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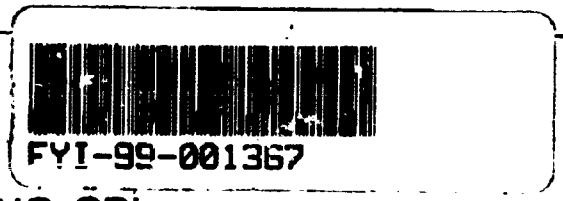

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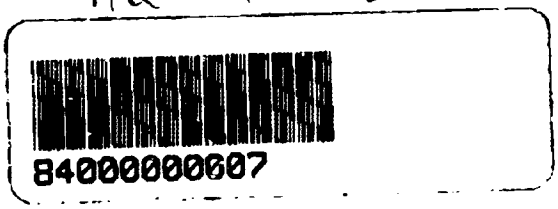

Document Control Office:

In compliance with the National Toxicology Program's (NTP) mission to keep our colleagues informed of the current NTP findings during on-going studies, a copy of the Pathology Working Group (PWG) report and the Summary Pathology Tables for the chronic dosed water studies on Sodium Nitrite (CAS No. 7632-00-0) 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.

All study data are subject to an NTP retrospective audit and the interpretation may be modified based on the findings. The technical report for this study is currently being prepared for presentation to the NTP Board of Scientific Counselors' Technical Reports Review Subcommittee with an anticipated peer-review date of May 2000.

The Summary Pathology Tables along with a wide variety of NTP information are 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 may be viewed electronically with access to the internet and a Web browser such as Netscape Navigator or Internet Explorer.

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To locate the NTP home page, use the URL http://ntp-server.niehs.nih.gov/. The NTP individual animal and summary pathology tables, survival tables, and survival and growth curves may be accessed from the NTP homepage selecting "Testing Information and Study Results" and then choosing "Data of Completed Studies." Comments on the usefulness of this site and suggestions for improvement are encouraged.

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

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

Sincerely,

William Eastin

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

Encls: PWG, Pathology Summary Tables (Rats and Mice)
cc: Dr. J. Bucher
Dr. J. Roycroft
Central Data Management

National Toxicology Program

TR-495 Sodium Nitrite

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

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PATHOLOGY WORKING GROUP CHAIRPERSON'S REPORT

2-Year Chronic Study of **Sodium Nitrite** in F344 Rats

Participants: Drs. M. Jokinen (PAI - PWG Chairperson), A. Brix (EPL), E. Gaillard, EPL (QA-Pathologist), R. Hailey (NIEHS), R. Herbert (NIEHS), J. Seely (Pathco), and R. Sills (NIEHS)

Date: May 13, 1999
Site: NIEHS, Research Triangle Park, NC

The PWG was convened to evaluate selected slides from F344 rats administered sodium nitrite by dosed water for two years. The doses and numbers of animals examined microscopically per group were as follows:

Dose	M	F
0.0%	50	50
0.075%	50	50
0.15%	50	50
0.30%	50	50

The study was conducted at Battelle Columbus. The Study Pathologist (SP) was Dr. J. Yarrington. The Quality Assessment Pathologists (QAP) were Drs. S. Botts and E. Gaillard of EPL.

A number of organs were reviewed by the QAP for potential treatment-related effects; the QAP reviewed these organs in all animals for all diagnoses, neoplastic and nonneoplastic. Organs reviewed for all diagnoses were as follows:

Male Rats	Female Rats
Stomach, Forestomach	Stomach, Forestomach
Thyroid, C-Cell	Thyroid, C-cell

In addition, a number of tissues were examined in both males and females for the presence of specific lesions. These were are follows:

Adrenal Cortex – Hyperplasia, Hypertrophy, Adenoma, Carcinoma
Adrenal Medulla – Hyperplasia, Pheochromocytoma (benign and malignant)
Intestine Large, Rectum - Fibroma
Liver – Inflammation, Altered Cellular Foci, Adenoma, Carcinoma
Liver/Spleen – Mononuclear Cell Leukemia
Lung – Alveolar Epithelial Hyperplasia, Alveolar/Bronchiolar Adenoma and Carcinoma

Mammary Gland – Hyperplasia, Fibroadenoma (single and multiple), Adenoma (single and multiple), Carcinoma
Pituitary Gland, Pars Distalis – Hyperplasia, Adenoma
Skin – Proliferative Lesions
Stomach, Glandular – Adenoma
Stomach, Glandular, Epithelium – Hyperplasia

Although the SP had detected no treatment-related effect in the lung and glandular stomach in rats, these tissues were reviewed since treatment-related lesions had been observed in these tissues in the mouse study of sodium nitrite.

Other tissues were reviewed for specific diagnoses only in males or only in females. These were as follows:

Males
Epididymis -- Mesothelioma (benign and malignant)
Kidney – Inflammation, Nephropathy
Pancreas, Acinus – Atrophy
Seminal Vesicle – Atrophy
Testes – Mesothelioma (benign and malignant)
Testes, Interstitial Cell – Hyperplasia, Adenoma

Females
Clitoral Gland – Hyperplasia, Adenoma, Carcinoma

In addition to the above, the QAP reviewed all tumor diagnoses in all animals.

SUMMARY OF REVIEW FINDINGS

Incidences of slight **Stomach, Forestomach, Epithelium – Hyperplasia** were greater in treated groups of males and females as compared with controls.

Incidences of **Mammary Gland – Fibroadenoma** and **Mammary Gland – Fibroadenoma, Multiple** were greater in treated groups of females as compared with controls, and were lower in 0.30% males as compared with control males and other treated male groups.

Incidences of **Pancreas, Acinus – Atrophy** were greater in treated groups of males as compared with controls.

Incidences of minimal **Liver – Inflammation, Chronic Active** were greater in all treated male groups and in the 0.15% and 0.30% female groups as compared with respective controls

Incidences of **Leukemia, Mononuclear Cell** were lower in all treated male and female groups as compared with respective controls, and the incidences were lowest in the 0.15% and 0.30% dose groups.

Combined incidences of **Thyroid Gland, C-cell – Adenoma** and **Carcinoma** were lower in treated groups of males as compared with controls, and the incidence was lowest in the 0.30% male group.

Combined incidences of **Clitoral Gland – Adenoma** and **Carcinoma** were lower in the 0.15% and 0.30% female groups than in the control and 0.075% female groups.

The incidence of **Lung, Alveolar Epithelium – Hyperplasia** was lower in the 0.30% female group than in the control and other treated female groups.

Incidences of slight **Adrenal Cortex – Hypertrophy** were slightly lower in treated groups of females as compared with controls.

CONDUCT OF THE PWG

Prior to the PWG, the PWG Chairperson reviewed the pathology tables, the SP's narrative, the Pathology Data Review, the Quality Assessment Report, and microslides of tissues selected for QA review. The PWG Chair then selected slides for review by the PWG, including representative examples of lesions, and lesions for which there was a difference in diagnosis among the SP, QAP, and PWG Chair.

RESULTS OF THE PWG REVIEW

Forestomach

The SP had diagnosed greater incidences of **Stomach, Forestomach – Hyperkeratosis**, generally of minimal severity, in the 0.30% groups of males and females as compared with the other treated and control groups of males and females. The QAP also added a number of diagnoses of **Stomach, Forestomach, Epithelium – Hyperplasia**, generally of minimal severity, primarily to the 0.30% groups of males and females, but also to each of the treated groups and the control groups. The QAP's findings indicated that a slight degree of hyperplasia and hyperkeratosis both occurred with substantially greater incidences in the 0.30% males and females as compared with the other treated groups and the controls. The PWG chair noted that a slight degree of hyperplasia occurred along with the hyperkeratosis in numerous forestomachs in which only hyperkeratosis had been diagnosed, as well as in some forestomachs in which no diagnosis had been made previously, and added a diagnosis of hyperplasia in each of those cases.

The PWG examined a considerable number of forestomachs, including examples in which the SP, QAP, and PWG chair agreed concerning the presence of lesions, examples of diagnoses added by the QAP, and examples of diagnoses added by the PWG chair. The PWG also examined forestomachs in which a diagnosis of squamous cell papilloma had been made. After examining over half of the slides the PWG chair had selected for review for the presence of hyperkeratosis and hyperplasia, the PWG reached a unanimous decision in each case. Based upon this the PWG decided it had seen enough examples to be certain what changes were present, and decided it was unnecessary to review all of the slides selected by the PWG chair.

In all the examples examined by the PWG in which only hyperkeratosis had been diagnosed, whether the diagnosis had been made by the SP or by the QAP, the PWG noted that hyperplasia was also present. The PWG concluded that hyperplasia was the primary change and that the hyperkeratosis occurred secondary to the hyperplasia. The PWG also examined one example in which no diagnosis had been made by the SP or QAP and noted that hyperkeratosis was present, but hyperplasia was not. The PWG examined some examples of hyperplasia that had been diagnosed by the QAP and confirmed the QAP's diagnoses. The PWG also examined some cases in which the PWG chair had added a diagnosis of hyperplasia and confirmed that hyperplasia was present. Based upon these findings the PWG concluded that if both hyperplasia and hyperkeratosis were present then only hyperplasia should be diagnosed. If hyperkeratosis was present without hyperplasia, then hyperkeratosis should be diagnosed. The PWG directed that, as a Post-PWG Action Item, the PWG chair review all forestomachs from all animals in the study, using the forestomachs examined by the PWG for reference, to ensure that hyperplasia and hyperkeratosis were diagnosed consistently in accord with the PWG's findings. The PWG also concluded the PWG chair's findings from this review should be added to the pathology data. The PWG chair conducted this review and the PWG chair's findings were entered onto the Pathology Quality Assessment Worksheets.

Microscopically, **Stomach, Forestomach, Epithelium – Hyperplasia** was, in general, a minimal change affecting the epithelium of the limiting ridge at the junction of the forestomach and glandular stomach, although a few cases of more severe hyperplasia were seen both at and away from the limiting ridge. Hyperplasia was characterized primarily by variable degrees of folding of the epithelium, and usually was accompanied by a variable degree of thickening of the overlying keratin layer. Sometimes slight thickening of the epithelium due to an increase in the number of cell layers was observed, especially in the more severe cases, but usually was not a prominent feature of the hyperplasia. **Stomach, Forestomach – Hyperkeratosis** was characterized by thickening of the keratin layer of the epithelium. In a few forestomachs both hyperplasia and

hyperkeratosis were present as separate lesions, and in this case the PWG chair diagnosed both changes in the same forestomach.

The PWG also reviewed four lesions diagnosed either by the SP or QAP as **Stomach, Forestomach – Squamous Cell Papilloma**. The PWG confirmed the diagnosis of papilloma in two cases and considered the lesions in the other two cases to represent hyperplasia of the forestomach epithelium. The papillomas appeared to be incidental findings unrelated to the test compound.

Acinar Pancreas

The SP had diagnosed greater incidences of **Pancreas, Acinus – Atrophy** in treated groups of males. Microscopically, **Pancreas, Acinus – Atrophy** had the typical appearance of this lesion as it occurs in F344 rats, and was a focal to multifocal to diffuse lesion characterized by loss of normal acini, a decrease in the size of the remaining acini, and an increase in small duct-like structures. The SP's findings were confirmed by the QA/PWG review; however, the significance of the greater incidences of atrophy of the acinar pancreas in treated groups of males was unclear. The QAP agreed with the SP's diagnoses of atrophy and added several additional diagnoses to each of the male groups, but added more to the treated groups, which increased the magnitude of the dose-related increase in incidence. The PWG chair agreed with the QAP in almost every instance, thus confirming the QAP's findings, and also added a few additional diagnoses of atrophy to each of the male groups. Although the pancreas in females had not been reviewed by the QAP, the PWG chair noted that atrophy occurred in a few animals in each of the female groups and had not been diagnosed previously. For the sake of completeness, the PWG chair reviewed the acinar pancreas in all females, and diagnosed atrophy in all females in which it occurred but had not been diagnosed previously. The PWG chair also noted a number of cases of **Pancreas, Acinus – Hyperplasia** scattered across the control and treated male and female groups that had not been previously diagnosed, and diagnosed these as well. The PWG first examined several examples of the diagnoses of atrophy made by the SP and QAP and agreed with the diagnoses in each case. The PWG then reviewed examples of the additional diagnoses of atrophy made by the PWG chair, and agreed with the PWG chair in all but one case. Based upon this, the PWG recommended adding the additional diagnoses of Atrophy made by the PWG chair. The PWG also reviewed the diagnoses of hyperplasia made by the PWG chair and agreed with the PWG chair's diagnosis in each case.

Liver

The SP had diagnosed higher incidences of **Inflammation, Chronic Active** in each of the treated groups of males and females as compared with respective controls. The QAP added a few additional diagnoses in each of the male groups

and confirmed the higher incidences in treated males as compared with controls. The QAP also added some additional diagnoses to each of the female groups and decreased the difference between the control and treated groups such that the incidences as diagnosed by the QAP were slightly higher in the 0.15% and 0.30% female groups than in female controls. The PWG chair added some additional diagnoses in each of the treated male groups which somewhat increased the differences between the control and treated groups. The PWG chair also added several diagnoses to each of the female groups which increased total incidence in each of the groups but did not alter the QAP's basic finding of a small increase in incidence in the 0.15% and 0.30% groups as compared with controls. The PWG first examined a number of examples of the diagnoses of chronic active inflammation made by the SP and QAP and agreed with the diagnoses in each case. The PWG then examined a number of examples of the diagnoses added by the PWG chair and agreed with the PWG chair in each case. Based upon this the PWG recommended adding all of the additional diagnoses made by the PWG chair to the pathology findings.

Microscopically, **Inflammation, Chronic Active** was generally a slight lesion consisting of few to several scattered aggregates of mixed mononuclear inflammatory cells, mainly lymphocytes and macrophages. The significance of the slightly greater incidences of this minor lesion in treated groups was unclear. Possibly, the higher incidence of this change seen in the treated groups of males and females was due to the fact that the incidences of mononuclear cell leukemia were lower in these groups. Since the presence of leukemic infiltrate can obscure the presence of other changes, the lower incidence of leukemia in these groups could have allowed these changes to be detected more readily in treated animals than in the controls, which had higher incidences of leukemia.

The SP and QAP diagnosed low, marginally increased incidences of **Angiectasis**, a minor lesion characterized by small clusters of dilated, blood filled sinusoids, in the treated groups of females. The PWG chair confirmed the presence of this change. As was the case with the chronic active inflammation, it is possible the incidences were higher in the treated groups of females due to the lower incidence of mononuclear cell leukemia in these groups which allowed this change to be detected in more treated animals than in control animals.

The QAP added several additional diagnoses of **Clear Cell Focus**, **Eosinophilic Focus**, **Basophilic Focus**, **Mixed Cell Focus**, and **Bile Duct – Hyperplasia** to the control and each of the treated groups in both the males and the females. With the exception of slightly greater incidences of eosinophilic focus in the 0.075% and 0.15% male groups as compared with control males, the incidences were similar in control and treated groups. Since there was good agreement concerning these diagnoses between the QAP and PWG chair and since none of them represented potential treatment related effects, the PWG opted not to review any examples

Mammary Gland

The **Mammary Gland** was reviewed for **Hyperplasia**, **Fibroadenoma** (single and multiple), **Adenoma** (single and multiple), and **Carcinoma**. The SP had not diagnosed **Hyperplasia** in any of the mammary glands in any of the animals in the study. The QAP diagnosed hyperplasia, characterized by variable numbers of scattered acinar lobules and ducts lined by slightly increased numbers of epithelial cells, in a few animals in each of the control and treated groups of males and females. The PWG chair generally agreed with the QAP's diagnoses except for a few cases in the control and lower dose groups. The incidences of hyperplasia as diagnosed by the QAP and agreed upon by the PWG chair were relatively similar across groups and did not indicate the presence of a compound related effect. The incidences of **Fibroadenoma** as diagnosed by the SP did not indicate any compound related effect, except that the incidence in the 0.30% group was lower than in the control and other treated male groups. This finding was confirmed by the QA/PWG review. The QAP agreed with the SP's diagnoses of fibroadenoma in all groups of males and females, except that in many instances the SP had used the term **Fibroadenoma** when more than one fibroadenoma was present; in these instances the QAP used the NTP preferred terminology of **Fibroadenoma, Multiple**. In females, the QAP considered several of the neoplasms diagnosed by the SP as **Adenoma** to be **Fibroadenoma**, and added a few additional diagnoses of fibroadenoma in the control females and in each of the treated female groups. The incidences of fibroadenoma as diagnosed by the QAP were somewhat greater in treated groups of females, especially in the 0.15% group, than in control females. The QAP also considered some of the neoplasms diagnosed by the SP as **Carcinoma** to be **Adenoma**. The PWG chair confirmed the QAP's findings. The PWG reviewed two cases of disagreements between the QAP and PWG chair. Otherwise, since there was excellent agreement between QAP and PWG chair, the PWG opted not to review any examples of mammary gland lesions.

