2 (50%)			
Bilateral, Adenoma		1 (50%)		

A 02

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
URINARY SYSTEM				
Kidney	(50)	(50)	(49)	(50)
Hemangiosarcoma	1 (2%)			
Leiomyosarcoma, Metastatic, Uterus	1 (2%)			
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)			
Hemangiosarcoma, Metastatic, Bone Marrow				1 (2%)
Leiomyosarcoma, Metastatic, Intestine Small, Ileum				1 (2%)
Sarcoma NOS, Metastatic, Uncertain Primary Site	1 (2%)			
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Histiocytic Sarcoma		1 (2%)		1 (2%)
Lymphoma Malignant	9 (18%)	7 (14%)	7 (14%)	2 (4%)

(a) Animals with any tissue examined microscopically

A 03

B6C3F1 MICE FEMALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	34	28	29	21
Total Primary Neoplasms	55	39	46	31
Total Animals with Benign Neoplasms	24	15	20	13
Total Benign Neoplasms	32	20	25	14
Total Animals with Malignant Neoplasms	20	17	17	14
Total Malignant Neoplasms	23	19	21	17
Total Animals with Metastatic Neoplasms	8	2	9	4
Total Metastatic Neoplasm	23	3	26	22
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

A 04

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Natural Death	9	5	4	3
Moribund Sacrifice	5	2	3	
Dosing Accident				1
Accidently Killed				24
Survivors				
Terminal Sacrifice	34	43	41	22
Natural Death	1		2	
Missing	1			
Animals Examined Microscopically	49	50	50	50
ALIMENTARY SYSTEM				
Intestine Large, Cecum	(49)	(50)	(50)	(50)
Adenocarcinoma		1 (2%)		
Intestine Small, Duodenum	(49)	(49)	(50)	(50)
Adenocarcinoma		1 (2%)	1 (2%)	
Adenoma	2 (4%)		2 (4%)	1 (2%)
Intestine Small, Jejunum	(49)	(50)	(50)	(50)
Adenocarcinoma	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Liver	(49)	(50)	(50)	(50)
Carcinoma, Metastatic, Harderian Gland			1 (2%)	
Carcinoma, Metastatic, Intestine Small, Duodenum			1 (2%)	
Hemangiosarcoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Hepatoblastoma	1 (2%)			
Hepatocellular Carcinoma	10 (20%)	7 (14%)	7 (14%)	4 (8%)
Hepatocellular Carcinoma, Multiple	3 (6%)			
Hepatocellular Adenoma	13 (27%)	15 (30%)	16 (32%)	6 (12%)
Hepatocellular Adenoma, Multiple	4 (8%)	12 (24%)	8 (16%)	6 (12%)
Hepatocholangiocarcinoma	1 (2%)	2 (4%)	1 (2%)	
Sarcoma, Metastatic, Pancreas		1 (2%)		
Mesentery	(3)	(6)	(6)	(1)
Carcinoma, Metastatic, Intestine Small, Duodenum			1 (17%)	
Hemangiosarcoma		1 (17%)		
Hepatocholangiocarcinoma, Metastatic, Liver		1 (17%)		
Sarcoma, Metastatic, Pancreas		1 (17%)		
Pancreas	(49)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)			
Sarcoma		1 (2%)		
Salivary Glands	(49)	(50)	(50)	(50)

A 05

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
ALIMENTARY SYSTEM - cont				
Stomach, Forestomach	(49)	(50)	(50)	(50)
Squamous Cell Papilloma	1 (2%)	2 (4%)	1 (2%)	
Stomach, Glandular	(49)	(50)	(50)	(50)
Tooth	(6)		(1)	(2)
Odontoma	1 (17%)			
CARDIOVASCULAR SYSTEM				
Heart	(48)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
ENDOCRINE SYSTEM				
Adrenal Cortex	(49)	(50)	(50)	(50)
Capsule, Adenoma	5 (10%)	4 (8%)	3 (6%)	
Subcapsular, Adenoma			1 (2%)	
Adrenal Medulla	(49)	(50)	(50)	(50)
Pheochromocytoma Benign				1 (2%)
Islets, Pancreatic	(49)	(50)	(50)	(50)
Adenoma	2 (4%)		1 (2%)	
Thyroid Gland	(49)	(50)	(50)	(50)
C-Cell, Carcinoma	1 (2%)			
Follicular Cell, Adenoma			1 (2%)	1 (2%)
Follicular Cell Carcinoma	1 (2%)			
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Epididymis	(49)	(50)	(50)	(50)
Preputial Gland	(49)	(50)	(50)	(49)
Prostate	(49)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)			
Sarcoma, Metastatic, Pancreas		1 (2%)		
Seminal Vesicle	(49)	(50)	(50)	(50)
Carcinoma, Metastatic, Intestine Small, Duodenum			1 (2%)	
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
Sarcoma, Metastatic, Pancreas		1 (2%)		
Testes	(49)	(50)	(50)	(50)
Interstitial Cell, Adenoma		1 (2%)		

A 06

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
HEMATOPOIETIC SYSTEM				
Bone Marrow	(49)	(50)	(50)	(50)
Lymph Node	(3)	(5)	(3)	(3)
Bronchial, Hepatocholangiocarcinoma, Metastatic, Liver	1 (33%)			
Mediastinal, Carcinoma, Metastatic Intestine Small, Duodenum			1 (33%)	
Mediastinal, Hepatocholangiocarcinoma, Metastatic, Liver		1 (20%)		
Pancreatic, Sarcoma, Metastatic, Pancreas		1 (20%)		
Lymph Node, Mandibular	(46)	(48)	(50)	(47)
Carcinoma, Metastatic, Harderian Gland			2 (4%)	
Lymph Node, Mesenteric	(46)	(43)	(49)	(47)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
Histiocytic Sarcoma		1 (2%)		
Spleen	(49)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)			
Thymus	(40)	(48)	(46)	(49)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
INTEGUMENTARY SYSTEM				
Skin	(49)	(50)	(50)	(50)
Keratoacanthoma	1 (2%)			
Subcutaneous Tissue, Hemangioma		1 (2%)		
Subcutaneous Tissue, Lipoma	1 (2%)	1 (2%)		
MUSCULOSKELETAL SYSTEM				
Skeletal Muscle	(1)		(2)	(1)
Carcinoma, Metastatic, Harderian Gland			1 (50%)	
Carcinoma, Metastatic, Intestine Small, Duodenum			1 (50%)	
Hepatocholangiocarcinoma, Metastatic, Liver	1 (100%)			
NERVOUS SYSTEM				
None				

A 07

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
RESPIRATORY SYSTEM				
Lung	(49)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	2 (4%)	11 (22%)	7 (14%)	4 (8%)
Alveolar/Bronchiolar Adenoma, Multiple			1 (2%)	1 (2%)
Alveolar/Bronchiolar Carcinoma	4 (8%)	2 (4%)	1 (2%)	1 (2%)
Alveolar/Bronchiolar Carcinoma, Multiple		1 (2%)		
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung		1 (2%)		
Carcinoma, Metastatic, Harderian Gland			2 (4%)	
Carcinoma, Metastatic, Intestine Small, Duodenum			1 (2%)	
Hepatocellular Carcinoma, Metastatic, Liver	6 (12%)	2 (4%)	4 (8%)	
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)	1 (2%)	1 (2%)	
Mediastinum, Carcinoma, Metastatic, Harderian Gland			1 (2%)	
Mediastinum, Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)	1 (2%)		
Serosa, Hepatocholangiocarcinoma, Metastatic, Liver			1 (2%)	
Nose	(49)	(50)	(50)	(50)
Carcinoma, Metastatic, Harderian Gland			1 (2%)	
SPECIAL SENSES SYSTEM				
Harderian Gland	(3)	(2)	(7)	(1)
Adenoma	3 (100%)	2 (100%)	5 (71%)	1 (100%)
Carcinoma			2 (29%)	
URINARY SYSTEM				
Kidney	(49)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)	1 (2%)		
Renal Tubule, Adenoma				1 (2%)
Renal Tubule, Carcinoma		1 (2%		
Urinary Bladder	(49)	(50)	(50)	(50)
SYSTEMIC LESIONS				
Multiple Organs	*(49)	*(50)	*(50)	*(50)
Histiocytic Sarcoma		1 (2%)		
Lymphoma Malignant	2 (4%)	3 (6%)	3 (6%)	1 (2%)