Mononuclear Cell Leukemia

The SP had diagnosed lower incidences of mononuclear cell leukemia in treated groups of males and females. All livers and spleens were reviewed by the QAP, and the SP's findings were confirmed. There were a few cases in which there was disagreement among the SP, QAP, or PWG chair concerning the presence of leukemia, and these were reviewed by the PWG. Otherwise there was very good agreement among the SP, QAP, and PWG Chair concerning the diagnoses of mononuclear cell leukemia.

Clitoral Gland

The **Clitoral Gland** was reviewed for **Hyperplasia**, **Adenoma**, and **Carcinoma**. The SP had diagnosed a lower incidence of **Adenoma** in the 0.15% and 0.30%

female groups as compared with the 0.075% female group and female controls The QAP considered many of the lesions diagnosed by the SP as **Carcinoma** to be **Adenoma**. The PWG chair agreed with the QAP in some instances but not in others. The QAP also added a few diagnoses of adenoma in some groups, and several diagnoses of **Hyperplasia** in the control and each of the treated groups. The PWG chair generally confirmed the QAP's findings, but disagreed with the QAP in some cases as to whether a lesion represented adenoma or hyperplasia, and as to whether or not hyperplasia was present or the gland was normal; these disagreements were reviewed by the PWG. The results of the QA/PWG review indicated the total combined incidences of adenoma and carcinoma of the clitoral gland were somewhat lower in the 0.15% and 0.30% female groups, as compared with the 0.075% female group and female controls.

Thyroid Gland, C-Cell

Thyroid glands from males and females were reviewed for the presence of proliferative C-Cell lesions. The QAP added several diagnoses of **Adenoma** and **Hyperplasia** in the control and each of the treated groups of males and females. The PWG chair agreed with most but not all of the QAP's diagnoses, and also noted a few instances of hyperplasia that had not been diagnosed previously. The PWG reviewed representative examples of adenoma and hyperplasia in which there was agreement on the diagnoses, and then reviewed all cases in which the PWG chair disagreed with the previous diagnosis. The QAP's findings indicated somewhat lower incidences of adenoma and somewhat higher incidences of hyperplasia in the treated male groups as compared with control males. Incidences of hyperplasia were somewhat increased in treated groups of females as compared with controls, but the incidences of adenoma were similar across groups.

Adrenal Cortex

The **Adrenal Gland, Cortex** was reviewed for **Hypertrophy**, **Hyperplasia**, **Adenoma**, and **Carcinoma**. The SP had not diagnosed **Hypertrophy**, focal lesions composed of enlarged cortical cells with an increased amount of cytoplasm, in any of the adrenal glands in any group of animals. The QAP found hypertrophy in a number of animals in each of the treatment groups. The SP had diagnosed **Hyperplasia**, focal lesions composed of increased numbers of cortical cells which were normal sized or slightly smaller than normal, in only two animals out of all the animals in the study. The QAP added diagnoses of hyperplasia in several animals in each of the control and treated groups of males and females. The SP had also diagnosed very lower incidences (one or two) of neoplasms (**Adenoma** and **Carcinoma**) of the adrenal cortex. The QAP generally confirmed these findings, but disagreed with a few of the SP's diagnoses. The PWG chair generally confirmed the QAP's findings, and also added a few diagnoses of hypertrophy and hyperplasia. The PWG examined all

disagreements between the QAP and PWG chair. The incidences of adrenal cortical hypertrophy, hyperplasia, and neoplasia, as diagnosed by the QAP and PWG chair were similar among the control and treatment groups of males and females.

Adrenal Medulla

The **Adrenal Gland, Medulla** was reviewed for **Hyperplasia** and **Pheochromocytoma (Benign and Malignant)**. The SP had diagnosed hyperplasia in only a few animals. The QAP diagnosed hyperplasia in a number of animals in each of the control and treated groups of males and females, and added a few diagnoses of pheochromocytoma. The PWG chair generally confirmed the QAP's findings, and added a few additional diagnoses of hyperplasia and pheochromocytoma. The PWG examined all cases in which the PWG chair disagreed with the previous diagnosis. The incidences of hyperplasia and pheochromocytoma, as diagnosed by the QAP and PWG chair, were similar among the control and treated groups of males and females.

Lung

The lungs of males and females were reviewed for the presence of proliferative epithelial lesions (**Alveolar Epithelium – Hyperplasia**, **Alveolar/Bronchiolar Adenoma**, and **Alveolar/Bronchiolar Carcinoma**). The incidences of proliferative epithelial lesions as diagnosed by the SP were similar across treatment groups with no indication of a compound related effect. The QAP disagreed with a few of the diagnoses of neoplasms, and added **Alveolar Epithelium – Hyperplasia** to a number of animals in each of the treatment groups. The PWG chair generally agreed with the QAP's findings. Other than a higher incidence of **Alveolar Epithelium – Hyperplasia** in the 0.15% males as compared with control males, and a lower incidence of **Alveolar Epithelium – Hyperplasia** in 0.30% females as compared with control females, the incidences of neoplasia and hyperplasia, as diagnosed by the QAP, were similar across groups of males and females. The PWG reviewed one unusual lung neoplasm. Otherwise, since there was good agreement among the SP, QAP and PWG chair concerning neoplasms, and the QAP and PWG chair concerning hyperplasias, and since there was no indication of a compound related effect on the incidences of proliferative epithelial lesions in the lung, the PWG opted not to review any examples.

Pituitary Gland

Pituitary gland was reviewed for the presence of proliferative lesions of the pars distalis. The SP had diagnosed proliferative lesions of the pars distalis using the site designation of **Pituitary** (e.g., **Pituitary – Adenoma**). The QAP recommended use of the NTP preferred site designation of **Pituitary, Pars**

Distalis (e.g., **Pituitary, Pars Distalis – Adenoma**) and changed all diagnoses to use this terminology; the PWG chair agreed with the QAP's recommendation. The SP had diagnosed similar incidences of adenoma of the pars distalis in control and treated groups of males and females. In general, the QAP agreed with the SP's diagnoses of adenoma, but added several additional diagnoses of **Adenoma, Pars Distalis – Hyperplasia** in each of the control and treated groups of males and females. The PWG chair generally agreed with the QAP's diagnoses. The incidences of **Pars Distalis – Adenoma** and **Pars Distalis – Hyperplasia** as diagnosed by the QAP were similar in control and treated groups of males and females, with the exceptions that the incidences of hyperplasia in the 0.15% male and female groups were increased over those of respective controls, and the incidence of adenoma in the 0.15% female group was decreased as compared with control females. The PWG examined all disagreements in diagnosis between the PWG chair and the SP and/or QAP.

Kidney

The SP had diagnosed a slightly greater incidence of **Inflammation, Chronic Active** in the treated male groups. The change diagnosed as chronic active inflammation consisted of a few scattered aggregates of basophilic regenerative tubules, sometimes accompanied by a slight mononuclear cell infiltrate. In each case the QAP considered the change diagnosed as chronic active inflammation to represent minimal **Nephropathy**; the PWG chair agreed without exception. Since this was a very minor change, there was complete agreement between the QAP and PWG chair, and there was no indication of a treatment related effect, the PWG opted not to review any of the kidneys.

Epididymis

The Epididymis was reviewed for the presence of **Mesothelioma, Benign** and **Mesothelioma, Malignant**. The QAP noted two additional mesotheliomas that had not been diagnosed previously, and the PWG chair concurred with the QAP. However, the incidences of mesothelioma as diagnosed by either the SP or the QAP did not indicate any treatment related effect. Since there was agreement concerning these diagnoses between the QAP and PWG chair and since mesothelioma did not represent a potential treatment related effect, the PWG opted not to review any examples.

Testes

The Testes were reviewed for the presence of **Mesothelioma, Benign**; **Mesothelioma, Malignant**; **Interstitial Cell – Hyperplasia**; and **Interstitial Cell – Adenoma**. The QAP noted five additional mesotheliomas that had not been diagnosed previously, and the PWG chair concurred with the QAP. However, the incidences of mesothelioma as diagnosed by either the SP or the QAP did

not indicate any treatment related effect. The QAP also noted several additional cases of interstitial cell hyperplasia in each of the male groups that had not been diagnosed previously; the PWG chair confirmed the QAP's findings. The incidences of interstitial cell hyperplasia as diagnosed by either the SP or the QAP did not indicate any treatment related effect. In addition, the QAP found that the SP had in numerous instances diagnosed **Interstitial Cell – Adenoma** when **Interstitial Cell – Adenoma, Bilateral** was present, and in these cases diagnosed bilateral adenoma; the PWG chair confirmed the QAP's findings. The incidences of interstitial cell adenoma or bilateral adenoma as diagnosed by either the SP or the QAP did not indicate any treatment related effect. Since there was good agreement concerning these diagnoses between the QAP and PWG chair and since none of these lesions represented potential compound related effects, the PWG opted not to review any examples.

Stomach, Glandular

The glandular stomach was reviewed for the presence of hyperplasia or adenoma of the epithelium, since these lesions had occurred in mice treated with sodium nitrite. No indications of any treatment-related effects were seen in the glandular stomach as a result of the QA/PWG review. The SP had diagnosed an adenoma of the glandular stomach in a single animal (a 0.075% male); the SP's diagnosis was not confirmed by the QAP or PWG chair. The SP had diagnosed a leiomyosarcoma of the glandular stomach in a control male and this was confirmed by the QAP and PWG chair. The QAP diagnosed a carcinoid tumor in a single animal (a 0.3% male); this was confirmed by the PWG chair. The QAP also diagnosed hyperplasia of the glandular stomach in a single animal (a 0.30%) male; this lesion was shown to the PWG which confirmed its presence. The PWG chair noted erosion or ulcer in the glandular stomach of a few animals which had not been diagnosed previously. These were shown to the PWG which in most cases confirmed the PWG chair's diagnosis. The ulcers and erosions usually occurred in early death animals, often animals with mononuclear cell leukemia, and appeared to be a result of the moribund condition of the animals.

Seminal Vesicle

The SP had diagnosed somewhat greater incidences of **Seminal Vesicle – Atrophy** in treated male groups as compared with controls. The QAP added numerous diagnoses of atrophy to each of the male groups such that the incidences of atrophy as diagnosed by the QAP were similar across dose groups, thus, not confirming the SP's findings. The PWG chair agreed with the QAP's diagnoses in each case. The PWG examined one slide of atrophy and agreed it was there but considered it to be a normal aging change. Atrophy was characterized microscopically by shrinkage of the seminal vesicle due to attenuation of the glandular epithelium and loss of secretory material from the lumen.

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Skin

Skin was reviewed for the presence of proliferative lesions. No indication of a treatment related effect in the skin was seen as a result of the QA/PWG review. The SP had diagnosed slightly greater incidences of **Squamous Cell Papilloma** in treated groups of males as compared with control males. The QAP considered these lesions to represent **Keratoacanthoma** rather than squamous cell papilloma; the PWG chair confirmed the QAP's findings. A few additional neoplasms were observed but these occurred with low incidences and were scattered across treatment groups with no apparent relationship to treatment.

Large Intestine, Rectum

The QAP observed a **Fibroma** arising in the rectum of one animal in the study which had not been diagnosed previously and as a consequence, all rectums were evaluated to determine if additional neoplasms were present. No additional neoplasms were found. The PWG chair confirmed the QAP's findings. The fibroma was considered to be an incidental finding unrelated to treatment.

POST-PWG ACTION ITEMS

The PWG chair was directed to review all forestomachs from all animals in the study, using the forestomachs examined by the PWG for reference, to ensure that hyperplasia and hyperkeratosis are diagnosed consistently in accord with the PWG's findings. This review was performed and the findings were entered onto the Pathology Quality Assessment Worksheets.

8/27/99

Micheal P. Jokinen, DVM
Diplomate, ACVP
PWG Chairperson

Date

FINAL #1 CORE STUDY RATS

REASONS FOR REMOVAL: ALL

REMOVAL DATE RANGE: ALL

TREATMENT GROUPS: INCLUDE ALL

R 04

NTP
LAB: Battelle Columbus

STATISTICAL ANALYSIS OF PRIMARY TUMORS
SODIUM NITRITE

REPORT: PEIRPT08
DATE: 10/18/99

TIME: 13:52:44

EXPERIMENT: 88007 TEST: 05
TEST TYPE: CHRONIC
CONT: NO1-ES-55384
PATHOLOGIST: YARRINGTON, JOHN

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED WATER

NTP C#: C88007
CAS: 7632-00-0

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
Ovary
Pancreas
Parathyroid Gland
Pituitary Gland
Spleen
Testes
Thyroid Gland
Urinary Bladder

B 05

NTP
LAB: Battelle Columbus
EXPERIMENT: 88007 TEST: 05
TEST TYPE: CHRONIC
CONT: NO1-ES-55384
PATHOLOGIST: YARRINGTON, JOHN

STATISTICAL ANALYSIS OF PRIMARY TUMORS
SODIUM NITRITE

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED WATER

REPORT: PEIRPT08
DATE: 10/18/99
TIME: 13:52:44

NTP C#: C88007
CAS: 7632-00-0

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

Male Rats

Organ	Morphology
Islets, Pancreatic	Adenoma
	Carcinoma or Adenoma
Mammary Gland	Fibroadenoma
	Fibroma, Fibroadenoma or Adenoma
Skin	Fibroma
	Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma
Testes	Adenoma
Thyroid Gland: C-Cell	Adenoma
	Carcinoma or Adenoma
All Organs	Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated
	Benign Tumors
	Malignant Tumors
	Malignant and Benign Tumors

Female Rats

Organ	Morphology
Clitoral/Preputial Gland	Adenoma
	Carcinoma or Adenoma
Mammary Gland	Fibroadenoma
	Fibroma, Fibroadenoma, Carcinoma, or Adenoma
All Organs	Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated
	Malignant Tumors

B 06

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Adrenal Medulla Pheochromocytoma Benign								
TUMOR RATES								
OVERALL (a)	6/50 (12%)	10/50 (20%)	6/50 (12%)	10/50 (20%)	4/50 (8%)	2/50 (4%)	0/45 (0%)	2/49 (4%)
POLY-3 ADJUSTED (b)	14.7%	21.7%	13.1%	21.7%	9.0%	4.5%	0.0%	4.6%
TERMINAL (d)	5/29 (17%)	7/38 (18%)	4/36 (11%)	8/36 (22%)	3/33 (9%)	2/31 (7%)	0/31 (0%)	1/32 (3%)
FIRST INCIDENCE	620	481	724	605	669	730 (T)	---	715
STATISTICAL TESTS								
LIFE TABLE	P=0.374	P=0.389	P=0.464N	P=0.360	P=0.233N	P=0.360N	P=0.070N	P=0.338N
POLY 3	P=0.336	P=0.287	P=0.535N	P=0.287	P=0.243N	P=0.339N	P=0.074N	P=0.346N
POLY 1.5	P=0.307	P=0.253	P=0.569N	P=0.255	P=0.244N	P=0.339N	P=0.075N	P=0.348N
POLY 6	P=0.368	P=0.334	P=0.493N	P=0.328	P=0.241N	P=0.338N	P=0.072N	P=0.341N
LOGISTIC REGRESSION	P=0.331	P=0.261	P=0.464N	P=0.314	P=0.236N	P=0.333N	P=0.075N	P=0.338N
COCH-ARM / FISHERS	P=0.257	P=0.207	P=0.620N	P=0.207	P=0.245N	P=0.339N	P=0.072N	P=0.349N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Adrenal Medulla Pheochromocytoma: Benign, Complex, Malignant, NOS								
TUMOR RATES								
OVERALL (a)	7/50 (14%)	10/50 (20%)	6/50 (12%)	11/50 (22%)	4/50 (8%)	2/50 (4%)	0/45 (0%)	2/49 (4%)
POLY-3 ADJUSTED (b)	17.2%	21.7%	13.1%	23.9%	9.0%	4.5%	0.0%	4.6%
TERMINAL (d)	6/29 (21%)	7/38 (18%)	4/36 (11%)	9/36 (25%)	3/33 (9%)	2/31 (7%)	0/31 (0%)	1/32 (3%)
FIRST INCIDENCE	620	481	724	605	669	730 (T)	---	715
STATISTICAL TESTS								
LIFE TABLE	P=0.360	P=0.509	P=0.340N	P=0.387	P=0.233N	P=0.360N	P=0.070N	P=0.338N
POLY 3	P=0.314	P=0.397	P=0.408N	P=0.307	P=0.243N	P=0.339N	P=0.074N	P=0.346N
POLY 1.5	P=0.288	P=0.356	P=0.444N	P=0.271	P=0.244N	P=0.339N	P=0.075N	P=0.348N
POLY 6	P=0.343	P=0.451	P=0.365N	P=0.351	P=0.241N	P=0.338N	P=0.072N	P=0.341N
LOGISTIC REGRESSION	P=0.321	P=0.372	P=0.330N	P=0.346	P=0.236N	P=0.333N	P=0.075N	P=0.338N
COCH-ARM / FISHERS	P=0.242	P=0.298	P=0.500N	P=0.218	P=0.245N	P=0.339N	P=0.072N	P=0.349N

B 07

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Clitoral/Preputial Gland Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	3/50 (6%)	1/50 (2%)	2/50 (4%)	8/46 (17%)	10/48 (21%)	9 (12%)	3/49 (6%)
POLY-3 ADJUSTED (b)	0.0%	6.7%	2.2%	4.4%	19.2%	23.5%	[illegible] 6%	6.7%
TERMINAL (d)	0/29 (0%)	3/38 (8%)	0/36 (0%)	1/36 (3%)	8/32 (25%)	9/30 (30%)	6/35 (17%)	1/33 (3%)
FIRST INCIDENCE	---	729 (T)	697	698	730 (T)	680	730 (T)	680
STATISTICAL TESTS								
LIFE TABLE	P=0.398	P=0.172	P=0.562	P=0.297	P=0.030N*	P=0.338	P=0.314N	P=0.090N
POLY 3	P=0.397	P=0.139	P=0.526	P=0.265	P=0.029N*	P=0.417	P=0.343N	P=0.077N
POLY 1.5	P=0.374	P=0.131	P=0.516	P=0.255	P=0.031N*	P=0.421	P=0.344N	P=0.079N
POLY 6	P=0.424	P=0.151	P=0.539	P=0.279	P=0.027N*	P=0.414	P=0.338N	P=0.073N
LOGISTIC REGRESSION	P=0.383	P=0.172	P=0.514	P=0.272	P=0.027N*	P=0.385	P=0.314N	P=0.076N
COCH-ARM / FISHERS	P=0.337	P=0.121	P=0.500	P=0.247	P=0.033N*	P=0.436	P=0.338N	P=0.081N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Clitoral/Preputial Gland Carcinoma								
TUMOR RATES								
OVERALL (a)	5/50 (10%)	1/50 (2%)	7/50 (14%)	5/50 (10%)	2/46 (4%)	1/48 (2%)	0/49 (0%)	1/49 (2%)
POLY-3 ADJUSTED (b)	12.0%	2.2%	15.3%	10.6%	4.7%	2.4%	0.0%	2.2%
TERMINAL (d)	3/29 (10%)	1/38 (3%)	5/36 (14%)	2/36 (6%)	1/32 (3%)	1/30 (3%)	0/35 (0%)	0/33 (0%)
FIRST INCIDENCE	400	729 (T)	724	523	567	730 (T)	---	626
STATISTICAL TESTS								
LIFE TABLE	P=0.415	P=0.069N	P=0.516	P=0.534N	P=0.356N	P=0.515N	P=0.230N	P=0.491N
POLY 3	P=0.397	P=0.085N	P=0.446	P=0.555N	P=0.348N	P=0.498N	P=0.228N	P=0.479N
POLY 1.5	P=0.374	P=0.092N	P=0.418	P=0.585N	P=0.349N	P=0.494N	P=0.226N	P=0.480N
POLY 6	P=0.422	P=0.076N	P=0.483	P=0.518N	P=0.347N	P=0.502N	P=0.228N	P=0.478N
LOGISTIC REGRESSION	P=0.275	P=0.134N	P=0.376	P=0.436	P=0.349N	P=0.465N	P=0.190N	P=0.439N
COCH-ARM / FISHERS	P=0.338	P=0.102N	P=0.380	P=0.630N	P=0.350N	P=0.484N	P=0.232N	P=0.476N

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Clitoral/Preputial Gland Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	5/50 (10%)	4/50 (8%)	8/50 (16%)	7/50 (14%)	10/46 (22%)	11/48 (23%)	6/49 (12%)	4/49 (8%)
POLY-3 ADJUSTED (b)	12.0%	8.9%	17.4%	14.9%	23.7%	25.8%	13.6%	8.9%
TERMINAL (d)	3/29 (10%)	4/38 (11%)	5/36 (14%)	3/36 (8%)	9/32 (28%)	10/30 (33%)	6/35 (17%)	1/33 (3%)
FIRST INCIDENCE	400	729 (T)	697	523	567	680	730 (T)	626
STATISTICAL TESTS								
LIFE TABLE	P=0.321	P=0.369N	P=0.418	P=0.499	P=0.021N*	P=0.439	P=0.152N	P=0.069N
POLY 3	P=0.301	P=0.455N	P=0.340	P=0.465	P=0.019N*	P=0.511	P=0.177N	P=0.054N
POLY 1.5	P=0.273	P=0.473N	P=0.313	P=0.431	P=0.020N*	P=0.521	P=0.175N	P=0.055N
POLY 6	P=0.335	P=0.428N	P=0.379	P=0.509	P=0.017N*	P=0.502	P=0.176N	P=0.050N
LOGISTIC REGRESSION	P=0.205	P=0.528N	P=0.275	P=0.227	P=0.019N*	P=0.512	P=0.167N	P=0.058N
COCH-ARM / FISHERS	P=0.231	P=0.500N	P=0.277	P=0.380	P=0.022N*	P=0.544	P=0.168N	P=0.057N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Islets, Pancreatic Adenoma								
TUMOR RATES								
OVERALL (a)	4/50 (8%)	0/50 (0%)	0/50 (0%)	1/49 (2%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	9.9%	0.0%	0.0%	2.2%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	4/29 (14%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	729 (T)	---	---	638	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.099N	P=0.034N*	P=0.039N*	P=0.121N	(e)	(e)	(e)	(e)
POLY 3	P=0.135N	P=0.047N*	P=0.045N*	P=0.147N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.130N	P=0.052N	P=0.051N	P=0.161N	(e)	(e)	(e)	(e)
POLY 6	P=0.143N	P=0.042N*	P=0.039N*	P=0.132N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.109N	(e)	(e)	P=0.140N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.128N	P=0.059N	P=0.059N	P=0.187N	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Islets, Pancreatic Carcinoma								
TUMOR RATES								
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/49 (4%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY 3 ADJUSTED (b)	2.5%	0.0%	0.0%	4.5%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/29 (3%)	0/38 (0%)	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	729 (T)	---	---	636	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.275	P=0.446N	P=0.457N	P=0.576	(e)	(e)	(e)	(e)
POLY 3	P=0.245	P=0.478N	P=0.475N	P=0.537	(e)	(e)	(e)	(e)
POLY 1.5	P=0.244	P=0.487N	P=0.485N	P=0.520	(e)	(e)	(e)	(e)
POLY 6	P=0.246	P=0.467N	P=0.462N	P=0.558	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.275	(e)	(e)	P=0.520	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.2	P=0.500N	P=0.500N	P=0.492	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Islets, Pancreatic Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	5/50 (10%)	0/50 (0%)	0/50 (0%)	3/49 (6%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	12.4%	0.0%	0.0%	6.6%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	5/29 (17%)	0/38 (0%)	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	729 (T)	---	---	636	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.342N	P=0.015N*	P=0.017N*	P=0.246N	(e)	(e)	(e)	(e)
POLY 3	P=0.426N	P=0.022N*	P=0.021N*	P=0.295N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.419N	P=0.025N*	P=0.025N*	P=0.323N	(e)	(e)	(e)	(e)
POLY 6	P=0.439N	P=0.019N*	P=0.017N*	P=0.262N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.380N	(e)	(e)	P=0.299N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.412N	P=0.028N*	P=0.028N*	P=0.369N	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Lung Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	3/50 (6%)	2/50 (4%)	2/50 (4%)	3/50 (6%)	2/50 (4%)	3/50 (6%)	2/50 (4%)
POLY-3 ADJUSTED (b)	5.0%	6.7%	4.4%	4.4%	6.8%	4.5%	6.7%	4.5%
TERMINAL (d)	2/29 (7%)	3/38 (8%)	1/36 (3%)	1/36 (3%)	2/33 (6%)	1/31 (3%)	3/36 (8%)	2/33 (6%)
FIRST INCIDENCE	729 (T)	729 (T)	716	622	693	680	730 (T)	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.459N	P=0.623	P=0.610N	P=0.616N	P=0.437N	P=0.515N	P=0.624N	P=0.495N
POLY 3	P=0.474N	P=0.549	P=0.647N	P=0.647N	P=0.455N	P=0.499N	P=0.656N	P=0.498N
POLY 1.5	P=0.492N	P=0.529	P=0.666N	P=0.665N	P=0.457N	P=0.501N	P=0.660N	P=0.501N
POLY 6	P=0.454N	P=0.574	P=0.621N	P=0.625N	P=0.449N	P=0.496N	P=0.649N	P=0.493N
LOGISTIC REGRESSION	P=0.467N	P=0.623	P=0.597N	P=0.661N	P=0.440N	P=0.498N	P=0.639N	P=0.485N
COCH-ARM / FISHERS	P=0.523N	P=0.500	P=0.691N	P=0.691N	P=0.456N	P=0.500N	P=0.661N	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Lung Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	3/50 (6%)	3/50 (6%)	2/50 (4%)	3/50 (6%)	2/50 (4%)	4/50 (8%)	2/50 (4%)
POLY-3 ADJUSTED (b)	5.0%	6.7%	6.5%	4.4%	6.8%	4.5%	8.9%	4.5%
TERMINAL (d)	2/29 (7%)	3/38 (8%)	2/36 (6%)	1/36 (3%)	2/33 (6%)	1/31 (3%)	4/36 (11%)	2/33 (6%)
FIRST INCIDENCE	729 (T)	729 (T)	716	622	693	680	730 (T)	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.476N	P=0.623	P=0.602	P=0.616N	P=0.459N	P=0.515N	P=0.545	P=0.495N
POLY 3	P=0.487N	P=0.549	P=0.559	P=0.647N	P=0.477N	P=0.499N	P=0.508	P=0.498N
POLY 1.5	P=0.508N	P=0.529	P=0.535	P=0.665N	P=0.480N	P=0.501N	P=0.503	P=0.501N
POLY 6	P=0.465N	P=0.574	P=0.588	P=0.625N	P=0.471N	P=0.496N	P=0.517	P=0.493N
LOGISTIC REGRESSION	P=0.481N	P=0.623	P=0.623	P=0.661N	P=0.461N	P=0.498N	P=0.532	P=0.485N
COCH-ARM / FISHERS	P=0.544N	P=0.500	P=0.500	P=0.691N	P=0.479N	P=0.500N	P=0.500	P=0.500N

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (e)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	3/50 (6%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	4.5%	2.3%	0.0%	6.7%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	2/33 (6%)	1/31 (3%)	0/36 (0%)	3/33 (9%)
FIRST INCIDENCE	---	---	---	---	730 (T)	730 (T)	---	730 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.346	P=0.522N	P=0.219N	P=0.500
POLY 3	(e)	(e)	(e)	(e)	P=0.339	P=0.499N	P=0.233N	P=0.503
POLY 1.5	(e)	(e)	(e)	(e)	P=0.338	P=0.501N	P=0.236N	P=0.500
POLY 6	(e)	(e)	(e)	(e)	P=0.342	P=0.497N	P=0.229N	P=0.510
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.346	P=0.522N	(e)	P=0.500
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.337	P=0.500N	P=0.247N	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	2.2%	0.0%	2.3%	2.3%	4.4%	4.4%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	1/36 (3%)	0/36 (0%)	1/33 (3%)	1/31 (3%)	2/36 (6%)	0/33 (0%)
FIRST INCIDENCE	---	---	729 (T)	---	730 (T)	730 (T)	730 (T)	361
STATISTICAL TESTS								
LIFE TABLE	P=0.715	(e)	P=0.543	(e)	P=0.350	P=0.748	P=0.530	P=0.512
POLY 3	P=0.726	(e)	P=0.525	(e)	P=0.351	P=0.760N	P=0.506	P=0.511
POLY 1.5	P=0.715	(e)	P=0.515	(e)	P=0.345	P=0.760	P=0.503	P=0.505
POLY 6	P=0.738	(e)	P=0.538	(e)	P=0.361	P=0.759N	P=0.513	P=0.519
LOGISTIC REGRESSION	(e)	(e)	P=0.543	(e)	P=0.346	P=0.748	P=0.530	P=0.594
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)	P=0.337	P=0.753N	P=0.500	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/50 (4%)	2/50 (4%)	2/50 (4%)	5/50 (10%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	2.2%	0.0%	4.5%	4.5%	4.4%	11.0%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	1/36 (3%)	0/36 (0%)	2/33 (6%)	2/31 (7%)	2/36 (6%)	3/33 (9%)
FIRST INCIDENCE	---	---	729 (T)	---	730 (T)	730 (T)	730 (T)	361
STATISTICAL TESTS								
LIFE TABLE	P=0.715	(e)	P=0.543	(e)	P=0.122	P=0.673	P=0.664N	P=0.226
POLY 3	P=0.726	(e)	P=0.525	(e)	P=0.121	P=0.694N	P=0.687N	P=0.228
POLY 1.5	P=0.715	(e)	P=0.515	(e)	P=0.118	P=0.693	P=0.691N	P=0.223
POLY 6	P=0.738	(e)	P=0.538	(e)	P=0.126	P=0.692N	P=0.681N	P=0.237
LOGISTIC REGRESSION	(e)	(e)	P=0.543	(e)	P=0.114	P=0.673	P=0.664N	P=0.224
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)	P=0.114	P=0.691N	P=0.691N	P=0.218

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Fibroadenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	5/50 (10%)	3/50 (6%)	0/50 (0%)	21/50 (42%)	27/50 (54%)	31/50 (62%)	25/50 (50%)
POLY-3 ADJUSTED (b)	7.3%	11.1%	6.5%	0.0%	45.7%	58.5%	66.7%	54.4%
TERMINAL (d)	1/29 (3%)	5/38 (13%)	2/36 (6%)	0/36 (0%)	15/33 (46%)	17/31 (55%)	26/36 (72%)	16/33 (49%)
FIRST INCIDENCE	589	729 (T)	708	---	547	541	541	626
STATISTICAL TESTS								
LIFE TABLE	P=0.014N*	P=0.487	P=0.566N	P=0.096N	P=0.363	P=0.148	P=0.092	P=0.315
POLY 3	P=0.047N*	P=0.405	P=0.611N	P=0.102N	P=0.268	P=0.149	P=0.029 *	P=0.263
POLY 1.5	P=0.052N	P=0.386	P=0.631N	P=0.108N	P=0.265	P=0.149	P=0.030 *	P=0.260
POLY 6	P=0.042N*	P=0.428	P=0.586N	P=0.096N	P=0.289	P=0.154	P=0.030 *	P=0.280
LOGISTIC REGRESSION	P=0.052N	P=0.395	P=0.567N	P=0.145N	P=0.292	P=0.155	P=0.039 *	P=0.279
COCH-ARM / FISHERS	P=0.064N	P=0.357	P=0.661N	P=0.121N	P=0.283	P=0.158	P=0.036 *	P=0.274

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Fibroma, Fibroadenoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	5/50 (10%)	3/50 (6%)	0/50 (0%)	23/50 (46%)	27/50 (54%)	31/50 (62%)	28/50 (56%)
POLY 3 ADJUSTED (b)	7.3%	11.1%	6.5%	0.0%	50.1%	58.5%	66.7%	61.0%
TERMINAL (d)	1/29 (3%)	5/38 (13%)	2/36 (6%)	0/36 (0%)	17/33 (52%)	17/31 (55%)	26/36 (72%)	19/33 (58%)
FIRST INCIDENCE	589	729 (T)	708	---	547	541	541	626
STATISTICAL TESTS								
LIFE TABLE	P=0.044N*	P=0.487	P=0.566N	P=0.096N	P=0.265	P=0.241	P=0.173	P=0.255
POLY 3	P=0.047N*	P=0.405	P=0.611N	P=0.102N	P=0.169	P=0.270	P=0.073	P=0.196
POLY 1.5	P=0.052N	P=0.386	P=0.631N	P=0.108N	P=0.169	P=0.266	P=0.075	P=0.195
POLY 6	P=0.042N*	P=0.428	P=0.586N	P=0.096N	P=0.181	P=0.280	P=0.076	P=0.211
LOGISTIC REGRESSION	P=0.052N	P=0.395	P=0.667N	P=0.145N	P=0.192	P=0.272	P=0.089	P=0.217
COCH-ARM / FISHERS	P=0.064N	P=0.357	P=0.661N	P=0.121N	P=0.187	P=0.274	P=0.080	P=0.212