* Number of animals with any tissue examined microscopically

A 08

B6C3F1 MICE MALE	0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	40	41	39	24
Total Primary Neoplasms	62	72	64	31
Total Animals with Benign Neoplasms	29	35	33	19
Total Benign Neoplasms	35	49	46	22
Total Animals with Malignant Neoplasms	24	17	16	8
Total Malignant Neoplasms	27	[illegible]	18	9
Total Animals with Metastatic Neoplasms	7	5	8	
Total Metastatic Neoplasm	12	17	20	
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

A 09

A 10

END OF REPORT

NTP
LAB: Battelle Columbus
EXPERIMENT: 88050 TEST: 06
TEST TYPE: CHRONIC
CONT. [illegible]-55388
PATHOLOGIST: [illegible]PT, JOHN

STATISTICAL ANALYSIS OF PRIMARY TUMORS
METHACRYLONITRILE

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

REPORT: PETERSON
DATE: [illegible]
TIME: [illegible]
PAGE: [illegible]
NTP [illegible]
CAS: [illegible]

CORE STUDY MICE FINAL#1

REASONS FOR REMOVAL: ALL

REMOVAL DATE RANGE: ALL

TREATMENT GROUPS: INCLUDE ALL

A 11

NTP
L/J. Battelle Columbus

STATISTICAL ANALYSIS OF PRIMARY TUMORS
METHACRYLONITRILE

REPORT OF PSTA-
DATE: 10 19 90

EXPERIMENT: 88050 TEST: 00
TEST TYPE: CHRONIC
CONT: N01-ES-55388
PATHOLOGIST TOFT, JOHN

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

TIME: 12:44 14

NTP CS PROG 5
DA 12:52

Mice(B6C3F1)

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
Pancreas
Pituitary Gland
Prostate
Spleen
Testes
Thyroid Gland
Urinary Bladder

A 12

NTP
LAB: Battelle Columbus
EXPERIMENT: 28050 TEST: 06
TEST TYPE: CHRONIC
CONT: N01-ES 55188
PATHOLOGIST: TOPT, JOHN

STATISTICAL ANALYSIS OF PRIMARY TUMORS
METHACRYLONITRILE

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

SUMMARY OF STATISTICALLY SIGNIFICANT (P<.05) RESULTS
IN THE ANALYSIS OF METHACRYLONITRILE

Male Mice

Organ	Morphology
Adrenal Cortex	Adenoma
Liver	Hepatocellular Adenoma
	Hepatocellular Carcinoma
	Hepatocellular Carcinoma or Hepatoblastoma
	Hepatocellular Carcinoma or Hepatocellular Adenoma
	Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma
Lung	Alveolar/Bronchiolar Adenoma
All Organs	Benign Tumors
	Malignant Tumors
	Malignant and Benign Tumors

Female Mice

Organ	Morphology
Intestine Large: Cecum	Leiomyoma
Lung	Alveolar/Bronchiolar Adenoma
Mammary Gland	Carcinoma
All Organs	Hemangiosarcoma or Hemangioma
	Malignant Lymphoma: Histiocytic, Lymphocytic, Mixed, NOS, or Undifferentiated Cell Type
	Benign Tumors
	Malignant and Benign Tumors

A 13

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Adrenal Cortex Adenoma								
TUMOR RATES								
OVERALL (a)	5/49 (10%)	4/50 (8%)	4/50 (8%)	0/25 (0%)	0/49 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	11.1%	8.4%	8.5%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (c)	5/35 (14%)	3/43 (7%)	4/43 (9%)	0/22 (0%)	0/34 (0%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	544	729 (T)		---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.069N	P=0.380N	P=0.372N	P=0.386N	(e)	(e)	(e)	(e)
POLY 3	P=0.083N	P=0.460N	P=0.474N	P=0.078N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.058N	P=0.472N	P=0.482N	P=0.054N	(e)	(e)	(e)	(e)
POLY 6	P=0.111N	P=0.442N	P=0.456N	P=0.105N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.078N	P=0.457N	P=0.372N	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.028N*	P=0.487N	P=0.484N	P=0.027N*	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Harderian Gland Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	2/50 (4%)	5/50 (10%)	1/50 (2%)	2/50 (4%)	2/50 (4%)	2/50 (4%)	[illegible]
POLY 3 ADJUSTED (b)	6.7%	4.2%	10.7%	3.2%	4.6%	4.6%	4.2%	[illegible]
TERMINAL (d)	3/35 (9%)	2/43 (5%)	5/43 (12%)	1/22 (5%)	2/35 (6%)	1/35 (3%)	3/43 (7%)	2/25 (8%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	729 (T)	730 (T)	638	589	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.530N	P=0.406N	P=0.473	P=0.482N	P=0.473	P=0.689	P=0.655N	P=[illegible]
POLY 3	P=0.534N	P=0.474N	P=0.380	P=0.446N	P=0.493	P=0.679	P=0.571N	P=[illegible]
POLY 1.5	P=0.454N	P=0.481N	P=0.372	P=0.388N	P=0.527	P=0.682	P=0.680N	P=[illegible]
POLY 6	P=0.512	P=0.463N	P=0.396	P=0.499N	P=0.468	P=0.684	P=0.650N	P=[illegible]
LOGISTIC REGRESSION	P=0.530N	P=0.406N	P=0.473	P=0.482N	P=0.532	P=0.682	P=0.675	P=[illegible]
COCH-ARM / FISHERS	P=0.319N	P=0.500N	P=0.357	P=0.309N	P=0.595	P=0.591N	P=0.591N	P=[illegible]

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Harderian Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	4.2%	0.0%	4.4%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	1/43 (2%)	0/22 (0%)	2/35 (6%)	0/35 (0%)	0/43 (0%)	0/22 (0%)
FIRST INCIDENCE	---	---	502	---	730 (T)			
STATISTICAL TESTS								
LIFE TABLE	P=0.490	(e)	P=0.262	(e)	P=0.124N	P=0.238N	P=0.154N	P=0.[illegible]N
POLY 3	P=0.350	(e)	P=0.250	(e)	P=0.094N	P=0.248N	P=0.226N	P=0.[illegible]N
POLY 1.5	P=0.448	(e)	P=0.246	(e)	P=0.102N	P=0.246N	P=0.230N	P=0.[illegible]N
POLY 6	P=0.285	(e)	P=0.258	(e)	P=0.086N	P=0.247N	P=0.[illegible]N	P=0.[illegible]N
LOGISTIC REGRESSION	P=0.679	(e)	P=0.187	(e)	P=0.124N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.595	(e)	P=0.247	(e)	P=0.115N	P=0.247N	P=0.247N	P=0.247N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Harderian Gland Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	2/50 (4%)	7/50 (14%)	1/50 (2%)	4/50 (8%)	2/50 (4%)	2/50 (4%)	2/50 (4%)
POLY-3 ADJUSTED (b)	6.7%	4.2%	14.7%	3.2%	8.9%	4.6%	4.2%	5.7%
TERMINAL (d)	3/35 (9%)	2/43 (5%)	6/43 (14%)	1/22 (5%)	4/35 (11%)	1/35 (3%)	1/43 (2%)	2/22 (9%)
FIRST INCIDENCE	729 (T)	729 (T)	502	729 (T)	730 (T)	638	589	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.558	P=0.406N	P=0.244	P=0.482N	P=0.411N	P=0.341N	P=0.262N	P=0.500N
POLY 3	P=0.464	P=0.474N	P=0.181	P=0.446N	P=0.344N	P=0.356N	P=0.309N	P=0.462N
POLY 1.5	P=0.543N	P=0.481N	P=0.173	P=0.388N	P=0.329N	P=0.353N	P=0.321N	P=0.417N
POLY 6	P=0.368	P=0.463N	P=0.196	P=0.499N	P=0.349N	P=0.350N	P=0.293N	P=0.500N
LOGISTIC REGRESSION	P=0.575N	P=0.406N	P=0.164	P=0.482N	P=0.370N	P=0.357N	P=0.338N	P=0.500N
COCH-ARM / FISHERS	P=0.367N	P=0.500N	P=0.159	P=0.309N	P=0.292N	P=0.339N	P=0.339N	P=0.339N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Large: Cecum Leiomyoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	3/50 (6%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	6.6%	2.3%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	3/35 (9%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	---		---		730 (T)	730 (T)	---	
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.050N	P=0.305N	P=0.087N	P=0.184N
POLY 3	(e)	(e)	(e)	(e)	P=0.040N*	P=0.323N	P=0.110N	P=0.172N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.042N*	P=0.319N	P=0.120N	P=0.152N
POLY 6	(e)	(e)	(e)	(e)	P=0.038N*	P=0.320N	P=0.100N	P=0.191N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.050N	P=0.305N	(e)	(e)
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.044N*	P=0.309N	P=0.120N	P=0.120N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Small: Duodenum Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	[illegible] (4%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.5%	[illegible]	4.7%	3.2%	2.2%	2.3%	0.0%	0.0%
TERMINAL (d)	[illegible]	[illegible]	2/43 (5%)	1/22 (5%)	1/35 (3%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	730 (T)		729 (T)	729 (T)	730 (T)	730 (T)	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.582	P=0.194N	P=0.619N	P=0.660N	P=0.264N	P=0.762	P=0.459N	P=0.567N
POLY 3	P=0.560	P=0.225N	P=0.679N	P=0.623N	P=0.235N	P=0.750	P=0.499N	P=0.541N
POLY 1.5	P=0.591N	P=0.228N	P=0.684N	P=0.576N	P=0.236N	P=0.752	P=0.494N	P=0.543N
POLY 6	P=0.529	P=0.239N	P=0.668N	P=0.664N	P=0.223N	P=0.751	P=0.484N	P=0.567N
LOGISTIC REGRESSION	P=0.582	(e)	P=0.619N	P=0.660N	P=0.264N	P=0.762	(e)	(e)
COCH-ARM / FISHERS	P=0.531N	P=0.247N	P=0.691N	P=0.500N	P=0.236N	P=0.753N	P=0.500N	P=0.500N