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Mammary Gland Fibroma, Fibroadenoma, Carcinoma, or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	5/50 (10%)	4/50 (8%)	0/50 (0%)	23/50 (46%)	27/50 (54%)	33/50 (66%)	30/50 (60%)
POLY-3 ADJUSTED (b)	7.3%	11.1%	8.7%	0.0%	50.1%	58.5%	71.0%	63.8%
TERMINAL (d)	1/29 (3%)	5/38 (13%)	3/36 (8%)	0/36 (0%)	17/33 (52%)	17/31 (55%)	28/36 (78%)	19/33 (58%)
FIRST INCIDENCE	589	729 (T)	708	---	547	541	541	361
STATISTICAL TESTS								
LIFE TABLE	P=0.054N	P=0.487	P=0.607	P=0.096N	P=0.150	P=0.241	P=0.093	P=0.164
POLY 3	P=0.058N	P=0.405	P=0.559	P=0.102N	P=0.092	P=0.270	P=0.027 *	P=0.124
POLY 1.5	P=0.064N	P=0.386	P=0.536	P=0.108N	P=0.086	P=0.266	P=0.028 *	P=0.117
POLY 6	P=0.052N	P=0.428	P=0.587	P=0.096N	P=0.108	P=0.280	P=0.027 *	P=0.143
LOGISTIC REGRESSION	P=0.063N	P=0.395	P=0.518	P=0.145N	P=0.083	P=0.272	P=0.038 *	P=0.112
COCH-ARM / FISHERS	P=0.079N	P=0.357	P=0.500	P=0.121N	P=0.085	P=0.274	P=0.035 *	P=0.115

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Oral Cavity (Oral Mucosa, Tongue, Pharynx, Tooth, Gingiva) Squamous Cell Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	2.2%	0.0%	2.3%	4.5%	2.2%	0.0%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	---	---	593	---	662	609	658	---
STATISTICAL TESTS								
LIFE TABLE	P=0.710	(e)	P=0.528	(e)	P=0.243N	P=0.519	P=0.755N	P=0.495N
POLY 3	P=0.726	(e)	P=0.527	(e)	P=0.247N	P=0.504	P=0.757N	P=0.500N
POLY 1.5	P=0.714	(e)	P=0.516	(e)	P=0.249N	P=0.501	P=0.759N	P=0.501N
POLY 6	P=0.738	(e)	P=0.541	(e)	P=0.244N	P=0.508	P=0.753N	P=0.498N
LOGISTIC REGRESSION	P=0.625	(e)	P=0.417	(e)	P=0.236N	P=0.527	P=0.759N	P=0.492N
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)	P=0.247N	P=0.500	P=0.753N	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Oral Cavity (Oral Mucosa, Tongue, Pharynx, Tooth, Gingiva) Squamous Cell Carcinoma, Papilloma Squamous, or Papilloma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	2.2%	0.0%	2.3%	4.5%	2.2%	0.0%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	---	---	593	---	662	609	658	---
STATISTICAL TESTS								
LIFE TABLE	P=0.710	(e)	P=0.528	(e)	P=0.243N	P=0.519	P=0.755N	P=0.495N
POLY 3	P=0.726	(e)	P=0.527	(e)	P=0.247N	P=0.504	P=0.757N	P=0.500N
POLY 1.5	P=0.714	(e)	P=0.516	(e)	P=0.249N	P=0.501	P=0.759N	P=0.501N
POLY 6	P=0.738	(e)	P=0.541	(e)	P=0.244N	P=0.508	P=0.753N	P=0.498N
LOGISTIC REGRESSION	P=0.625	(e)	P=0.417	(e)	P=0.236N	P=0.527	P=0.759N	P=0.492N
COCH-ARM / FISHERS	P=0.694	(e)	P=0.500	(e)	P=0.247N	P=0.500	P=0.753N	P=0.500N

C 01

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Pancreas Carcinoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/49 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	4.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/29 (0%)	1/38 (3%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	---	669	---	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.371N	P=0.301	(e)	(e)	(e)	(e)	(e)	(e)
POLY 3	P=0.367N	P=0.263	(e)	(e)	(e)	(e)	(e)	(e)
POLY 1.5	P=0.383N	P=0.252	(e)	(e)	(e)	(e)	(e)	(e)
POLY 6	P=0.348N	P=0.278	(e)	(e)	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.400N	P=0.252	(e)	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.409N	P=0.247	(e)	(e)	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Pancreas Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	1/50 (2%)	0/49 (0%)	0/50 (0%)	0/50 (0%)	0/49 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	4.4%	2.2%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/29 (0%)	1/38 (3%)	1/36 (3%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	---	669	729 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.420N	P=0.301	P=0.543	(e)	(e)	(e)	(e)	(e)
POLY 3	P=0.417N	P=0.263	P=0.525	(e)	(e)	(e)	(e)	(e)
POLY 1.5	P=0.435N	P=0.252	P=0.515	(e)	(e)	(e)	(e)	(e)
POLY 6	P=0.395N	P=0.278	P=0.538	(e)	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.442N	P=0.252	P=0.543	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.466N	P=0.247	P=0.500	(e)	(e)	(e)	(e)	(e)

C 02

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Pituitary Gland: Pars Distalis or Unspecified Site								
Adenoma								
TUMOR RATES								
OVERALL (a)	13/50 (26%)	13/49 (27%)	15/50 (30%)	10/50 (20%)	24/50 (48%)	25/50 (50%)	17/50 (34%)	21/50 (42%)
POLY-3 ADJUSTED (b)	31.5%	28.8%	31.5%	21.8%	51.9%	53.9%	36.7%	45.6%
TERMINAL (d)	10/29 (35%)	10/37 (27%)	12/36 (33%)	9/36 (25%)	16/33 (49%)	16/31 (52%)	12/36 (33%)	14/33 (42%)
FIRST INCIDENCE	589	481	505	622	513	536	541	624
STATISTICAL TESTS								
LIFE TABLE	P=0.152N	P=0.330N	P=0.516N	P=0.144N	P=0.200N	P=0.437	P=0.086N	P=0.343N
POLY 3	P=0.191N	P=0.488N	P=0.587	P=0.218N	P=0.207N	P=0.507	P=0.099N	P=0.342N
POLY 1.5	P=0.218N	P=0.537N	P=0.518	P=0.252N	P=0.214N	P=0.498	P=0.105N	P=0.351N
POLY 6	P=0.168N	P=0.426N	P=0.515N	P=0.184N	P=0.191N	P=0.522	P=0.091N	P=0.321N
LOGISTIC REGRESSION	P=0.212N	P=0.499N	P=0.511	P=0.178N	P=0.207N	P=0.498	P=0.103N	P=0.338N
COCH-ARM / FISHERS	P=0.275N	P=0.567	P=0.412	P=0.318N	P=0.213N	P=0.500	P=0.111N	P=0.344N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin								
Basal Cell Adenoma, Basosquamous Tumor Benign, or Trichoepithelioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	0.0%	4.5%	0.0%	0.0%	2.3%	0.0%	0.0%	2.2%
TERMINAL (d)	0/29 (0%)	2/38 (5%)	0/36 (0%)	0/36 (0%)	1/33 (3%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	---	729 (T)	---	---	730 (T)	---	---	624
STATISTICAL TESTS								
LIFE TABLE	P=0.375N	P=0.299	(e)	(e)	P=0.604	P=0.512N	P=0.483N	P=0.753N
POLY 3	P=0.364N	P=0.262	(e)	(e)	P=0.597	P=0.500N	P=0.496N	P=0.757N
POLY 1.5	P=0.379N	P=0.252	(e)	(e)	P=0.596	P=0.500N	P=0.499N	P=0.760N
POLY 6	P=0.346N	P=0.275	(e)	(e)	P=0.600	P=0.499N	P=0.493N	P=0.753N
LOGISTIC REGRESSION	(e)	P=0.299	(e)	(e)	P=0.597	(e)	(e)	P=0.760N
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)	P=0.595	P=0.500N	P=0.500N	P=0.753N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Basal Cell Carcinoma, Basal Cell Adenoma, Basosquamous Tumor (benign, malignant or NOS), or Trichoepithelioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	2.5%	4.5%	0.0%	0.0%	4.5%	0.0%	0.0%	4.4%
TERMINAL (d)	0/29 (0%)	2/38 (5%)	0/36 (0%)	0/36 (0%)	1/33 (3%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	724	729 (T)	---	---	513	---	---	624
STATISTICAL TESTS								
LIFE TABLE	P=0.162N	P=0.589	P=0.453N	P=0.464N	P=0.506	P=0.249N	P=0.230N	P=0.687N
POLY 3	P=0.169N	P=0.537	P=0.475N	P=0.476N	P=0.504	P=0.240N	P=0.236N	P=0.692N
POLY 1.5	P=0.176N	P=0.522	P=0.485N	P=0.485N	P=0.502	P=0.240N	P=0.238N	P=0.693
POLY 6	P=0.162N	P=0.557	P=0.462N	P=0.466N	P=0.508	P=0.240N	P=0.233N	P=0.695N
LOGISTIC REGRESSION	P=0.155N	P=0.585	P=0.449N	P=0.456N	P=0.522	P=0.199N	P=0.208N	P=0.659N
COCH-ARM / FISHERS	P=0.188N	P=0.500	P=0.500N	P=0.500N	P=0.500	P=0.247N	P=0.247N	P=0.691N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Basal or Sq. Cell Carcinoma, Carcinoma, Basosq. Tumor (M or B), Basal Cell Adenoma, Adenoma, Papilloma, Sq Papilloma, Keratoacanthoma, Trichoepitheliom								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	6/50 (12%)	4/50 (8%)	4/50 (8%)	3/50 (6%)	0/50 (0%)	0/50 (0%)	3/50 (6%)
POLY-3 ADJUSTED (b)	7.3%	13.1%	8.7%	8.8%	6.7%	0.0%	0.0%	6.6%
TERMINAL (d)	1/29 (3%)	4/38 (11%)	4/36 (11%)	4/36 (11%)	1/33 (3%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	486	480	729 (T)	729 (T)	513	---	---	624
STATISTICAL TESTS								
LIFE TABLE	P=0.502N	P=0.355	P=0.602	P=0.600	P=0.457	P=0.128N	P=0.118N	P=0.647N
POLY 3	P=0.525N	P=0.299	P=0.560	P=0.555	P=0.449	P=0.122N	P=0.119N	P=0.661N
POLY 1.5	P=0.546N	P=0.276	P=0.536	P=0.535	P=0.446	P=0.121N	P=0.120N	P=0.660
POLY 6	P=0.503N	P=0.331	P=0.590	P=0.579	P=0.453	P=0.122N	P=0.117N	P=0.654N
LOGISTIC REGRESSION	P=0.568N	P=0.215	P=0.528	P=0.530	P=0.458	P=0.099N	P=0.105N	P=0.639N
COCH-ARM / FISHERS	P=0.551	P=0.243	P=0.500	P=0.500	P=0.444	P=0.121N	P=0.121N	P=0.661N

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Fibroma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	1/50 (2%)	6/50 (12%)	3/50 (6%)	1/50 (2%)	0/50 (0%)	2/50 (4%)	1/50 (2%)
POLY-3 ADJUSTED (b)	0.0%	2.2%	13.0%	6.6%	2.3%	0.0%	4.4%	2.2%
TERMINAL (d)	0/29 (0%)	1/38 (3%)	3/36 (8%)	2/36 (6%)	0/33 (0%)	0/31 (0%)	2/36 (6%)	0/33 (0%)
FIRST INCIDENCE	---	729 (T)	694	697	729	---	730 (T)	715
STATISTICAL TESTS								
LIFE TABLE	P=0.112	P=0.554	P=0.040 *	P=0.170	P=0.512	P=0.518N	P=0.527	P=0.754N
POLY 3	P=0.103	P=0.521	P=0.024 *	P=0.142	P=0.503	P=0.500N	P=0.506	P=0.759N
POLY 1.5	P=0.091	P=0.513	P=0.020 *	P=0.133	P=0.500	P=0.500N	P=0.503	P=0.760N
POLY 6	P=0.116	P=0.533	P=0.030 *	P=0.154	P=0.509	P=0.499N	P=0.513	P=0.755N
LOGISTIC REGRESSION	P=0.099	P=0.554	P=0.028 *	P=0.154	P=0.514	P=0.505N	P=0.531	P=0.756N
COCH-ARM / FISHERS	P=0.077	P=0.500	P=0.013 *	P=0.121	P=0.500	P=0.500N	P=0.500	P=0.753N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	7/50 (14%)	5/50 (10%)	1/50 (2%)	0/50 (0%)	2/50 (4%)	2/50 (4%)
POLY-3 ADJUSTED (b)	2.5%	2.2%	14.9%	10.8%	2.3%	0.0%	4.4%	4.5%
TERMINAL (d)	1/29 (3%)	1/38 (3%)	3/36 (8%)	3/36 (8%)	0/33 (0%)	0/31 (0%)	2/36 (6%)	1/33 (3%)
FIRST INCIDENCE	729 (T)	729 (T)	400	520	729	---	730 (T)	715
STATISTICAL TESTS								
LIFE TABLE	P=0.061	P=0.701N	P=0.070	P=0.161	P=0.257	P=0.518N	P=0.527	P=0.506
POLY 3	P=0.054	P=0.736N	P=0.050	P=0.136	P=0.248	P=0.500N	P=0.506	P=0.503
POLY 1.5	P=0.047 *	P=0.746N	P=0.041 *	P=0.122	P=0.247	P=0.500N	P=0.503	P=0.500
POLY 6	P=0.063	P=0.723N	P=0.063	P=0.154	P=0.253	P=0.499N	P=0.513	P=0.509
LOGISTIC REGRESSION	P=0.030 *	P=0.701N	P=0.026 *	P=0.105	P=0.258	P=0.505N	P=0.531	P=0.513
COCH-ARM / FISHERS	P=0.038 *	P=0.753N	P=0.030 *	P=0.102	P=0.245	P=0.500N	P=0.500	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Fibrosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	2.5%	0.0%	0.0%	4.3%	0.0%	0.0%	0.0%	2.2%
TERMINAL (d)	1/29 (3%)	0/38 (0%)	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	1/33 (3%)
FIRST INCIDENCE	729 (T)	---	---	520	---	---	---	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.270	P=0.446N	P=0.457N	P=0.560	P=0.201	(e)	(e)	P=0.500
POLY 3	P=0.251	P=0.478N	P=0.475N	P=0.546	P=0.200	(e)	(e)	P=0.501
POLY 1.5	P=0.250	P=0.487N	P=0.485N	P=0.529	P=0.199	(e)	(e)	P=0.500
POLY 6	P=0.251	P=0.467N	P=0.462N	P=0.566	P=0.202	(e)	(e)	P=0.504
LOGISTIC REGRESSION	P=0.205	(e)	(e)	P=0.453	(e)	(e)	(e)	P=0.500
COCH-ARM / FISHERS	P=0.246	P=0.500N	P=0.500N	P=0.500	P=0.198	(e)	(e)	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Female 0.0%	0.075%	0.15%	0.30%
Skin Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	2.5%	0.0%	2.1%	4.3%	0.0%	0.0%	0.0%	2.2%
TERMINAL (d)	1/29 (3%)	0/38 (0%)	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	1/33 (3%)
FIRST INCIDENCE	729 (T)	---	400	520	---	---	---	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.271	P=0.446N	P=0.734N	P=0.560	P=0.201	(e)	(e)	P=0.500
POLY 3	P=0.266	P=0.478N	P=0.727N	P=0.546	P=0.200	(e)	(e)	P=0.501
POLY 1.5	P=0.260	P=0.487N	P=0.740N	P=0.529	P=0.199	(e)	(e)	P=0.500
POLY 6	P=0.271	P=0.467N	P=0.710N	P=0.566	P=0.202	(e)	(e)	P=0.504
LOGISTIC REGRESSION	P=0.116	(e)	P=0.655	P=0.453	(e)	(e)	(e)	P=0.500
COCH-ARM / FISHERS	P=0.247	P=0.500N	P=0.753N	P=0.500	P=0.198	(e)	(e)	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Keratoacanthoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	3/50 (6%)	4/50 (8%)	4/50 (8%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.9%	6.6%	8.7%	8.8%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	1/29 (3%)	2/38 (5%)	4/36 (11%)	4/36 (11%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	486	680	729 (T)	729 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.328	P=0.593	P=0.425	P=0.426	(e)	(e)	(e)	(e)
POLY 3	P=0.310	P=0.543	P=0.389	P=0.385	(e)	(e)	(e)	(e)
POLY 1.5	P=0.294	P=0.526	P=0.368	P=0.367	(e)	(e)	(e)	(e)
POLY 6	P=0.326	P=0.567	P=0.417	P=0.407	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.298	P=0.481	P=0.344	P=0.346	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.264	P=0.500	P=0.339	P=0.339	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Lipoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)
POLY-3 ADJUSTED (b)	2.5%	0.0%	0.0%	0.0%	0.0%	0.0%	4.4%	0.0%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	1/36 (3%)	0/33 (0%)
FIRST INCIDENCE	724	---	---	---	---	---	554	---
STATISTICAL TESTS								
LIFE TABLE	P=0.286N	P=0.453N	P=0.453N	P=0.464N	P=0.598	(e)	P=0.252	(e)
POLY 3	P=0.324N	P=0.479N	P=0.475N	P=0.476N	P=0.597	(e)	P=0.244	(e)
POLY 1.5	P=0.317N	P=0.487N	P=0.485N	P=0.485N	P=0.595	(e)	P=0.240	(e)
POLY 6	P=0.335N	P=0.468N	P=0.462N	P=0.466N	P=0.604	(e)	P=0.250	(e)
LOGISTIC REGRESSION	P=0.281N	P=0.456N	P=0.449N	P=0.456N	P=0.607	(e)	P=0.247	(e)
COCH-ARM / FISHERS	P=0.306N	P=0.500N	P=0.500N	P=0.500N	P=0.595	(e)	P=0.247	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Squamous Cell Carcinoma, Basal Cell Carcinoma, Basosquamous Tumor (malignant or NOS), or Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	2.5%	2.2%	0.0%	0.0%	4.4%	0.0%	0.0%	4.5%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	724	480	---	---	513	---	---	658
STATISTICAL TESTS								
LIFE TABLE	P=0.222N	P=0.732N	P=0.453N	P=0.464N	P=0.507	P=0.239N	P=0.237N	P=0.684N
POLY 3	P=0.229N	P=0.733N	P=0.475N	P=0.476N	P=0.503	P=0.241N	P=0.237N	P=0.692
POLY 1.5	P=0.231N	P=0.744N	P=0.485N	P=0.485N	P=0.501	P=0.240N	P=0.238N	P=0.691
POLY 6	P=0.227N	P=0.718N	P=0.462N	P=0.466N	P=0.506	P=0.242N	P=0.236N	P=0.693N
LOGISTIC REGRESSION	P=0.315N	P=0.705	P=0.449N	P=0.456N	P=0.517	P=0.172N	P=0.183N	P=0.666N
COCH-ARM / FISHERS	P=0.236N	P=0.753N	P=0.500N	P=0.500N	P=0.500	P=0.247N	P=0.247N	P=0.691N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma or Keratoacanthoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	4/50 (8%)	4/50 (8%)	4/50 (8%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	4.9%	8.7%	8.7%	8.8%	2.3%	0.0%	0.0%	2.2%
TERMINAL (d)	1/29 (3%)	2/38 (5%)	4/36 (11%)	4/36 (11%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	486	480	729 (T)	729 (T)	669	---	---	718
STATISTICAL TESTS								
LIFE TABLE	P=0.389	P=0.422	P=0.425	P=0.426	P=0.606	P=0.495N	P=0.495N	P=0.748N
POLY 3	P=0.372	P=0.389	P=0.389	P=0.385	P=0.596	P=0.501N	P=0.497N	P=0.760N
POLY 1.5	P=0.354	P=0.368	P=0.368	P=0.367	P=0.595	P=0.501N	P=0.499N	P=0.760
POLY 6	P=0.392	P=0.418	P=0.417	P=0.407	P=0.598	P=0.501N	P=0.495N	P=0.758N
LOGISTIC REGRESSION	P=0.314	P=0.262	P=0.344	P=0.346	P=0.595	P=0.494N	P=0.498N	P=0.762N
COCH-ARM / FISHERS	P=0.320	P=0.339	P=0.339	P=0.339	P=0.595	P=0.500N	P=0.500N	P=0.753N

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Testes								
Adenoma								
TUMOR RATES								
OVERALL (a)	47/50 (94%)	46/50 (92%)	47/50 (94%)	46/50 (92%)				
POLY-3 ADJUSTED (b)	98.9%	96.3%	96.7%	95.1%				
TERMINAL (d)	29/29 (100%)	37/38 (97%)	35/36 (97%)	36/36 (100%)				
FIRST INCIDENCE	486	552	505	520				
STATISTICAL TESTS								
LIFE TABLE	P=0.075N	P=0.018N*	P=0.056N	P=0.038N*				
POLY 3	P=0.200N	P=0.416N	P=0.478N	P=0.248N				
POLY 1.5	P=0.254N	P=0.414N	P=0.534N	P=0.301N				
POLY 6	P=0.272N	P=0.470N	P=0.469N	P=0.330N				
LOGISTIC REGRESSION	P=0.043N*	P=0.133N	P=0.213N	P=0.050N				
COCH-ARM / FISHERS	P=0.463N	P=0.500N	P=0.661N	P=0.500N				
Thyroid Gland: C-Cell								
Adenoma								
TUMOR RATES								
OVERALL (a)	12/50 (24%)	8/50 (16%)	7/50 (14%)	5/50 (10%)	7/50 (14%)	4/49 (8%)	10/48 (21%)	7/50 (14%)
POLY-3 ADJUSTED (b)	29.3%	17.8%	15.2%	10.9%	15.8%	9.1%	22.7%	15.7%
TERMINAL (d)	10/29 (35%)	8/38 (21%)	5/36 (14%)	4/36 (11%)	7/33 (21%)	2/31 (7%)	7/36 (19%)	6/33 (18%)
FIRST INCIDENCE	620	729 (T)	708	636	730 (T)	616	658	680
STATISTICAL TESTS								
LIFE TABLE	P=0.020N*	P=0.075N	P=0.061N	P=0.018N*	P=0.418	P=0.287N	P=0.364	P=0.610N
POLY 3	P=0.028N*	P=0.157N	P=0.092N	P=0.028N*	P=0.399	P=0.263N	P=0.293	P=0.605N
POLY 1.5	P=0.033N*	P=0.183N	P=0.113N	P=0.036N*	P=0.394	P=0.270N	P=0.278	P=0.612N
POLY 6	P=0.024N*	P=0.129N	P=0.070N	P=0.021N*	P=0.413	P=0.252N	P=0.321	P=0.591N
LOGISTIC REGRESSION	P=0.019N*	P=0.102N	P=0.059N	P=0.023N*	P=0.411	P=0.270N	P=0.312	P=0.583N
COCH-ARM / FISHERS	P=0.045N*	P=0.227N	P=0.154N	P=0.054N	P=0.394	P=0.274N	P=0.266	P=0.613N

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Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Thyroid Gland: C-Cell Carcinoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	2/50 (4%)	0/49 (0%)	0/48 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)	5.0%	0.0%	4.3%	2.2%	4.5%	0.0%	0.0%	2.2%
TERMINAL (d)	2/29 (7%)	0/38 (0%)	1/36 (3%)	0/36 (0%)	2/33 (6%)	0/31 (0%)	0/36 (0%)	1/33 (3%)
FIRST INCIDENCE	729 (T)	---	582	705	730 (T)	---	---	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.482N	P=0.181N	P=0.624N	P=0.420N	P=0.453N	P=0.252N	P=0.219N	P=0.500N
POLY 3	P=0.518N	P=0.214N	P=0.643N	P=0.458N	P=0.459N	P=0.241N	P=0.240N	P=0.498N
POLY 1.5	P=0.522N	P=0.223N	P=0.664N	P=0.474N	P=0.459N	P=0.242N	P=0.244N	P=0.500N
POLY 6	P=0.517N	P=0.202N	P=0.616N	P=0.439N	P=0.458N	P=0.240N	P=0.234N	P=0.492N
LOGISTIC REGRESSION	P=0.525N	(e)	P=0.683N	P=0.428N	P=0.453N	(e)	(e)	P=0.500N
COCH-ARM / FISHERS	P=0.531N	P=0.247N	P=0.691N	P=0.500N	P=0.461N	P=0.253N	P=0.258N	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.07 %	0.15%	0.30%
Thyroid Gland: C-Cell Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	14/50 (28%)	8/50 (16%)	9/50 (18%)	6/50 (12%)	9/50 (18%)	4/49 (8%)	10/48 (21%)	7/50 (14%)
POLY-3 ADJUSTED (b)	34.1%	17.8%	19.4%	13.1%	20.4%	9.1%	22.7%	15.7%
TERMINAL (d)	12/29 (41%)	8/38 (21%)	6/36 (17%)	4/36 (11%)	9/33 (27%)	2/31 (7%)	7/36 (19%)	6/33 (18%)
FIRST INCIDENCE	620	729 (T)	582	636	730 (T)	616	658	680
STATISTICAL TESTS								
LIFE TABLE	P=0.019N*	P=0.025N*	P=0.064N	P=0.011N*	P=0.498N	P=0.135N	P=0.578	P=0.384N
POLY 3	P=0.027N*	P=0.066N	P=0.091N	P=0.017N*	P=0.518N	P=0.115N	P=0.498	P=0.382N
POLY 1.5	P=0.032N*	P=0.082N	P=0.119N	P=0.023N*	P=0.524N	P=0.120N	P=0.478	P=0.391N
POLY 6	P=0.022N*	P=0.049N*	P=0.064N	P=0.011N*	P=0.505N	P=0.107N	P=0.533	P=0.365N
LOGISTIC REGRESSION	P=0.020N*	P=0.036N*	P=0.072N	P=0.013N*	P=0.504N	P=0.121N	P=0.527	P=0.354N
COCH-ARM / FISHERS	P=0.045N*	P=0.114N	P=0.171N	P=0.039N*	P=0.525N	P=0.125N	P=0.460	P=0.393N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Thyroid Gland: Follicular Cell Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)	0/49 (0%)	1/48 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	4.9%	0.0%	2.2%	2.2%	4.5%	0.0%	2.3%	2.2%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	1/36 (3%)	0/36 (0%)	1/33 (3%)	0/31 (0%)	0/36 (0%)	1/33 (3%)
FIRST INCIDENCE	680	---	729 (T)	622	547	---	723	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.447N	P=0.186N	P=0.401N	P=0.417N	P=0.494N	P=0.251N	P=0.480N	P=0.505N
POLY 3	P=0.499N	P=0.216N	P=0.459N	P=0.459N	P=0.497N	P=0.244N	P=0.509N	P=0.502N
POLY 1.5	P=0.498N	P=0.224N	P=0.475N	P=0.474N	P=0.498N	P=0.244N	P=0.513N	P=0.503N
POLY 6	P=0.501N	P=0.206N	P=0.439N	P=0.442N	P=0.494N	P=0.245N	P=0.502N	P=0.499N
LOGISTIC REGRESSION	P=0.522N	P=0.234N	P=0.475N	P=0.542N	P=0.498N	P=0.216N	P=0.513N	P=0.491N
COCH-ARM / FISHERS	P=0.500N	P=0.247N	P=0.500N	P=0.500N	P=0.499N	P=0.253N	P=0.515N	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Uterus Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)					4.5%	2.3%	0.0%	0.0%
TERMINAL (d)					1/33 (3%)	1/33 (3%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE					548	730 (T)	---	---
STATISTICAL TESTS								
LIFE TABLE					P=0.099N	P=0.517N	P=0.230N	P=0.242N
POLY 3					P=0.100N	P=0.504N	P=0.236N	P=0.238N
POLY 1.5					P=0.100N	P=0.503N	P=0.237N	P=0.239N
POLY 6					P=0.099N	P=0.504N	P=0.233N	P=0.236N
LOGISTIC REGRESSION					P=0.099N	P=0.491N	P=0.220N	P=0.212N
COCH-ARM / FISHERS					P=0.101N	P=0.500N	P=0.247N	P=0.247N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Uterus Polyp Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					7/50 (14%)	3/50 (6%)	8/50 (16%)	7/50 (14%)
POLY-3 ADJUSTED (b)					15.8%	6.5%	17.6%	15.7%
TERMINAL (d)					7/33 (21%)	0/31 (0%)	6/36 (17%)	6/33 (18%)
FIRST INCIDENCE					730 (T)	332	626	680
STATISTICAL TESTS								
LIFE TABLE					P=0.397	P=0.180N	P=0.569	P=0.610N
POLY 3					P=0.364	P=0.138N	P=0.525	P=0.605N
POLY 1.5					P=0.364	P=0.147N	P=0.511	P=0.612N
POLY 6					P=0.371	P=0.130N	P=0.549	P=0.591N
LOGISTIC REGRESSION					P=0.373	P=0.137N	P=0.535	P=0.583N
COCH-ARM / FISHERS					P=0.372	P=0.159N	P=0.500	P=0.613N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Uterus Sarcoma Stromal or Polyp Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					7/50 (14%)	3/50 (6%)	9/50 (18%)	7/50 (14%)
POLY-3 ADJUSTED (b)					15.8%	6.5%	19.8%	15.7%
TERMINAL (d)					7/33 (21%)	0/31 (0%)	7/36 (19%)	6/33 (18%)
FIRST INCIDENCE					730 (T)	332	626	680
STATISTICAL TESTS								
LIFE TABLE					P=0.386	P=0.180N	P=0.463	P=0.610N
POLY 3					P=0.352	P=0.138N	P=0.417	P=0.605N
POLY 1.5					P=0.352	P=0.147N	P=0.404	P=0.612N
POLY 6					P=0.360	P=0.130N	P=0.441	P=0.591N
LOGISTIC REGRESSION					P=0.361	P=0.137N	P=0.428	P=0.583N
COCH-ARM / FISHERS					P=0.361	P=0.159N	P=0.393	P=0.613N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Zymbal's Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	2.5%	0.0%	0.0%	4.4%	0.0%	0.0%	2.2%	2.2%
TERMINAL (d)	0/29 (0%)	0/38 (0%)	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	610	---	---	655	---	---	596	474
STATISTICAL TESTS								
LIFE TABLE	P=0.275	P=0.476N	P=0.471N	P=0.569	P=0.235	(e)	P=0.504	P=0.492
POLY 3	P=0.250	P=0.481N	P=0.477N	P=0.540	P=0.243	(e)	P=0.506	P=0.505
POLY 1.5	P=0.249	P=0.488N	P=0.486N	P=0.525	P=0.239	(e)	P=0.503	P=0.502
POLY 6	P=0.250	P=0.471N	P=0.465N	P=0.557	P=0.248	(e)	P=0.511	P=0.509
LOGISTIC REGRESSION	P=0.211	P=0.554N	P=0.568N	P=0.464	P=0.273	(e)	P=0.542	P=0.744
COCH-ARM / FISHERS	P=0.246	P=0.500N	P=0.500N	P=0.500	P=0.236	(e)	P=0.500	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Leukemia: Lymphocytic, Monocytic, Mononuclear, or Undifferentiated								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	17/50 (34%)	12/50 (24%)	7/50 (14%)	3/50 (6%)	15/50 (30%)	10/50 (20%)	1/50 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	37.9%	25.7%	15.0%	6.6%	32.1%	21.9%	2.2%	2.2%
TERMINAL (d)	7/29 (24%)	7/38 (18%)	1/36 (3%)	1/36 (3%)	8/33 (24%)	4/31 (13%)	0/36 (0%)	1/33 (3%)
FIRST INCIDENCE	486	552	620	698	513	616	638	730 (T)
STATISTICAL TESTS								
LIFE TABLE	P<0.001N**	P=0.085N	P=0.008N**	P<0.001N**	P<0.001N**	P=0.215N	P<0.001N**	P<0.001N**
POLY 3	P<0.001N**	P=0.151N	P=0.010N*	P<0.001N**	P<0.001N**	P=0.191N	P<0.001N**	P<0.001N**
POLY 1.5	P<0.001N**	P=0.163N	P=0.012N*	P<0.001N**	P<0.001N**	P=0.188N	P<0.001N**	P<0.001N**
POLY 6	P<0.001N**	P=0.137N	P=0.008N**	P<0.001N**	P<0.001N**	P=0.192N	P<0.001N**	P<0.001N**
LOGISTIC REGRESSION	P<0.001N**	P=0.241N	P=0.030N*	P<0.001N**	P<0.001N**	P=0.174N	P<0.001N**	P<0.001N**
COCH-ARM / FISHERS	P<0.001N**	P=0.189N	P=0.017N*	P<0.001N**	P<0.001N**	P=0.178N	P<0.001N**	P<0.001N**