B 02

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Small: Jejunum Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	2/50 (4%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	2.1%	4.3%	6.3%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	1/43 (2%)	2/43 (5%)	0/22 (0%)	0/35 (0%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	481	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.204	P=0.715N	P=0.572	P=0.396	(e)	(e)	(e)	(e)
POLY 3	P=0.214	P=0.748N	P=0.515	P=0.384	(e)	(e)	(e)	(e)
POLY 1.5	P=0.255	P=0.751N	P=0.510	P=0.428	(e)	(e)	(e)	(e)
POLY 6	P=0.192	P=0.742N	P=0.525	P=0.347	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.296	P=0.715N	P=0.572	P=0.503	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.337	P=0.753N	P=0.500	P=0.500	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Small: Site Unspecified Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.5%	0.0%	4.3%	3.2%	2.2	2.3%	0.0%	0.0%
TERMINAL (d)	2/35 (6%)	0/43 (0%)	2/43 (5%)	1/22 (5%)	1/35 (3%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	---	729 (T)	729 (T)	730 (T)	730 (T)	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.582	P=0.194N	P=0.619N	P=0.660N	P=0.264N	P=0.762	P=0.459N	P=0.567N
POLY 3	P=0.560	P=0.225N	P=0.679N	P=0.523N	P=0.231N	P=0.750	P=0.490N	P=0.551N
POLY 1.5	P=0.591N	P=0.228N	P=0.684N	P=0.576N	P=0.236N	P=0.752	P=0.494N	P=0.533N
POLY 6	P=0.529	P=0.219N	P=0.668N	P=0.664N	P=0.223N	P=0.751	P=0.484N	P=0.565N
LOGISTIC REGRESSION	P=0.582	(e)	P=0.619N	P=0.660N	P=0.264N	P=0.762	(e)	(e)
COCH-ARM / FISHERS	P=0.531N	P=0.247N	P=0.691N	P=0.500N	P=0.236N	P=0.753N	P=0.500N	P=0.500N

B 03

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Small: Site Unspecified Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	3/50 (6%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	4.2%	6.4%	6.3%	0.0%	0.0%	2.1%	0.0%
TERMINAL (d)	1/35 (3%)	2/43 (5%)	2/43 (5%)	0/22 (0%)	0/35 (0%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	612	481	---	---	589	---
STATISTICAL TESTS								
LIFE TABLE	P=0.234	P=0.572	P=0.367	P=0.396	P=0.656	(e)	P=0.504	(e)
POLY 3	P=0.233	P=0.520	P=0.324	P=0.384	P=0.662	(e)	P=0.512	(e)
POLY 1.5	P=0.290	P=0.514	P=0.317	P=0.428	P=0.614	(e)	P=0.507	(e)
POLY 6	P=0.198	P=0.528	P=0.336	P=0.347	P=0.613	(e)	P=0.519	(e)
LOGISTIC REGRESSION	P=0.376	P=0.572	P=0.304	P=0.503	P=0.734N	(e)	P=0.365	(e)
COCH-ARM / FISHERS	P=0.404	P=0.500	P=0.309	P=0.500	P=0.694	(e)	P=0.500	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Intestine Small: Site Unspecified Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	2/50 (4%)	5/50 (10%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	6.7%	4.2%	10.6%	9.4%	2.2%	2.3%	2.1%	0.0%
TERMINAL (d)	3/35 (9%)	2/43 (5%)	4/43 (9%)	1/22 (5%)	1/35 (3%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	612	481	730 (T)	730 (T)	589	---
STATISTICAL TESTS								
LIFE TABLE	P=0.251	P=0.406N	P=0.[illegible]22	P=0.478	P=0.374N	P=0.762	P=0.735N	P=0.560N
POLY 3	P=0.269	P=0.474N	P=0.385	P=0.497	P=0.354N	P=0.750	P=0.746N	P=0.551N
POLY 1.5	P=0.339	P=0.481N	P=0.375	P=0.563	P=0.341N	P=0.752	P=0.752N	P=0.533N
POLY 6	P=0.225	P=0.463N	P=0.404	P=0.438	P=0.361N	P=0.752	P=0.738N	P=0.565N
LOGISTIC REGRESSION	P=0.339	P=0.406N	P=0.375	P=0.529	P=0.312N	P=0.762	P=0.719	(e)
COCH-ARM / FISHERS	P=0.481	P=0.500N	P=0.357	P=0.661N	P=0.311N	P=0.753N	P=0.753N	P=0.500N

B 04

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Islets, Pancreatic Adenoma								
TUMOR RATES								
OVERALL (a)	2/49 (4%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)
POLY-3 ADJUSTED (b)	4.4%	0.0%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	1/43 (2%)	0/22 (0%)	0/35 (0%)	0/35 (0%)	0/63 (0%)	0/25 (0%)
FIRST INCIDENCE	677	---	729 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.255N	P=0.222N	P=0.452N	P=0.371N	(e)	(e)	(e)	(e)
POLY 3	P=0.212N	P=0.226N	P=0.488N	P=0.330N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.206N	P=0.229N	P=0.491N	P=0.291N	(e)	(e)	(e)	(e)
POLY 6	P=0.226N	P=0.222N	P=0.480N	P=0.367N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.205N	P=0.257N	P=0.494N	P=0.289N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.185N	P=0.242N	P=0.492N	P=0.242N	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver Hepatocellular Adenoma								
TUMOR RATES								
OVERALL (a)	17/49 (35%)	27/50 (54%)	24/50 (48%)	12/50 (24%)	9/50 (18%)	9/50 (18%)	12/49 (24%)	5/50 (10%)
POLY-3 ADJUSTED (b)	26.3%	54.7%	49.2%	34.7%	19.8%	20.8%	25.5%	14.1%
TERMINAL (d)	12/35 (34%)	22/43 (51%)	21/43 (49%)	7/22 (32%)	7/35 (20%)	8/35 (23%)	12/63 (28%)	4/25 (16%)
FIRST INCIDENCE	501	605	429	481	653	638	730 (T)	480
STATISTICAL TESTS								
LIFE TABLE	P=0.512	P=0.168	P=0.318	P=0.518	P=0.384N	P=0.599	P=0.507	P=0.411N
POLY 3	P=0.442N	P=0.053	P=0.143	P=0.531N	P=0.380N	P=0.559	P=0.341	P=0.355N
POLY 1.5	P=0.253N	P=0.046 *	P=0.135	P=0.380N	P=0.305N	P=0.569	P=0.322	P=0.292N
POLY 6	P=0.448	P=0.064	P=0.159	P=0.517	P=0.440N	P=0.563	P=0.367	P=0.411N
LOGISTIC REGRESSION	P=0.123N	P=0.030 *	P=0.119	P=0.296N	P=0.386N	P=0.564	P=0.408	P=0.370N
COCH-ARM / FISHERS	P=0.051N	P=0.041 *	P=0.127	P=0.172N	P=0.183N	P=0.602N	P=0.294	P=0.194N