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Mesothelioma: Benign, Malignant, NOS								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	3/50 (6%)	4/50 (8%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	7.3%	6.6%	8.6%	2.2%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	2/29 (7%)	2/38 (5%)	2/36 (6%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	558	641	593	705	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.193N	P=0.552N	P=0.605	P=0.243N	(e)	(e)	(e)	(e)
POLY-3	P=0.211N	P=0.615N	P=0.569	P=0.267N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.224N	P=0.634N	P=0.541	P=0.281N	(e)	(e)	(e)	(e)
POLY 6	P=0.198N	P=0.589N	P=0.604	P=0.252N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.253N	P=0.656N	P=0.491	P=0.307N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.248N	P=0.661N	P=0.500	P=0.309N	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Mesothelioma: Malignant								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	3/50 (6%)	3/50 (6%)	4/50 (8%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	7.3%	6.6%	8.6%	2.2%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	2/29 (7%)	2/38 (5%)	2/36 (6%)	0/36 (0%)	0/33 (0%)	0/31 (0%)	0/36 (0%)	0/33 (0%)
FIRST INCIDENCE	558	641	593	705	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.193N	P=0.552N	P=0.605	P=0.243N	(e)	(e)	(e)	(e)
POLY 3	P=0.211N	P=0.615N	P=0.569	P=0.267N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.224N	P=0.634N	P=0.541	P=0.281N	(e)	(e)	(e)	(e)
POLY 6	P=0.198N	P=0.589N	P=0.604	P=0.252N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.253N	P=0.656N	P=0.491	P=0.307N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.248N	P=0.661N	P=0.500	P=0.309N	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	47/50 (94%)	48/50 (96%)	49/50 (98%)	49/50 (98%)	42/50 (84%)	42/50 (84%)	46/50 (92%)	42/50 (84%)
POLY-3 ADJUSTED (b)	98.9%	99.0%	99.7%	99.1%	87.5%	84.6%	95.2%	89.4%
TERMINAL (d)	29/29 (100%)	38/38 (100%)	36/36 (100%)	36/36 (100%)	29/33 (88%)	25/31 (81%)	35/36 (97%)	29/33 (88%)
FIRST INCIDENCE	486	481	505	520	511	332	541	624
STATISTICAL TESTS								
LIFE TABLE	P=0.181N	P=0.041N*	P=0.106N	P=0.114N	P=0.469N	P=0.462	P=0.516	P=0.540N
POLY 3	P=0.775	P=0.973	P=0.951	P=0.946	P=0.303	P=0.452N	P=0.140	P=0.517
POLY 1.5	P=0.457	P=0.784	P=0.608	P=0.685	P=0.354	P=0.519N	P=0.142	P=0.533
POLY 6	P=0.995N	P=1.000	P=1.000	P=1.000N	P=0.300	P=0.374N	P=0.156	P=0.549
LOGISTIC REGRESSION	P=0.359N	P=0.794	P=0.995	P=0.536N	P=0.472	P=0.604	P=0.165	P=0.593
COCH-ARM / FISHERS	P=0.199	P=0.500	P=0.309	P=0.309	P=0.500	P=0.607N	P=0.178	P=0.607N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Malignant Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	30/50 (60%)	22/50 (44%)	21/50 (42%)	20/50 (40%)	23/50 (46%)	16/50 (32%)	12/50 (24%)	12/50 (24%)
POLY-3 ADJUSTED (b)	63.1%	45.3%	43.1%	40.6%	47.8%	34.0%	25.1%	25.5%
TERMINAL (d)	14/29 (48%)	13/38 (34%)	10/36 (28%)	8/36 (22%)	13/33 (39%)	7/31 (23%)	5/36 (14%)	5/33 (15%)
FIRST INCIDENCE	400	480	400	520	513	480	337	361
STATISTICAL TESTS								
LIFE TABLE	P=0.028N*	P=0.027N*	P=0.022N*	P=0.018N*	P=0.023N*	P=0.166N	P=0.023N*	P=0.032N*
POLY 3	P=0.029N*	P=0.058N	P=0.036N*	P=0.020N*	P=0.013N*	P=0.121N	P=0.016N*	P=0.018N*
POLY 1.5	P=0.033N*	P=0.064N	P=0.041N*	P=0.023N*	P=0.013N*	P=0.118N	P=0.016N*	P=0.017N*
POLY 6	P=0.026N*	P=0.051N	P=0.031N*	P=0.016N*	P=0.014N*	P=0.122N	P=0.016N*	P=0.018N*
LOGISTIC REGRESSION	P=0.112N	P=0.142N	P=0.116N	P=0.106N	P=0.012N*	P=0.104N	P=0.018N*	P=0.015N*
COCH-ARM / FISHERS	P=0.044N*	P=0.080N	P=0.055N	P=0.036N*	P=0.014N*	P=0.109N	P=0.018N*	P=0.018N*

D 01

Statistical Analysis of Primary Tumors in Rats(FISCHER 344) - SODIUM NITRITE
Terminal Sacrifice at 105 weeks

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
All Organs Malignant and Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	49/50 (98%)	49/50 (98%)	50/50 (100%)	50/50 (100%)	45/50 (90%)	45/50 (90%)	49/50 (98%)	45/50 (90%)
POLY-3 ADJUSTED (b)	99.9%	99.6%	100.0%	100.0%	90.8%	90.0%	98.0%	92.6%
TERMINAL (d)	29/29 (100%)	38/38 (100%)	36/36 (100%)	36/36 (100%)	29/33 (88%)	26/31 (84%)	35/36 (97%)	30/33 (91%)
FIRST INCIDENCE	400	480	400	520	511	332	337	361
STATISTICAL TESTS								
LIFE TABLE	P=0.150N	P=0.033N*	P=0.085N	P=0.091N	P=0.468N	P=0.465	P=0.516	P=0.539N
POLY 3	P=0.998	P=1.000N	P=1.000	P=1.000	P=0.333	P=0.581N	P=0.124	P=0.519
POLY 1.5	P=0.676	P=0.947N	P=1.000	P=1.000	P=0.389	P=0.603N	P=0.113	P=0.559
POLY 6	P=1.000	P=1.000N	P=1.000	P=1.000	P=0.297	P=0.552N	P=0.142	P=0.494
LOGISTIC REGRESSION	P=0.900	P=0.415N	(e)	(e)	P=0.500	P=0.627	P=0.100	P=0.617
COCH-ARM / FISHERS	P=0.236	P=0.753N	P=0.500	P=0.500	P=0.500	P=0.630N	P=0.102	P=0.630N

(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).

D 02

D 03

CHAIRPERSON'S REPORT
PATHOLOGY WORKING GROUP (PWG) REVIEW

THE CHRONIC DOSED-WATER TOXICITY/CARCINOGENICITY STUDY OF SODIUM NITRITE (CAS NO. 7632-00-0) IN B6C3F1 MICE (G003333-C)
CONDUCTED AT BATTELLE

TDMS NUMBER: 88007-06
BATTELLE STUDY NUMBER G003333-C

Date of PWG: December 1, 1998
Site of PWG: National Toxicology Program (NTP/NIEHS), Research Triangle Park, NC
PWG Participants: Mark Butt, DVM (PAI, Chairperson)
James Hailey, DVM (NIEHS)
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Cynthia Shackelford, DVM, MS, PhD (EPL)
John Seely, DVM (Pathco)
Study Pathologist: John Toft, II, DVM, MS (Battelle)
QA Pathologist: Suzanne Botts, DVM, PhD (EPL)

I. INTRODUCTION

Sodium nitrite was recommended for carcinogenicity studies by the FDA in June of 1985 based on its widespread use and potential for human exposure. Doses for the current carcinogenicity study were selected based on the results of repeated-dose and subchronic studies. The in-life phase of this study was conducted by Battelle, Columbus OH.

II. CONFLICT STATEMENT

The PWG Chairperson has had no involvement in the generation or previous evaluation of data in this study. Further, he has no relevant connection with the originating laboratory.

III. CONDUCT OF THE PWG

Before the PWG, the chairperson reviewed the study report prepared by the testing facility, all TDMS generated pathology tables and all documents supplied by the quality assessment pathologist (QAP). Tissues to be examined by the PWG chairperson were those examined by the QAP pathologist as prescribed by the NTP. Subsets of slides were selected by the PWG chairperson for review by the full PWG and are listed later in this report.

IV. BACKGROUND

General

Sodium nitrite is approved by the Food and Drug Administration (FDA) for use as a food additive in meats and canned pet food. It has also been used as a pharmacologic in human and veterinary medicine as a vasodilator, bronchial dilator, intestinal relaxant and as an antidote for cyanide poisoning. Sodium nitrite has two known pharmacologic actions *in vivo*: relaxation of smooth muscle and the conversion of hemoglobin to methemoglobin. The two main health hazards associated with the ingestion of sodium nitrite in drinking water are the induction of methemoglobin (predominantly a problem in infants) and the potential formation of carcinogenic nitrosamines. Previous toxicity studies have established the oral LD50 in mice to be 216 mg/kg and the MTD in drinking water to vary from 1 g/L to 5 g/L depending on the strain of mouse.

Reproductive Toxicity

Sodium nitrite in drinking water had no adverse effect on reproductive parameters in female C57BL/6 mice (0.31 g/kg) but has been associated with maternal anemia and increased incidence of abortion and fetal mortality.

Genetic Toxicity

Sodium nitrite has been shown to be mutagenic in assay systems with *Escherichia coli*, *Saccharomyces cerevisiae*, and *Salmonella typhimurium*. An intraperitoneal dose (20 mg/kg) has been associated with increased sister chromatid exchanges in bone marrow cells of mice. Five hundred mg/kg (orally) causes micronucleus formation in cultures of embryonic hamster cells.

Carcinogenicity

Previous carcinogenicity studies in mice evaluating the effects of sodium nitrite in the drinking water have shown no evidence of a carcinogenic effect. Carcinogenicity/chronic studies with sodium nitrite in rats (feed or drinking water) have produced increased incidences of malignant lymphoma, lymphoreticular tumors, forestomach squamous papillomas, and liver tumors in various strains.

Subchronic Toxicity Study

A subchronic toxicity study utilizing doses of 0, 0.0375, 0.075, 0.15, 0.3, and 0.5% sodium nitrite in the drinking water was previously conducted at Microbiological Associates. In mice, there was no effect on survival, clinical signs or food consumption at any dose level. There was a dose-dependent decrease in water consumption in males and females. Body weights were decreased in male mice at doses $\geq 0.3\%$ and showed a slight reduction in females at 0.5%. Various statistically significant organ weight increases (absolute and/or relative) were present in the spleen, testes and kidney of males at doses of 0.3% and/or 0.5%. In females, increased organ weights (absolute and/or relative) in the heart, spleen, kidney and/or liver were noted in the 0.3% and/or 0.5% dose groups. Minimal squamous epithelial hyperplasia of the forestomach at the limiting ridge was observed in the 0.5% group of both sexes. Increased extramedullary hematopoiesis in males at doses $\geq 0.3\%$ and females at doses $\geq 0.15\%$ was noted. Testicular degeneration was noted in the 0.5% males. None of the microscopic lesions were considered adverse enough to have any effect on survival in a chronic study.

V. CURRENT STUDY

Study Design

Mice (50/sex) were assigned to three treated groups (0.075%, 0.15% and 0.30%) and one untreated group (0%). The test material was provided in the drinking water for the duration of the study. Terminal sacrifices were conducted after 105 weeks of treatment.

Methods

The study pathologist (SP) evaluated all protocol tissues from all mice.

The QAP reviewed the following.
-all diagnoses for the small intestine, lung, stomach forestomach, stomach glandular, kidney (males)
-all diagnoses for the stomach forestomach and lung (females)
-spleen-extramedullary hematopoiesis (males and females)
-liver-necrosis (males) and pigmentation (females)
-mesentery-inflammation and fibrosis (females)
-adrenal cortex, zona glomerulosa-hyperplasia
-skin-fibrosarcoma
-skin-Schwannoma, Malignant
-all tumors from all organs in all animals

Slides from all of these tissues/organs/diagnoses were assembled into the slide set presented for review by the PWG Chairperson. The QAP provided Slide Review Work Sheets to the PWG Chairperson. Those work sheets listed, by CID number order, potential target organs, neoplasms, and nontumor pathology which were examined by the QAP. Entries under reviewing pathologist's comments indicated a disagreement with the study pathologist's diagnosis. Additionally, all data from the Slide Review Work Sheets were provided to the PWG Chairperson electronically on disk. During his review, the PWG Chairperson entered his findings directly into the Pathology Quality Assurance System, PWG Module.

During the PWG Chairperson's review, selected slides were assembled by dot group into a PWG slide set. These slides were then reviewed by the full PWG.

The consensus of the PWG members for each of the selected slides/findings is provided in Appendix I to this report.

Results

Survival

Survival in the treated groups was similar to the control group for both sexes.

Clinical Signs

There were no clinical signs interpreted to be related to sodium nitrite.

Body Weights
There was a slight, transient decrease of body weight in the high dose males and females which was resolved by study termination.

Water Consumption
There was a dose related decrease of water consumption in all treated male and female groups. Exposure index data showed an increase in exposure to sodium nitrite proportional to the increase in the dosed-water concentration. At each dose level, males had a 1.5 to 1.6 times higher exposure level as compared to females.

Toxicokinetics
Plasma nitrite and blood methemoglobin concentrations were determined at 12 months. Plasma nitrite levels were slightly elevated in the 0.15% and 0.30% males but below the limit of quantitation for all female groups and the control and 0.075% males. Methemoglobin concentrations were similar in all female dose groups (including controls) but elevated (at the earliest time point) in the high dose males.

Gross Lesions
There was a treatment related increase of forestomach nodules in high dose females (see Table 1). There were no gross changes indicating increased methemoglobin levels in the treated mice.

Table 1. Test Material Related Gross Lesions

Macroscopic Observations								
	Male				Female			
Dose (Percent)	0.0	0.075	0.15	0.30	0.0	0.075	0.15	0.30
Number Examined	50	50	50	50	50	50	50	50
Forestomach Nodule	2	1	1	1	2	1	2	5

Microscopic Lesions (determined by PWG Chairperson and PWG review)
Forestomach
An increased incidence of squamous cell papillomas of the forestomach was noted by the SP and QAP for the high dose females. All proliferative lesions in the forestomach of female mice were reviewed by the entire PWG.

PWG review confirmed the increase of forestomach papillomas in the high dose females and also revealed an increased incidence of squamous cell carcinoma and forestomach epithelium hyperplasia in the high dose females.

Glandular Stomach
An increased incidence of hyperplasia of the glandular stomach epithelium was noted by the SP and QAP in the high dose males. PWG review confirmed this increase, agreeing with the QAP that two of the mid dose males also had "Glandular Stomach Epithelium, Hyperplasia" (and diagnosing an additional high dose male with the same lesion).

The glandular epithelium hyperplasia noted in the high and mid dose males was consistently focally extensive and characterized by a distorted and irregular arrangement of the glandular elements of the gastric mucosa. Typically, the proportion of the gastric glands comprised by mucus secreting cells was reduced from about 50% in the normal areas to 25% in the hyperplastic areas. The parietal cells in the mid portion of the gastric glands were less distinct in the hyperplastic areas. Instead of large, cuboidal cells with eosinophilic cytoplasm (characteristic of normal parietal cells), the parietal cell area tended to be composed of smaller, elongated, basophilic cells with vesiculated, fusiform nuclei and relatively scant cytoplasm. The mitotic rate among these cells often averaged 2 to 3 per 40X field. The base of the gastric glands, populated by basophilic chief cells with basal nuclei and abundant secretory granules in the apical cytoplasm in the normal areas, was largely populated by fewer and smaller chief cells intermixed with normal appearing parietal cells. The PWG agreed that there was no evidence of neoplastic lesions in the glandular stomach.

Small Intestine, Jejunum

There was an unusual increased incidence of carcinomas in the small intestine of the control males (Intestine Small Jejunum - Carcinoma, 5/50; 10%) noted by the QAP. This increased incidence was confirmed by the PWG chairperson. NTP data for dosed water studies in B6C3F$_1$ mice indicate an incidence among control males of 0.595% (2/340 animals) for this lesion. An explanation for this increase was not apparent but no relationship to the test material was considered since the increase was highest in the control group. The slides of these lesions were pulled for review by the NTP study pathologist but were not reviewed by the entire PWG since this was not a treatment related effect. All primary intestinal carcinomas were traceable gross lesions.

Lung

The PWG reviewed a sample of proliferative lung lesions for which there was agreement between the SP and QAP and also all proliferative lung lesions for which there was a disagreement between the SP and QAP. PWG review confirmed the increased incidence of proliferative lung lesions in the mid and high dose males and high dose females, noting that only "Alveolar Epithelium, Hyperplasia" was increased in males (mid and high dose) and only "Alveolar/Bronchiolar Adenoma" and "Alveolar Epithelium, Hyperplasia" were increased in females.

NTP incidence data for dosed water studies in B6C3F$_1$ mice indicate an incidence range of "Alveolar/Bronchiolar Adenoma" for control females to be 3% (2/59) to 8% (4/50) with an overall average (6 studies) of 5.9%. The incidence of "Alveolar/Bronchiolar Adenoma" of 5/50 (10%) in the high dose females in this study was thus above the control reference range. Additionally, the incidence in the control females was below the reference range.

Subcutaneous Tissue - Fibrosarcoma

An unusual incidence of "Fibrosarcoma" was diagnosed in the subcutaneous tissue of the low dose females with fewer occurring in the mid and high dose females. These diagnoses were confirmed by PWG review. (A fibrosarcoma diagnosed in the pinna of a single high dose female was determined to be a fibroma by the PWG.) The cause of this increased incidence of

fibrosarcomas was not precisely determined. The PWG did not consider the unusual incidence of fibrosarcomas to be related to the test material because of the lack of any semblance of a dose response. The fibrosarcomas were generally microscopic correlates to gross lesions at various locations of the body.

Mesentery Fat - Necrosis

Both the SP and QAP noted an apparent increased incidence of "Fibrosis" and "Inflammation, Chronic Active" in the mesentery of females. The PWG chairperson noted that these lesions were nearly always associated with mesenteric fat necrosis and that "Fibrosis", "Inflammation, Chronic Active", "Mineralization" and "Pigment" were inconsistently diagnosed in conjunction with the fat necrosis. The PWG reviewed and discussed the issue and determined that the proper diagnosis should be "Mesentery, Fat - Necrosis" alone without splitting the lesion out into its various associated components such as inflammation, fibrosis, mineralization and pigment. Thus, for all animals for which a diagnosis of "Mesentery, Fat - Necrosis" was made by the SP/QAP and confirmed by the PWG Chairperson, the associated diagnoses of "Inflammation, Chronic Active", "Fibrosis", "Mineralization" and "Pigment" were deleted. "Mesentery, Fat - Necrosis" was not considered to be treatment related.

Adrenal Cortex - Hyperplasia

The SP frequently diagnosed two lesions in the adrenal gland: "Adrenal Cortex, Capsule - Hyperplasia"; and "Adrenal Cortex, Zona Glomerulosa - Hyperplasia". This issue was discussed at the PWG. In the opinion of the QAP, PWG Chairperson and PWG, both these lesions represented components of adrenal cortical hyperplasia and felt that it was appropriate to diagnose only "Adrenal Cortex, Capsule - Hyperplasia". Thus, the diagnosis of "Adrenal Cortex, Zona Glomerulosa - Hyperplasia" was deleted.

Kidney, Renal Tubule - Hyperplasia

In male mice, there was an increased incidence of renal tubule hyperplasia diagnosed in the high dose animals. In the opinion of the QAP, these hyperplasias were a component of nephropathy. The PWG reviewed the renal tubule hyperplasia from the four high dose males. The PWG agreed with the QAP that in general, the hyperplasia was minimal and a component of nephropathy; consequently, it was the consensus of the PWG that for 3/4 of the high dose animals, the diagnosis of renal tubule hyperplasia was deleted. For the other male, it was the consensus of the PWG that the correct diagnosis was renal tubule hypertrophy, mild, focal. This change was made to the raw data.

Spleen - Extramedullary Hematopoiesis

Extramedullary hematopoiesis in the spleen was specifically evaluated by the QAP and the PWG chairperson. The incidence of this change was found to be approximately equal across all dose groups.

Liver - Necrosis and Pigment

There was a decreased incidence of necrosis in the liver of the high dose males as compared to the control animals. The reason for this difference was not apparent but was confirmed by the PWG chairperson. Pigmentation in the liver of female mice was slightly increased in the high dose

group as compared to controls. The PWG chairperson confirmed the observation of the QAP that the pigmentation was generally related to small areas of inflammation of a chronic nature. The PWG chairperson observed that the pigment was consistent with lipofuscin and did not consider the slightly increased incidence of pigment in the liver to have any relationship to the test material.

Mark T. Butt

Mark T. Butt, DVM
Diplomate, American College of Veterinary Pathologists
PWG Chairperson

3/25/99

Date

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
SODIUM NITRITE

2 YEAR CHRONIC MICE

Facility: Battelle Columbus Laboratory

Chemical CAS #: 7632-00-0

Lock Date: 03/20/98

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

D11

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
SODIUM NITRITE

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	1	7	2	4
Natural Death	9	9	11	5
Survivors				
Terminal Sacrifice	40	34	37	41
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Gallbladder	(48)	(50)	(50)	(49)
Cyst	1 (2%)	1 (2%)		
Infiltration Cellular, Mononuclear Cell		3 (6%)	1 (2%)	4 (8%)
Epithelium, Cytoplasmic Alteration		1 (2%)		
Epithelium, Hyperplasia		1 (2%)		
Intestine Small, Duodenum	(50)	(48)	(50)	(49)
Epithelium, Inflammation, Chronic Active	1 (2%)			
Epithelium, Ulcer	1 (2%)			
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Necrosis	1 (2%)			
Peyer's Patch, Hyperplasia, Lymphoid				1 (2%)
Intestine Small, Ileum	(49)	(49)	(50)	(50)
Inflammation, Chronic Active				1 (2%)
Liver	(50)	(50)	(50)	(50)
Angiectasis				2 (4%)
Basophilic Focus	3 (6%)	4 (8%)	3 (6%)	1 (2%)
Clear Cell Focus	2 (4%)	3 (6%)	3 (6%)	2 (4%)
Congestion				1 (2%)
Eosinophilic Focus	7 (14%)	3 (6%)	4 (8%)	5 (10%)
Hematopoietic Cell Proliferation	2 (4%)	5 (10%)	3 (6%)	4 (8%)
Hemorrhage	1 (2%)			
Infiltration Cellular, Mononuclear Cell	30 (60%)	32 (64%)	29 (58%)	35 (70%)
Inflammation, Chronic Active	36 (72%)	35 (70%)	30 (60%)	35 (70%)
Mineralization	1 (2%)	1 (2%)	1 (2%)	
Mixed Cell Focus	3 (6%)	1 (2%)		
Necrosis	5 (10%)	4 (8%)	3 (6%)	2 (4%)
Pigmentation	12 (24%)	17 (34%)	16 (32%)	18 (36%)
Thrombosis		1 (2%)		
Vacuolization Cytoplasmic	10 (20%)	17 (34%)	12 (24%)	13 (26%)
Bile Duct, Cyst			1 (2%)	
Bile Duct, Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Centrilobular, Necrosis				2 (4%)
Centrilobular, Vacuolization Cytoplasmic				1 (2%)
Hepatocyte, Centrilobular, Hypertrophy	1 (2%)			

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

D 12

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - CONT				
Mesentery	(14)	(19)	(17)	(13)
Congestion		1 (5%)		
Hemorrhage			1 (6%)	
Infiltration Cellular, Mononuclear Cell				1 (8%)
Inflammation, Chronic Active		1 (5%)		
Inflammation, Granulomatous	1 (7%)			
Pigmentation, Hemosiderin			1 (6%)	
Thrombosis		1 (5%)		
Artery, Inflammation, Chronic Active				1 (8%)
Fat, Necrosis	10 (71%)	7 (37%)	10 (59%)	11 (85%)
Oral Mucosa	(1)		(2)	(3)
Gingival, Foreign Body	1 (100%)		2 (100%)	3 (100%)
Gingival, Inflammation, Chronic Active	1 (100%)		2 (100%)	2 (67%)
Pancreas	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	14 (28%)	10 (20%)	7 (14%)	13 (26%)
Inflammation, Chronic Active		1 (2%)		
Acinus, Atrophy	1 (2%)			1 (2%)
Acinus, Hyperplasia			1 (2%)	
Acinus, Hypertrophy				1 (2%)
Artery, Inflammation, Chronic Active			1 (2%)	1 (2%)
Duct, Cyst	1 (2%)	1 (2%)		
Salivary Glands	(49)	(49)	(48)	(50)
Atrophy				2 (4%)
Infiltration Cellular, Mononuclear Cell	34 (69%)	36 (73%)	40 (83%)	35 (70%)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell		1 (2%)		
Ulcer	1 (2%)	2 (4%)	2 (4%)	
Epithelium, Hyperkeratosis				1 (2%)
Epithelium, Hyperplasia	2 (4%)	3 (6%)	3 (6%)	6 (12%)
Epithelium, Inflammation, Chronic Active	2 (4%)	3 (6%)	3 (6%)	1 (2%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Mineralization	1 (2%)			
Epithelium, Hyperplasia			1 (2%)	1 (2%)
Epithelium, Necrosis			1 (2%)	
Glands, Ectasia	19 (38%)	16 (32%)	10 (20%)	21 (42%)
Glands, Necrosis			1 (2%)	
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell			1 (2%)	
Aorta, Inflammation, Chronic Active				1 (2%)
Aorta, Mineralization	2 (4%)			
Pulmonary Artery, Mineralization	1 (2%)			
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy		1 (2%)		

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

D13

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
CARDIOVASCULAR SYSTEM - CONT				
Infiltration Cellular, Mononuclear Cell	1 (2%)			
Inflammation, Chronic Active		1 (2%)	1 (2%)	
Mineralization	1 (2%)	2 (4%)		1 (2%)
Artery, Inflammation, Chronic Active				1 (2%)
Artery, Mineralization		1 (2%)		
Valve, Inflammation, Chronic Active	2 (4%)			
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(49)	(50)
Accessory Adrenal Cortical Nodule	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Degeneration, Fatty			1 (2%)	2 (4%)
Hematopoietic Cell Proliferation	1 (2%)	2 (4%)		2 (4%)
Inflammation, Chronic Active		1 (2%)		
Capsule, Hyperplasia	49 (98%)	50 (100%)	49 (100%)	49 (98%)
Zona Fasciculata, Hyperplasia			1 (2%)	1 (2%)
Zona Fasciculata, Hypertrophy	1 (2%)	1 (2%)		
Zona Glomerulosa, Hyperplasia		1 (2%)		1 (2%)
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	45 (90%)	44 (88%)	40 (80%)	42 (84%)
Pigmentation			1 (2%)	
Parathyroid Gland	(33)	(32)	(31)	(37)
Cyst			1 (3%)	
Pituitary Gland	(48)	(47)	(43)	(48)
Pars Distalis, Angiectasis	1 (2%)	3 (6%)		3 (6%)
Pars Distalis, Cyst			2 (5%)	2 (4%)
Pars Distalis, Hyperplasia	2 (4%)	3 (6%)	4 (9%)	6 (13%)
Thyroid Gland	(49)	(49)	(48)	(49)
Inflammation, Chronic Active	2 (4%)	1 (2%)		1 (2%)
Follicle, Cyst		2 (4%)		1 (2%)
Follicular Cell, Hyperplasia			1 (2%)	
GENERAL BODY SYSTEM				
Peritoneum		(1)		(1)
Inflammation, Granulomatous				1 (100%)
GENITAL SYSTEM				
Clitoral Gland	(50)	(49)	(50)	(48)
Infiltration Cellular, Mononuclear Cell	7 (14%)	4 (8%)	13 (26%)	3 (6%)
Inflammation, Chronic Active	1 (2%)			1 (2%)
Inflammation, Suppurative		2 (4%)	2 (4%)	
Duct, Cyst	1 (2%)			

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

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
GENITAL SYSTEM - CONT				
Ovary	(47)	(49)	(50)	(49)
Angiectasis				1 (2%)
Cyst	6 (13%)	9 (18%)	9 (18%)	7 (14%)
Hemorrhage	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Hyperplasia, Adenomatous		1 (2%)		
Mineralization	3 (6%)			1 (2%)
Pigmentation				1 (2%)
Thrombosis	2 (4%)		1 (2%)	1 (2%)
Uterus	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)		
Hydrometra	32 (64%)	31 (62%)	33 (66%)	37 (74%)
Infiltration Cellular, Mononuclear Cell	2 (4%)			
Inflammation, Suppurative	1 (2%)		2 (4%)	
Endometrium, Hyperplasia, Cystic	13 (26%)	10 (20%)	16 (32%)	18 (36%)
Submucosa, Hyperplasia, Stromal			1 (2%)	
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Atrophy				2 (4%)
Hyperplasia				1 (2%)
Myelofibrosis			2 (4%)	
Myeloid Cell, Hyperplasia	2 (4%)	3 (6%)	1 (2%)	3 (6%)
Lymph Node	(7)	(7)	(8)	(4)
Inflammation, Granulomatous				1 (25%)
Inguinal, Hyperplasia, Lymphoid			1 (13%)	
Lumbar, Hyperplasia, Lymphoid				1 (25%)
Mediastinal, Hematopoietic Cell Proliferation				1 (25%)
Mediastinal, Hyperplasia, Lymphoid			3 (38%)	1 (25%)
Mediastinal, Pigmentation, Hemosiderin		1 (14%)		
Renal, Ectasia	1 (14%)		1 (13%)	
Renal, Hemorrhage	1 (14%)		1 (13%)	
Lymph Node, Mandibular	(47)	(46)	(48)	(48)
Hematopoietic Cell Proliferation				1 (2%)
Hyperplasia, Lymphoid	1 (2%)		5 (10%)	5 (10%)
Hyperplasia, Plasma Cell		1 (2%)	1 (2%)	
Lymph Node, Mesenteric	(50)	(49)	(47)	(49)
Ectasia	1 (2%)	1 (2%)	2 (4%)	
Fibrosis			1 (2%)	
Hematopoietic Cell Proliferation				1 (2%)
Hyperplasia, Lymphoid		1 (2%)	2 (4%)	
Inflammation, Granulomatous				1 (2%)
Spleen	(49)	(50)	(50)	(50)
Hematopoietic Cell Proliferation	37 (76%)	39 (78%)	35 (70%)	39 (78%)
Hyperplasia, Lymphoid	4 (8%)	3 (6%)	4 (8%)	1 (2%)
Metaplasia, Osseous		1 (2%)		

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

E 01

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
HEMATOPOIETIC SYSTEM - CONT				
Capsule, Inflammation, Chronic Active				1 (2%)
Thymus	(46)	(47)	(44)	(46)
Cyst	10 (22%)	12 (26%)	17 (39%)	16 (35%)
Ectopic Parathyroid Gland	1 (2%)	5 (11%)	3 (7%)	2 (4%)
Hyperplasia, Lymphoid			1 (2%)	
INTEGUMENTARY SYSTEM				
Mammary Gland	(49)	(50)	(49)	(50)
Hyperplasia, Cystic	1 (2%)	3 (6%)		1 (2%)
Skin	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)	3 (6%)	2 (4%)	
Ulcer	1 (2%)	1 (2%)	1 (2%)	
Epidermis, Hyperplasia		1 (2%)	1 (2%)	
Subcutaneous Tissue, Fibrosis	2 (4%)			
Subcutaneous Tissue, Infiltration Cellular, Mononuclear Cell				2 (4%)
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Periosteum, Synovial Tissue, Inflammation, Chronic Active				1 (2%)
Skeletal Muscle	(3)	(2)	(1)	(3)
Artery, Inflammation, Chronic Active				1 (33%)
NERVOUS SYSTEM				
Brain	(50)	(50)	(49)	(50)
Degeneration	1 (2%)			
Hemorrhage	1 (2%)	1 (2%)		
Peripheral Nerve				(2)
Sciatic, Inflammation, Chronic Active				1 (50%)
Spinal Cord				(2)
Demyelination				2 (100%)
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Hemorrhage			1 (2%)	
Infiltration Cellular, Mononuclear Cell	1 (2%)	2 (4%)		1 (2%)
Inflammation, Chronic Active	2 (4%)	3 (6%)	2 (4%)	
Metaplasia, Osseous				1 (2%)