Statistical Analysis of Primary Tumors in Mice (B6C3F1) METHACRYLONITRILE

Terminal Sacrifice at 104 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver								
Hepatocellular Carcinoma								
TUMOR RATES								
OVERALL (a)	13/49 (27%)	7/50 (14%)	7/50 (14%)	4/50 (8%)	2/50 (4%)	2/50 (4%)	4/49 (8%)	1/50 (2%)
POLY-3 ADJUSTED (b)	27.5%	14.4%	14.9%	12.4%	4.4%	4.7%	8.5%	2.9%
TERMINAL (d)	6/35 (17%)	3/43 (7%)	6/43 (14%)	1/22 (5%)	0/35 (0%)	2/35 (6%)	3/43 (7%)	1/25 (4%)
FIRST INCIDENCE	501	625	694	481	662	730 (T)	653	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.112N	P=0.074N	P=0.064N	P=0.161N	P=0.565N	P=0.692N	P=0.412	P=0.621N
POLY 3	P=0.063N	P=0.091N	P=0.106N	P=0.097N	P=0.565N	P=0.674	P=0.356	P=0.591N
POLY 1.5	P=0.040N*	P=0.093N	P=0.103N	P=0.049N*	P=0.520N	P=0.679	P=0.345	P=0.5[illegible]N
POLY 6	P=0.087N	P=0.087N	P=0.105N	P=0.165N	P=0.534	P=0.674	P=0.371	P=0.618N
LOGISTIC REGRESSION	P=0.010N*	P=0.155N	P=0.097N	P=0.019N*	P=0.537N	P=0.682	P=0.309	P=0.5[illegible]N
COCH-ARM / FISHERS	P=0.014N*	P=0.096N	P=0.096N	P=0.014N*	P=0.433N	P=0.691N	P=0.329	P=0.5[illegible]N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver								
Hepatocellular Carcinoma or Hepatoblastoma								
TUMOR RATES								
OVERALL (a)	14/49 (29%)	7/50 (14%)	7/50 (14%)	4/50 (8%)	2/50 (4%)	2/50 (4%)	4/49 (8%)	1/50 (2%)
POLY-3 ADJUSTED (b)	29.6%	14.4%	14.9%	12.4%	4.4%	4.7%	8.5%	2.9%
TERMINAL (d)	7/35 (20%)	3/43 (7%)	6/43 (14%)	1/22 (5%)	0/35 (0%)	2/35 (6%)	3/43 (7%)	1/25 (4%)
FIRST INCIDENCE	501	625	694	481	662	730 (T)	653	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.079N	P=0.047N*	P=0.040N*	P=0.123N	P=0.565N	P=0.692N	P=0.412	P=0.62[illegible]N
POLY 3	P=0.040N*	P=0.058N	P=0.069N	P=0.067N	P=0.565N	P=0.674	P=0.356	P=0.59[illegible]N
POLY 1.5	P=0.025N*	P=0.060N	P=0.067N	P=0.031N*	P=0.520N	P=0.679	P=0.345	P=0.5[illegible]N
POLY 6	P=0.056N	P=0.055N	P=0.069N	P=0.124N	P=0.534	P=0.674	P=0.371	P=0.6[illegible]N
LOGISTIC REGRESSION	P=0.006N**	P=0.104N	P=0.064N	P=0.013N*	P=0.537N	P=0.682	P=0.309	P=0.5[illegible]N
COCH-ARM / FISHERS	P=0.008N**	P=0.063N	P=0.063N	P=0.008N**	P=0.433N	P=0.691N	P=0.329	P=0.5[illegible]N

B 06

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver								
Hepatocellular Carcinoma or Hepatocellular Adenoma								
TUMOR RATES								
OVERALL (a)	24/49 (49%)	29/50 (58%)	28/50 (56%)	15/50 (30%)	10/50 (20%)	11/50 (22%)	14/49 (29%)	6/50 (12%)
POLY-3 ADJUSTED (b)	50.7%	58.6%	57.2%	41.9%	21.9%	25.4%	29.6%	16.9%
TERMINAL (d)	16/35 (46%)	23/43 (54%)	24/43 (56%)	7/22 (32%)	7/35 (20%)	10/35 (29%)	13/43 (30%)	5/25 (20%)
FIRST INCIDENCE	501	605	429	481	653	638	653	480
STATISTICAL TESTS								
LIFE TABLE	P=0.477N	P=0.539	P=0.538N	P=0.503N	P=0.414N	P=0.494	P=0.431	P=0.454N
POLY 3	P=0.256N	P=0.281	P=0.331	P=0.283N	P=0.410N	P=0.444	P=0.269	P=0.392N
POLY 1.5	P=0.117N	P=0.264	P=0.321	P=0.156N	P=0.322N	P=0.458	P=0.251	P=0.319N
POLY 6	P=0.410N	P=0.311	P=0.352	P=0.429N	P=0.483N	P=0.443	P=0.294	P=0.458N
LOGISTIC REGRESSION	P=0.050N	P=0.205	P=0.298	P=0.118N	P=0.400N	P=0.453	P=0.284	P=0.401N
COCH-ARM / FISHERS	P=0.014N*	P=0.243	P=0.309	P=0.042N*	P=0.181N	P=0.500	P=0.224	P=0.207N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver								
Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma								
TUMOR RATES								
OVERALL (a)	24/49 (49%)	29/50 (58%)	28/50 (56%)	15/50 (30%)	10/50 (20%)	11/50 (22%)	14/49 (29%)	6/50 (12%)
POLY-3 ADJUSTED (b)	50.7%	58.6%	57.2%	41.9%	21.9%	25.4%	29.6%	16.9%
TERMINAL (d)	16/35 (46%)	23/43 (54%)	24/43 (56%)	7/22 (32%)	7/35 (20%)	10/35 (29%)	13/43 (30%)	5/25 (20%)
FIRST INCIDENCE	501	605	429	481	653	638	653	480
STATISTICAL TESTS								
LIFE TABLE	P=0.477N	P=0.539	P=0.538N	P=0.503N	P=0.414N	P=0.494	P=0.431	P=0.454N
POLY 3	P=0.256N	P=0.281	P=0.331	P=0.283N	P=0.410N	P=0.444	P=0.269	P=0.392N
POLY 1.5	P=0.117N	P=0.264	P=0.321	P=0.156N	P=0.322N	P=0.458	P=0.251	P=0.319N
POLY 6	P=0.410N	P=0.311	P=0.352	P=0.429N	P=0.483N	P=0.443	P=0.294	P=0.458N
LOGISTIC REGRESSION	P=0.050N	P=0.205	P=0.298	P=0.118N	P=0.400N	P=0.453	P=0.284	P=0.401N
COCH-ARM / FISHERS	P=0.014N*	P=0.243	P=0.309	P=0.042N*	P=0.181N	P=0.500	P=0.224	P=0.207N

Statistical Analysis of Primary Tumors in Mice(B6C3F1)

Terminal Sacrifice at 105 weeks

METHACRYLONITRILE

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Liver								
Hepatocholangiocarcinoma								
TUMOR RATES								
OVERALL (a)	1/49 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	4.2%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	1/43 (2%)	0/43 (0%)	0/22 (0%)	0/35 (0%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	513	625	694	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.368N	P=0.536	P=0.750N	P=0.630N	(e)	(e)	(e)	(e)
POLY 3	P=0.330N	P=0.518	P=0.754N	P=0.574N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.301N	P=0.513	P=0.756N	P=0.545N	(e)	(e)	(e)	(e)
POLY 6	P=0.366N	P=0.525	P=0.748N	P=0.598N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.130N	P=0.315	P=0.716N	P=0.316N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.243N	P=0.508	P=0.747N	P=0.495N	(e)	(e)	(e)	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Lung								
Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	2/49 (4%)	11/50 (22%)	8/50 (16%)	5/50 (10%)	6/50 (12%)	3/50 (6%)	1/50 (2%)	2/50 (4%)
POLY-3 ADJUSTED (b)	4.5%	22.9%	16.9%	15.7%	13.3%	7.0%	2.1%	5.7%
TERMINAL (d)	2/35 (6%)	9/43 (21%)	7/43 (16%)	4/22 (18%)	5/35 (14%)	3/35 (9%)	1/43 (2%)	1/25 (4%)
FIRST INCIDENCE	729 (T)	629	612	481	709	730 (T)	730 (T)	673
STATISTICAL TESTS								
LIFE TABLE	P=0.143	P=0.023 *	P=0.088	P=0.088	P=0.127N	P=0.239N	P=0.533N*	P=0.264N
POLY 3	P=0.165	P=0.010 *	P=0.054	P=0.104	P=0.092N	P=0.287N	P=0.048N*	P=0.273N
POLY 1.5	P=0.258	P=0.009 **	P=0.051	P=0.141	P=0.089N	P=0.261N	P=0.051N	P=0.139N
POLY 6	P=0.114	P=0.012 *	P=0.060	P=0.078	P=0.091N	P=0.264N	P=0.044N*	P=0.264N
LOGISTIC REGRESSION	P=0.185	P=0.012 *	P=0.055	P=0.088	P=0.134N	P=0.240N	P=0.038N*	P=0.283N
COCH-ARM / FISHERS	P=0.485	P=0.008 **	P=0.049 *	P=0.226	P=0.079N	P=0.243N	P=0.056N	P=0.134N

B 08

Statistical Analysis of Primary Tumors in Mice(B6C3F1) METHAPYRILENE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Lung								
Alveolar/Bronchiolar Carcinoma								
TUMOR RATES								
OVERALL (a)	4/49 (8%)	3/50 (6%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (0%)
POLY-3 ADJUSTED (b)	8.9%	6.2%	2.1%	3.2%	2.2%	0.0%	2.1%	2.5%
TERMINAL (d)	4/35 (11%)	2/43 (5%)	1/43 (2%)	1/22 (5%)	1/35 (3%)	0/35 (0%)	1/43 (2%)	1/25 (4%)
FIRST INCIDENCE	729 (T)	563	729 (T)	729 (T)	730 (T)	---	730 (T)	[illegible]
STATISTICAL TESTS								
LIFE TABLE	P=0.172N	P=0.400N	P=0.123N	P=0.341N	P=0.050	P=0.500N	P=0.715N	P=0.199
POLY 3	P=0.128N	P=0.462N	P=0.166N	P=0.311N	P=0.077	P=0.510N	P=0.749N	P=0.226
POLY 1.5	P=0.118N	P=0.474N	P=0.170N	P=0.253N	P=0.082	P=0.507N	P=0.753N	P=0.285
POLY 6	P=0.136N	P=0.447N	P=0.158N	P=0.367N	P=0.074	P=0.509N	P=0.742N	P=0.206
LOGISTIC REGRESSION	P=0.150N	P=0.501N	P=0.123N	P=0.341N	P=0.062	(e)	P=0.715N	P=0.219
COCH-ARM / FISHERS	P=0.089N	P=0.489N	P=0.175N	P=0.175N	P=0.097	P=0.500N	P=0.753N	P=0.309

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Lung								
Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	6/49 (12%)	13/50 (26%)	9/50 (18%)	5/50 (10%)	6/50 (12%)	3/50 (6%)	2/50 (4%)	5/50 (10%)
POLY-3 ADJUSTED (b)	13.4%	26.8%	19.1%	15.7%	13.3%	7.0%	4.2%	14.1%
TERMINAL (d)	6/35 (17%)	10/43 (23%)	8/43 (19%)	4/22 (18%)	5/35 (14%)	3/35 (9%)	2/43 (5%)	2/25 (8%)
FIRST INCIDENCE	729 (T)	563	612	481	709	730 (T)	730 (T)	641
STATISTICAL TESTS								
LIFE TABLE	P=0.506	P=0.145	P=0.439	P=0.463	P=0.470	P=0.239N	P=0.081N	P=0.524
POLY 3	P=0.534	P=0.087	P=0.325	P=0.515	P=0.547N	P=0.267N	P=0.117N	P=0.586
POLY 1.5	P=0.424N	P=0.078	P=0.312	P=0.608	P=0.537N	P=0.261N	P=0.124N	P=0.610N
POLY 6	P=0.442	P=0.100	P=0.350	P=0.431	P=0.547N	P=0.266N	P=0.109N	P=0.546
LOGISTIC REGRESSION	P=0.528N	P=0.075	P=0.334	P=0.442	P=0.476	P=0.240N	P=0.093N	P=0.543
COCH-ARM / FISHERS	P=0.218N	P=0.068	P=0.303	P=0.486N	P=0.500N	P=0.243N	P=0.134N	P=0.500N

B 09

Statistical Analysis of Primary Tumors in Mice(B6C3F1) METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Mammary Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	5.1%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	0/35 (0%)	0/25 (0%)	0/43 (0%)	1/25 (4%)
FIRST INCIDENCE	---	---	-	---	---	---	---	581
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.024 *	(e)	(e)	P=0.153
POLY 3	(e)	(e)	(e)	(e)	P=0.040 *	(e)	(e)	P=0.187
POLY 1.5	(e)	(e)	(e)	(e)	P=0.041 *	(e)	(e)	P=0.203
POLY 6	(e)	(e)	(e)	(e)	P=0.039 *	(e)	(e)	P=0.176
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.051	(e)	(e)	P=0.229
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.247

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Mammary Gland Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	0.0%	2.3%	0.0%	5.1%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	0/35 (0%)	1/35 (3%)	0/43 (0%)	1/25 (4%)
FIRST INCIDENCE	---				--	730 (T)	-	581
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.086	P=0.500	(e)	P=0.[illegible]
POLY 3	(e)	(e)	(e)	(e)	P=0.116	P=0.496	(e)	P=0.[illegible]
POLY 1.5	(e)	(e)	(e)	(e)	P=0.122	P=0.493	(e)	P=0.[illegible]
POLY 6	(e)	(e)	(e)	(e)	P=0.114	P=0.493	(e)	P=0.176
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.129	P=0.500	(e)	P=0.229
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.140	P=0.500	(e)	P=0.24[illegible]

B10

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Mammary Gland Fibroma, Fibroadenoma, Carcinoma, or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	0.0%	2.3%	0.0%	5.7%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	0/35 (0%)	1/35 (3%)	0/4[illegible] (0%)	2/[illegible] (0%)
FIRST INCIDENCE	---	---	---	---	---	730 (T)	[illegible]	[illegible]
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.086	P=0.500	(e)	P=0.161
POLY 3	(e)	(e)	(e)	(e)	P=0.116	P=0.490	(e)	P=0.187
POLY 1.5	(e)	(e)	(e)	(e)	P=0.122	P=0.493	(e)	P=0.203
POLY 6	(e)	(e)	(e)	(e)	P=0.114	P=0.491	(e)	P=0.176
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.129	P=0.500	(e)	P=0.228
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.140	P=0.500	(e)	P=0.247

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Ovary Cystadenoma								
TUMOR RATES								
OVERALL (a)					2/50 (4%)	1/50 (2%)	1/50 (2%)	1/49 (2%)
POLY-3 ADJUSTED (b)					4.4%	2.3%	2.1%	2.9%
TERMINAL (d)					2/35 (6%)	1/35 (3%)	1/43 (2%)	1/25 (4%)
FIRST INCIDENCE					730 (T)	730 (T)	730 (T)	730 (T)
STATISTICAL TESTS								
LIFE TABLE					P=0.499N	P=0.500N	P=0.428N	P=0.617N
POLY 3					P=0.444N	P=0.517N	P=0.482N	P=0.595N
POLY 1.5					P=0.438N	P=0.513N	P=0.489N	P=0.565N
POLY 6					P=0.444N	P=0.515N	P=0.471N	P=0.618N
LOGISTIC REGRESSION					P=0.499N	P=0.500N	P=0.428N	P=0.617N
COCH-ARM / FISHERS					P=0.416N	P=0.500N	P=0.500N	P=0.508N

Statistical Analysis of Primary Tumors in Mice(B6C3F1)

Terminal Sacrifice at 105 weeks

METHACRYLONITRILE

Dose	Males 0 MG/KG	Males 1.5 MG/KG	Males 3 MG/KG	Males 6 MG/KG	Females 0 MG/KG	Females 1.5 MG/KG	Females 3 MG/KG	Females 6 MG/KG
Ovary								
Hemangioma								
TUMOR RATES								
OVERALL (a)					2/50 (4%)	0/50 (0%)	0/50 (0%)	0/49 (0%)
POLY 3 ADJUSTED (b)					4.4%	0.0%	0.0%	0.0%
TERMINAL (d)					2/35 (6%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE					730 (T)	---	---	---
STATISTICAL TESTS								
LIFE TABLE					P=0.124N	P=0.238N	P=0.196N	P=0.315N
POLY 3					P=0.095N	P=0.248N	P=0.226N	P=0.304N
POLY 1.5					P=0.103N	P=0.245N	P=0.230N	P=0.281N
POLY 6					P=0.087N	P=0.247N	P=0.239N	P=0.322N
LOGISTIC REGRESSION					P=0.124N	(e)	(e)	(e)
COCH-ARM / FISHERS					P=0.115N	P=0.247N	P=0.247N	P=0.253N

Dose	Males 0 MG/KG	Males 1.5 MG/KG	Males 3 MG/KG	Males 6 MG/KG	Females 0 MG/KG	Females 1.5 MG/KG	Females 3 MG/KG	Females 6 MG/KG
Pituitary Gland: Pars Distalis or Unspecified Site								
Adenoma								
TUMOR RATES								
OVERALL (a)	0/48 (0%)	0/49 (0%)	0/49 (0%)	0/46 (0%)	2/49 (4%)	1/49 (2%)	2/49 (4%)	2/45 (4%
POLY 3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.5%	2.3%	4.3%	5.8%
TERMINAL (d)	0/35 (0%)	0/42 (0%)	0/42 (0%)	0/22 (0%)	2/25 (8%)	1/35 (3%)	2/43 (5%)	2/21 (9%
FIRST INCIDENCE	---	---	---	---	730 (T)	730 (T)	730 (T)	54
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.410	P=0.500N	P=0.519N	P=0.56
POLY 3	(e)	(e)	(e)	(e)	P=0.434	P=0.515N	P=0.674N	P=0.5[illegible]
POLY 1.5	(e)	(e)	(e)	(e)	P=0.464	P=0.522N	P=0.682N	P=0.6[illegible]
POLY 6	(e)	(e)	(e)	(e)	P=0.414	P=0.513N	P=0.664N	P=0.[illegible]6
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.418	P=0.500N	P=0.619N	P=0.59[illegible]
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.524	P=0.500N	P=0.621N	P=0.6[illegible]N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Pituitary Gland: Pars Intermedia Adenoma								
TUMOR RATES								
OVERALL (a)	0/48 (0%)	0/49 (0%)	0/49 (0%)	0/46 (0%)	2/49 (4%)	0/49 (0%)	0/49 (0%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.5%	0.0%	0.0%	[illegible]
TERMINAL (d)	0/35 (0%)	0/42 (0%)	0/42 (0%)	0/22 (0%)	2/35 (6%)	0/35 (0%)	0/43 (0%)	[illegible]
FIRST INCIDENCE	---	---	---	---	730 (T)	-		[illegible]
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.532N	P=0.238N	P=0.196N	[illegible]
POLY 3	(e)	(e)	(e)	(e)	P=0.421N	P=0.247N	P=0.225N	[illegible]
POLY 1.5	(e)	(e)	(e)	(e)	P=0.439N	P=0.245N	[illegible]	[illegible]
POLY 6	(e)	(e)	(e)	(e)	P=0.401N	P=0.246N	P=0.219N	[illegible]
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.533N	(e)	(e)	[illegible]
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.461N	P=0.267N	P=0.247N	[illegible]

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Skin Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	2/50 (4%)	5/50 (10%)	[illegible]
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.4%	4.6%	10.2%	2.9%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	1/35 (3%)	0/35 (0%)	1/43 (2%)	[illegible]
FIRST INCIDENCE	---	---	---	---	671	521	589	730 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.571	P=0.677	P=0.268	P=0.614N
POLY 3	(e)	(e)	(e)	(e)	P=0.528	P=0.683	P=0.250	P=0.590N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.559N	P=0.684	P=0.236	P=0.559N
POLY 6	(e)	(e)	(e)	(e)	P=0.472	P=0.688	P=0.269	P=0.616N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.365N	P=0.648N	P=0.125	P=0.606N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.456N	P=0.691N	P=0.238	P=0.500N

B 13

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Skin								
Fibrosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	5/50 (10%)	1/50 (2%
POLY 3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.4%	2.3%	10.2%	2.9%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	1/35 (3%)	0/35 (0%)	1/43 (2%)	1/25 (4%
FIRST INCIDENCE	---	---	---	---	671	521	589	705 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.521	P=0.510N	P=0.268	P=0.516N
POLY 3	(e)	(e)	(e)	(e)	P=0.477	P=0.513N	P=0.250	P=0.500N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.543	P=0.511N	P=0.236	P=0.550N
POLY 6	(e)	(e)	(e)	(e)	P=0.491	P=0.511N	P=0.264	P=0.516N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.438N	P=0.449N	P=0.125	P=0.506N
COCH ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.523N	P=0.500N	P=0.218	P=0.500N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Skin								
Fibrosarcoma Sarcoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	2/50 (4%)	5/50 (10%)	1/50 (2%
POLY 3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.4%	4.6%	10.2%	2.9%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	1/35 (3%)	0/35 (0%)	1/43 (2%)	1/25 (4%
FIRST INCIDENCE	---	---	---	---	671	521	589	705 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.571	P=0.577	P=0.258	P=0.516N
POLY 3	(e)	(e)	(e)	(e)	P=0.528	P=0.593	P=0.215	P=0.500N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.559N	P=0.584	P=0.236	P=0.550N
POLY 6	(e)	(e)	(e)	(e)	P=0.472	P=0.588	P=0.243	P=0.516N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.365N	P=0.448N	P=0.125	P=0.506N
COCH ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.456N	P=0.691N	P=0.218	P=0.500N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Skin								
Schwannoma Malignant								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.4%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	1/35 (3%)	0/35 (0%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	---	---	---	---	607			
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.133N	P=0.252N	P=0.210N	P=0.224N
POLY 3	(e)	(e)	(e)	(e)	P=0.093N	P=0.250N	P=0.228N	P=0.252N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.101N	P=0.247N	P=0.232N	P=0.248N
POLY 6	(e)	(e)	(e)	(e)	P=0.085N	P=0.250N	P=0.224N	P=0.238N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.101N	P=0.222N	P=0.222N	P=0.238N
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.115N	P=0.247N	P=0.247N	P=0.247N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Stomach, Forestomach								
Squamous Cell Papilloma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	4.2%	2.1%	0.0%	0.0%	0.0%	2.1%	0.0%
TERMINAL (d)	0/35 (0%)	2/43 (5%)	1/43 (2%)	0/22 (0%)	0/35 (0%)	0/35 (0%)	1/43 (2%)	0/25 (0%)
FIRST INCIDENCE	513	729 (T)	729 (T)	---	---	---	730 (T)	
STATISTICAL TESTS								
LIFE TABLE	P=0.350N	P=0.552	P=0.740N	P=0.630N	P=0.672	(e)	P=0.541	(e)
POLY 3	P=0.329N	P=0.515	P=0.754N	P=0.574N	P=0.563	(e)	P=0.510	(e)
POLY 1.5	P=0.300N	P=0.511	P=0.756N	P=0.545N	P=0.615	(e)	P=0.506	(e)
POLY 6	P=0.364N	P=0.521	P=0.749N	P=0.599N	P=0.515	(e)	P=0.516	(e)
LOGISTIC REGRESSION	P=0.229N	P=0.440	P=0.729	P=0.410N	(e)	(e)	P=0.541	(e)
COCH-ARM / FISHERS	P=0.247N	P=0.500	P=0.753N	P=0.500N	P=0.694	(e)	P=0.500	(e)

C 01

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Thyroid Gland: Follicular Cell Carcinoma								
TUMOR RATES								
OVERALL (a)	1/49 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	0.0%	0.0%	0.0%	0.0%	4.6%	0.0%	0.0%
TERMINAL (d)	1/35 (3%)	0/43 (0%)	0/43 (0%)	0/22 (0%)	0/35 (0%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	--	---	--	--	644		
STATISTICAL TESTS								
LIFE TABLE	P=0.344N	P=0.459N	P=0.459N	P=0.593N	P=0.455N	P=0.235	(e)	(e)
POLY 3	P=0.242N	P=0.488N	P=0.492N	P=0.571N	P=0.431N	P=0.231	(e)	(e)
POLY 1.5	P=0.271N	P=0.492N	P=0.494N	P=0.543N	P=0.425N	P=0.234	(e)	(e)
POLY 6	P=0.234N	P=0.484N	P=0.486N	P=0.595N	P=0.430N	P=0.233	(e)	(e)
LOGISTIC REGRESSION	P=0.344N	(e)	(e)	(e)	P=0.410N	P=0.242	(e)	(e)
COCH-ARM / FISHERS	P=0.303N	P=0.495N	P=0.495N	P=0.495N	P=0.402N	P=0.253	(e)	(e)

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
Thyroid Gland: Follicular Cell Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	1/49 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/49 (0%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.2%	0.0%	2.1%	3.1%	0.0%	4.5%	2.1%	0.0%
TERMINAL (d)	1/35 (3%)	0/43 (0%)	1/43 (2%)	0/22 (0%)	0/35 (0%)	1/35 (3%)	1/43 (2%)	0/25 (0%)
FIRST INCIDENCE	729 (T)	--	729 (T)	681	-	644	730 (T)	
STATISTICAL TESTS								
LIFE TABLE	P=0.463	P=0.459N	P=0.715N	P=0.710	P=0.539N	P=0.235	P=0.541	(e)
POLY 3	P=0.431	P=0.488N	P=0.751N	P=0.677	P=0.535N	P=0.231	P=0.514	(e)
POLY 1.5	P=0.469	P=0.492N	P=0.754N	P=0.712	P=0.510N	P=0.234	P=0.520	(e)
POLY 6	P=0.412	P=0.484N	P=0.745N	P=0.645	P=0.552N	P=0.233	P=0.519	(e)
LOGISTIC REGRESSION	P=0.648	(e)	P=0.715N	P=0.719N	P=0.498N	P=0.242	P=0.541	(e)
COCH-ARM / FISHERS	P=0.543	P=0.495N	P=0.747N	P=0.747N	P=0.457N	P=0.253	P=0.505	(e)

C 02

Dose	Males 0 MG/KG	Males 1.5 MG/KG	Males 3 MG/KG	Males 6 MG/KG	Females 0 MG/KG	Females 1.5 MG/KG	Females 3 MG/KG	Females 6 MG/KG
Uterus								
Hemangiosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)					0.0%	4.6%	0.0%	0.0%
TERMINAL (d)					0/35 (0%)	1/35 (3%)	0/43 (0%)	0/25 (0%)
FIRST INCIDENCE					---	711	---	---
STATISTICAL TESTS								
LIFE TABLE					P=0.459N	P=0.246	(e)	(e)
POLY 3					P=0.434N	P=0.227	(e)	(e)
POLY 1.5					P=0.428N	P=0.229	(e)	(e)
POLY 6					P=0.432N	P=0.228	(e)	(e)
LOGISTIC REGRESSION					P=0.460N	P=0.229	(e)	(e)
COCH-ARM / FISHERS					P=0.405N	P=0.247	(e)	(e)

Dose	Males 0 MG/KG	Males 1.5 MG/KG	Males 3 MG/KG	Males 6 MG/KG	Females 0 MG/KG	Females 1.5 MG/KG	Females 3 MG/KG	Females 6 MG/KG
All Organs								
Hemangioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	2.1%	0.0%	0.0%	4.4%	0.0%	0.0%	0.0%
TERMINAL (d)	0/35 (0%)	1/43 (2%)	0/43 (0%)	0/22 (0%)	2/35 (6%)	0/35 (0%)	0/43 (0%)	0/25 (0%
FIRST INCIDENCE	---	729 (T)	---	---	730 (T)	---	---	
STATISTICAL TESTS								
LIFE TABLE	P=0.646N	P=0.541	(e)	(e)	P=0.124N	P=0.238N	P=0.194N	P=0.315N
POLY 3	P=0.550N	P=0.512	(e)	(e)	P=0.094N	P=0.248N	P=0.226N	P=0.299N
POLY 1.5	P=0.561N	P=0.508	(e)	(e)	P=0.102N	P=0.246N	P=0.230N	P=0.276N
POLY 6	P=0.562N	P=0.516	(e)	(e)	P=0.086N	P=0.247N	P=0.219N	P=0.319N
LOGISTIC REGRESSION	(e)	P=0.541	(e)	(e)	P=0.124N	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.567N	P=0.500	(e)	(e)	P=0.115N	P=0.247N	P=0.247N	P=0.247N

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Hemangiosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	1/50 (2%)	1/50 (2%)	1/50 (2%)	2/50 (4%)	3/50 (6%)	0/50 (0%)	3/50 (6%)
POLY-3 ADJUSTED (b)	6.6%	2.1%	2.1%	3.1%	4.4%	6.8%	0.0%	8.6%
TERMINAL (d)	2/35 (6%)	1/43 (2%)	0/43 (0%)	0/22 (0%)	1/35 (3%)	1/35 (3%)	0/43 (0%)	3/25 (12%)
FIRST INCIDENCE	650	729 (T)	655	481	704	405		729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.354N	P=0.254N	P=0.263N	P=0.453N	P=0.388	P=0.505	P=0.202N	P=0.[illegible]49
POLY 3	P=0.280N	P=0.287N	P=0.291N	P=0.439N	P=0.444	P=0.487	P=0.225N	P=0.[illegible]63
POLY 1.5	P=0.272N	P=0.292N	P=0.296N	P=0.385N	P=0.459	P=0.489	P=0.232N	P=0.[illegible]
POLY 6	P=0.284N	P=0.281N	P=0.281N	P=0.490N	P=0.449	P=0.491	P=0.220N	P=0.[illegible]
LOGISTIC REGRESSION	P=0.196N	P=0.295N	P=0.311N	P=0.304N	P=0.484	P=0.544	P=0.125N	P=0.[illegible]41
COCH-ARM / FISHERS	P=0.242N	P=0.309N	P=0.309N	P=0.309N	P=0.500	P=0.550	P=0.247N	P=0.[illegible]

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Hemangiosarcoma or Hemangioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	4/50 (8%)	3/50 (6%)	0/50 (0%)	3/50 (6%)
POLY-3 ADJUSTED (b)	6.6%	4.2%	2.1%	3.1%	8.8%	6.8%	0.0%	8.6%
TERMINAL (d)	2/35 (6%)	2/43 (5%)	0/43 (0%)	0/22 (0%)	3/35 (9%)	1/35 (3%)	0/43 (0%)	3/25 (12%)
FIRST INCIDENCE	650	729 (T)	655	481	704	405		729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.309N	P=0.426N	P=0.263N	P=0.453N	P=0.490N	P=0.495N	P=0.043N	P=0.[illegible]
POLY 3	P=0.247N	P=0.477N	P=0.291N	P=0.439N	P=0.385N	P=0.516N	P=0.054N	P=0.[illegible]
POLY 1.5	P=0.235N	P=0.483N	P=0.296N	P=0.385N	P=0.387N	P=0.524N	P=0.057N	P=0.[illegible]
POLY 6	P=0.255N	P=0.468N	P=0.281N	P=0.490N	P=0.374N	P=0.511N	P=0.053N	P=0.[illegible]
LOGISTIC REGRESSION	P=0.171N	P=0.482N	P=0.311N	P=0.304N	P=0.414N	P=0.482N	P=0.059N	P=0.[illegible]
COCH-ARM / FISHERS	P=0.199N	P=0.500N	P=0.309N	P=0.309N	P=0.371N	P=0.530N	P=0.059N	P=0.[illegible]

C 04

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Malignant Lymphoma: Histiocytic, Lymphocytic, Mixed, NOS, or Undifferentiated Cell Type								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	3/50 (6%)	3/50 (6%)	1/50 (2%)	9/50 (18%)	7/50 (14%)	7/50 (14%)	2/50 (4%)
POLY-3 ADJUSTED (b)	4.5%	6.3%	6.4%	3.2%	19.5%	15.9%	16.7%	4.3%
TERMINAL (d)	2/35 (6%)	3/43 (7%)	3/43 (7%)	1/22 (5%)	5/35 (14%)	5/35 (14%)	7/43 (16%)	2/25 (8%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	729 (T)	623	289	729 (T)	729 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.536N	P=0.594	P=0.594	P=0.660N	P=0.060N	P=0.404N	P=0.263N	P=0.599N
POLY 3	P=0.509N	P=0.526	P=0.519	P=0.623N	P=0.065N	P=0.432N	P=0.367N	P=0.579N
POLY 1.5	P=0.449N	P=0.519	P=0.513	P=0.576N	P=0.047N*	P=0.419N	P=0.376N	P=0.551N
POLY 6	P=0.562N	P=0.537	P=0.532	P=0.664N	P=0.084N	P=0.436N	P=0.356N	P=0.650N
LOGISTIC REGRESSION	P=0.536N	P=0.594	P=0.594	P=0.660N	P=0.036N*	P=0.380N	P=0.269N	P=0.600N
COCH-ARM / FISHERS	P=0.343N	P=0.500	P=0.500	P=0.500N	P=0.023N*	P=0.393N	P=0.393N	P=0.626N*

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	29/50 (58%)	35/50 (70%)	33/50 (66%)	19/50 (38%)	24/50 (48%)	15/50 (30%)	20/50 (40%)	13/50 (26%)
POLY-3 ADJUSTED (b)	60.7%	70.8%	67.6%	52.7%	51.5%	34.6%	41.6%	30.1%
TERMINAL (d)	21/35 (60%)	29/43 (67%)	30/43 (70%)	12/22 (55%)	20/35 (57%)	14/35 (40%)	19/43 (44%)	10/25 (40%)
FIRST INCIDENCE	501	605	429	481	362	638	589	480
STATISTICAL TESTS								
LIFE TABLE	P=0.531N	P=0.547	P=0.464N	P=0.565N	P=0.204N	P=0.048N*	P=0.074N	P=0.190N
POLY 3	P=0.247N	P=0.201	P=0.309	P=0.303N	P=0.143N	P=0.076N	P=0.223N	P=0.116N
POLY 1.5	P=0.088N	P=0.188	P=0.306	P=0.145N	P=0.095N	P=0.069N	P=0.245N	P=0.064N
POLY 6	P=0.454N	P=0.227	P=0.321	P=0.502N	P=0.1[illegible]N	P=0.075N	P=0.192N	P=0.174N
LOGISTIC REGRESSION	P=0.083N	P=0.167	P=0.284	P=0.176N	P=0.186N	P=0.069N	P=0.220N	P=0.134N
COCH-ARM / FISHERS	P=0.008N**	P=0.149	P=0.268	P=0.036N*	P=0.036N*	P=0.050N	P=0.273N	P=0.019N*

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Statistical Analysis of Primary Tumors in Mice(B6C3F1) - METHACRYLONITRILE

Terminal Sacrifice at 105 weeks

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Malignant Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	24/50 (48%)	17/50 (34%)	16/50 (32%)	8/50 (16%)	19/50 (38%)	17/50 (34%)	17/50 (34%)	14/50 (28%)
POLY-3 ADJUSTED (b)	49.5%	34.3%	33.1%	23.8%	40.3%	36.4%	24.4%	36.7%
TERMINAL (d)	14/35 (40%)	11/43 (26%)	12/43 (28%)	3/22 (14%)	11/35 (31%)	9/35 (26%)	11/43 (26%)	8/25 (32%)
FIRST INCIDENCE	501	563	502	481	607	289	589	58
STATISTICAL TESTS								
LIFE TABLE	P=0.047N*	P=0.058N	P=0.037N*	P=0.065N	P=0.534N	P=0.442N	P=0.242N	P=0.528
POLY 3	P=0.015N*	P=0.092N	P=0.075N	P=0.016N*	P=0.452N	P=0.428N	P=0.349N	P=0.531N
POLY 1.5	P=0.005N**	P=0.094N	P=0.072N	P=0.004N**	P=0.354N	P=0.424N	P=0.374N	P=0.397N
POLY 6	P=0.033N*	P=0.088N	P=0.073N	P=0.050N	P=0.519N	P=0.431N	P=0.320N	P=0.539
LOGISTIC REGRESSION	P<0.001N**	P=0.158N	P=0.086N	P=0.002N**	P=0.230N	P=0.365N	P=0.469N	P=0.522N
COCH-ARM / FISHERS	P<0.001N**	P=0.111N	P=0.076N	P<0.001N**	P=0.174N	P=0.418N	P=0.418N	P=0.193N

Dose	Males 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG	Females 0 MG/KG	1.5 MG/KG	3 MG/KG	6 MG/KG
All Organs								
Malignant and Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	40/50 (80%)	41/50 (82%)	39/50 (78%)	24/50 (48%)	33/50 (66%)	28/50 (56%)	29/50 (58%)	21/50 (42%)
POLY-3 ADJUSTED (b)	81.9%	82.9%	78.2%	62.1%	68.8%	59.5%	58.7%	57.9%
TERMINAL (d)	27/35 (77%)	34/43 (79%)	33/43 (77%)	12/22 (55%)	24/35 (69%)	19/35 (54%)	23/43 (54%)	14/25 (56%)
FIRST INCIDENCE	501	563	429	481	362	289	589	480
STATISTICAL TESTS								
LIFE TABLE	P=0.360N	P=0.195N	P=0.121N	P=0.378N	P=0.268N	P=0.261N	P=0.076N	P=0.345N
POLY 3	P=0.017N*	P=0.595	P=0.418N	P=0.027N*	P=0.164N	P=0.230N	P=0.204N	P=0.181N
POLY 1.5	P=0.002N**	P=0.587	P=0.422N	P=0.005N**	P=0.082N	P=0.225N	P=0.233N	P=0.177N
POLY 6	P=0.071N	P=0.600N	P=0.415N	P=0.098N	P=0.244N	P=0.225N	P=0.170N	P=0.110N
LOGISTIC REGRESSION	P<0.001N**	P=0.539	P=0.490N	P=0.010N*	P=0.063N	P=0.208N	P=0.274N	P=0.139N
COCH-ARM / FISHERS	P<0.001N**	P=0.500	P=0.500N	P<0.001N**	P=0.013N*	P=0.205N	P=0.258N	P=0.1[illegible]N

(a) Number of tumor-bearing animals / number of animals examined at site
(b) Poly 3 adjusted lifetime tumor incidence
(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

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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
For all tests a negative trend is indicated by N
(e) Value of Statistic cannot be computed.
(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).

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