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

E 02

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
RESPIRATORY SYSTEM - CONT				
Mineralization		1 (2%)	1 (2%)	
Alveolar Epithelium, Hyperplasia		1 (2%)	4 (8%)	3 (6%)
Alveolus, Infiltration Cellular, Histiocyte		3 (6%)	2 (4%)	2 (4%)
Bronchus, Mineralization	1 (2%)			
Interstitium, Inflammation, Chronic Active				1 (2%)
Vein, Mineralization	1 (2%)	1 (2%)	1 (2%)	
Nose	(50)	(49)	(50)	(50)
Foreign Body			1 (2%)	
Inflammation, Chronic Active			1 (2%)	
Nasolacrimal Duct, Inflammation, Suppurative		1 (2%)	1 (2%)	1 (2%)
SPECIAL SENSES SYSTEM				
Eye			(1)	
Cataract			1 (100%)	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Accumulation, Hyaline Droplet		1 (2%)		
Infarct	2 (4%)	4 (8%)	3 (6%)	6 (12%)
Infiltration Cellular, Mononuclear Cell	35 (70%)	37 (74%)	34 (68%)	40 (80%)
Infiltration Cellular, Plasma Cell				1 (2%)
Inflammation, Suppurative	1 (2%)			
Mineralization	5 (10%)	8 (16%)	6 (12%)	4 (8%)
Nephropathy	20 (40%)	17 (34%)	13 (26%)	20 (40%)
Cortex, Cyst				1 (2%)
Vein, Inflammation, Chronic Active				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	25 (50%)	29 (58%)	24 (48%)	25 (50%)
Inflammation, Chronic Active	1 (2%)			1 (2%)
Mineralization	1 (2%)			

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

E 03

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
SODIUM NITRITE

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	3	2	3	1
Natural Death	8	3	5	10
Survivors				
Terminal Sacrifice	39	45	42	39
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Gallbladder	(50)	(50)	(49)	(49)
Cyst	1 (2%)			
Intestine Small, Duodenum	(49)	(50)	(48)	(49)
Ectasia		2 (4%)		2 (4%)
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Inflammation, Chronic Active			1 (2%)	
Intussusception			1 (2%)	
Peyer's Patch, Hyperplasia, Lymphoid		2 (4%)		
Peyer's Patch, Inflammation, Granulomatous				1 (2%)
Intestine Small, Ileum	(50)	(49)	(50)	(50)
Parasite Metazoan			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Basophilic Focus	3 (6%)	3 (6%)		1 (2%)
Clear Cell Focus	4 (8%)	6 (12%)	10 (20%)	7 (14%)
Eosinophilic Focus	12 (24%)	14 (28%)	14 (28%)	7 (14%)
Fibrosis	1 (2%)			
Hematopoietic Cell Proliferation			1 (2%)	1 (2%)
Infarct	2 (4%)			
Infiltration Cellular, Mononuclear Cell	2 (4%)		3 (6%)	1 (2%)
Inflammation, Chronic Active	25 (50%)	25 (50%)	31 (62%)	19 (38%)
Mineralization	1 (2%)	1 (2%)		2 (4%)
Mixed Cell Focus	6 (12%)	2 (4%)	7 (14%)	9 (18%)
Necrosis	12 (24%)	4 (8%)	6 (12%)	2 (4%)
Pigmentation	2 (4%)		2 (4%)	1 (2%)
Vacuolization Cytoplasmic	3 (6%)		3 (6%)	1 (2%)
Bile Duct, Cyst				1 (2%)
Bile Duct, Hyperplasia	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Hepatocyte, Karyomegaly			1 (2%)	
Mesentery	(7)	(6)	(7)	(5)
Infiltration Cellular, Mononuclear Cell	2 (29%)			
Inflammation, Granulomatous	2 (29%)		2 (29%)	
Mineralization	1 (14%)	1 (17%)		
Pigmentation		1 (17%)	1 (14%)	
Artery, Inflammation, Chronic Active		1 (17%)		

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

E 04

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - CONT				
Fat, Necrosis	4 (57%)	4 (67%)	3 (43%)	2 (40%)
Oral Mucosa	(26)	(27)	(17)	(19)
Gingival, Foreign Body	26 (100%)	27 (100%)	17 (100%)	19 (100%)
Gingival, Inflammation, Chronic Active	21 (81%)	22 (81%)	14 (82%)	11 (58%)
Pancreas	(49)	(50)	(50)	(50)
Fibrosis	1 (2%)			
Infiltration Cellular, Mononuclear Cell	2 (4%)	2 (4%)	3 (6%)	2 (4%)
Inflammation, Chronic Active	1 (2%)			
Acinus, Atrophy	1 (2%)	1 (2%)		
Acinus, Hypertrophy			1 (2%)	
Artery, Inflammation, Chronic Active		1 (2%)		
Salivary Glands	(50)	(50)	(50)	(50)
Atrophy	1 (2%)			
Infiltration Cellular, Mononuclear Cell	27 (54%)	28 (56%)	33 (66%)	32 (64%)
Mineralization	1 (2%)			1 (2%)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Ulcer	3 (6%)		1 (2%)	1 (2%)
Epithelium, Hyperplasia	6 (12%)	1 (2%)	2 (4%)	3 (6%)
Epithelium, Inflammation, Chronic Active	2 (4%)		2 (4%)	1 (2%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Mineralization			1 (2%)	
Epithelium, Erosion			1 (2%)	
Epithelium, Hyperplasia			2 (4%)	10 (20%)
Epithelium, Necrosis				1 (2%)
Glands, Ectasia	12 (24%)	18 (36%)	16 (32%)	14 (28%)
Tooth	(5)	(5)	(4)	(1)
Malformation	5 (100%)	4 (80%)	3 (75%)	1 (100%)
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(50)	(50)	(50)
Aorta, Inflammation, Chronic Active		1 (2%)		
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy				1 (2%)
Inflammation, Chronic Active		1 (2%)		
Mineralization	3 (6%)		1 (2%)	
Artery, Inflammation, Chronic Active		2 (4%)		
Atrium, Thrombosis	1 (2%)			
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule	2 (4%)		6 (12%)	4 (8%)
Degeneration, Fatty	1 (2%)		1 (2%)	
Pigmentation		1 (2%)		

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

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
ENDOCRINE SYSTEM - CONT				
Capsule, Hyperplasia	46 (92%)	42 (84%)	40 (80%)	40 (80%)
Zona Fasciculata, Hyperplasia		1 (2%)		1 (2%)
Zona Fasciculata, Hypertrophy	18 (36%)	24 (48%)	14 (28%)	21 (42%)
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia		1 (2%)		
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	46 (92%)	47 (94%)	49 (98%)	44 (88%)
Parathyroid Gland	(36)	(48)	(38)	(41)
Cyst			1 (3%)	
Pituitary Gland	(49)	(49)	(47)	(47)
Pars Distalis, Cyst	3 (6%)	2 (4%)	2 (4%)	4 (9%)
Pars Distalis, Hyperplasia		1 (2%)		
Thyroid Gland	(50)	(50)	(50)	(50)
Inflammation, Chronic Active		1 (2%)		
Follicle, Cyst	4 (8%)	1 (2%)	1 (2%)	2 (4%)
Follicular Cell, Hyperplasia		1 (2%)		
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Coagulating Gland		(1)		
Inflammation, Chronic Active		1 (100%)		
Epididymis	(50)	(50)	(50)	(50)
Granuloma Sperm	1 (2%)	1 (2%)		1 (2%)
Infiltration Cellular, Mononuclear Cell	21 (42%)	22 (44%)	25 (50%)	25 (50%)
Infiltration Cellular, Mixed Cell				1 (2%)
Inflammation, Chronic Active			1 (2%)	
Preputial Gland	(50)	(50)	(49)	(50)
Atrophy	1 (2%)		1 (2%)	
Infiltration Cellular, Mononuclear Cell	27 (54%)	28 (56%)	29 (59%)	25 (50%)
Inflammation, Chronic Active	7 (14%)	8 (16%)	4 (8%)	4 (8%)
Inflammation, Suppurative			2 (4%)	
Duct, Cyst	33 (66%)	32 (64%)	33 (67%)	39 (78%)
Prostate	(50)	(50)	(49)	(50)
Infiltration Cellular, Mononuclear Cell	15 (30%)	22 (44%)	29 (59%)	28 (56%)
Inflammation, Chronic Active	1 (2%)	2 (4%)	3 (6%)	
Inflammation, Suppurative	1 (2%)		1 (2%)	
Artery, Inflammation, Chronic Active		2 (4%)		
Seminal Vesicle	(50)	(50)	(50)	(50)
Congestion				1 (2%)
Dilatation	2 (4%)	2 (4%)		
Infiltration Cellular, Mononuclear Cell		1 (2%)	1 (2%)	1 (2%)

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

E 06

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
GENITAL SYSTEM - CONT				
Inflammation, Chronic Active	2 (4%)			
Inflammation, Suppurative			1 (2%)	
Bilateral, Dilatation	1 (2%)	1 (2%)	1 (2%)	
Testes	(50)	(50)	(50)	(50)
Mineralization				2 (4%)
Germinal Epithelium, Atrophy		1 (2%)		1 (2%)
Germinal Epithelium, Necrosis			1 (2%)	
Interstitial Cell, Hyperplasia			2 (4%)	
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(49)	(50)
Hemorrhage			1 (2%)	
Thrombosis			1 (2%)	
Myeloid Cell, Hyperplasia			1 (2%)	2 (4%)
Lymph Node	(1)	(1)	(3)	(5)
Lumbar, Hyperplasia, Plasma Cell			1 (33%)	
Mediastinal, Hemorrhage				1 (20%)
Mediastinal, Inflammation, Granulomatous				1 (20%)
Renal, Hyperplasia, Lymphoid		1 (100%)		
Renal, Hyperplasia, Plasma Cell			1 (33%)	
Lymph Node, Mandibular	(47)	(50)	(47)	(48)
Hyperplasia, Lymphoid	2 (4%)	1 (2%)	1 (2%)	
Lymph Node, Mesenteric	(49)	(49)	(48)	(49)
Ectasia		1 (2%)		
Hematopoietic Cell Proliferation				1 (2%)
Hyperplasia, Plasma Cell		2 (4%)	1 (2%)	
Hyperplasia, Lymphocyte	1 (2%)		1 (2%)	
Infiltration Cellular, Eosinophil		1 (2%)		
Inflammation, Chronic Active				1 (2%)
Inflammation, Granulomatous			1 (2%)	2 (4%)
Spleen	(50)	(50)	(50)	(50)
Hematopoietic Cell Proliferation	22 (44%)	11 (22%)	14 (28%)	20 (40%)
Hyperplasia, Lymphoid	1 (2%)		1 (2%)	
Thymus	(37)	(39)	(38)	(42)
Cyst	9 (24%)	14 (36%)	16 2%)	9 (21%)
Hemorrhage	1 (3%)			
Inflammation, Granulomatous	1 (3%)			
Necrosis	1 (3%)			

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

E 07

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
SODIUM NITRITE

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
INTEGUMENTARY SYSTEM				
Skin	(50)	(50)	(50)	(50)
Cyst Epithelial Inclusion	1 (2%)			
Inflammation, Chronic Active	4 (8%)	1 (2%)	1 (2%)	2 (4%)
Ulcer	3 (6%)	1 (2%)	1 (2%)	2 (4%)
Epidermis, Hyperplasia	2 (4%)	1 (2%)	1 (2%)	
Subcutaneous Tissue, Infiltration Cellular, Mononuclear Cell			1 (2%)	
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(49)	(50)
Cranium, Hyperostosis	1 (2%)			
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Neuron, Necrosis	2 (4%)			
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Inflammation, Chronic	1 (2%)			
Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	
Mineralization	4 (8%)		3 (6%)	
Necrosis				2 (4%)
Alveolar Epithelium, Hyperplasia	3 (6%)	2 (4%)	6 (12%)	9 (18%)
Alveolus, Infiltration Cellular, Histiocyte	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Interstitium, Inflammation, Chronic Active			1 (2%)	
Mediastinum, Inflammation, Chronic Active		1 (2%)		
Mediastinum, Inflammation, Suppurative			1 (2%)	
Mediastinum, Pigmentation		1 (2%)		
Nose	(50)	(50)	(49)	(50)
Foreign Body	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Inflammation, Suppurative	1 (2%)		1 (2%)	
Nasolacrimal Duct, Inflammation, Suppurative		1 (2%)		

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

E 08

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
SPECIAL SENSES SYSTEM				
Eye	(1)			
Atrophy	1 (100%)			
Harderian Gland	(5)	(4)	(6)	(1)
Hyperplasia		1 (25%)		
Inflammation, Chronic		1 (25%)		
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Hydronephrosis			1 (2%)	1 (2%)
Infarct	11 (22%)	10 (20%)	9 (18%)	13 (26%)
Infiltration Cellular, Mononuclear Cell	42 (84%)	41 (82%)	41 (82%)	45 (90%)
Infiltration Cellular, Plasma Cell			1 (2%)	
Inflammation, Chronic Active	2 (4%)	1 (2%)		1 (2%)
Inflammation, Suppurative	1 (2%)		1 (2%)	
Metaplasia, Osseous	2 (4%)	3 (6%)		
Mineralization	48 (96%)	50 (100%)	48 (96%)	46 (92%)
Necrosis	1 (2%)	1 (2%)		
Nephropathy	44 (88%)	49 (98%)	45 (90%)	42 (84%)
Pigmentation	1 (2%)			
Artery, Inflammation, Chronic Active		2 (4%)	1 (2%)	
Cortex, Cyst	5 (10%)	9 (18%)	6 (12%)	4 (8%)
Renal Tubule, Hypertrophy, Focal				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(49)
Infiltration Cellular, Mononuclear Cell	6 (12%)	7 (14%)	16 (32%)	10 (20%)
Inflammation, Suppurative		1 (2%)		

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

E2 09

END OF REPORT

2 YEAR CHRONIC MICE

Facility: Battelle Columbus Laboratory

Chemical CAS #: 7632-00-0

Lock Date: 03/20/98

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

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	1	7	2	4
Natural Death	9	9	11	5
Survivors				
Terminal Sacrifice	40	34	37	41
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Gallbladder	(48)	(50)	(50)	(49)
Intestine Large, Rectum	(49)	(50)	(50)	(50)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Intestine Small, Ileum	(49)	(49)	(50)	(50)
Leiomyosarcoma, Metastatic, Uterus			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Carcinoma, Metastatic, Islets, Pancreatic		1 (2%)		
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Hemangiosarcoma			1 (2%)	
Hepatocellular Carcinoma	2 (4%)	2 (4%)	4 (8%)	1 (2%)
Hepatocellular Adenoma	9 (18%)	6 (12%)	2 (4%)	5 (10%)
Hepatocellular Adenoma, Multiple		1 (2%)	1 (2%)	1 (2%)
Hepatocholangiocarcinoma	1 (2%)	1 (2%)		
Mesentery	(14)	(19)	(17)	(13)
Carcinoma, Metastatic, Islets, Pancreatic		1 (5%)		
Fibrosarcoma, Metastatic, Skin		1 (5%)	1 (6%)	
Hepatocholangiocarcinoma, Metastatic, Liver	1 (7%)	1 (5%)		
Osteosarcoma, Metastatic, Bone			1 (6%)	
Sarcoma			1 (6%)	
Pancreas	(50)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)	1 (2%)		
Salivary Glands	(49)	(49)	(48)	(50)
Schwannoma Malignant, Metastatic, Skin				1 (2%)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Carcinoma				2 (4%)
Squamous Cell Papilloma	1 (2%)		1 (2%)	3 (6%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		

F12

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(49)	(50)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)			
Osteosarcoma, Metastatic, Bone			1 (2%)	
Adrenal Medulla	(50)	(50)	(48)	(49)
Pheochromocytoma Benign		1 (2%)	1 (2%)	
Islets, Pancreatic	(50)	(50)	(50)	(50)
Adenoma			3 (6%)	
Carcinoma		1 (2%)		
Pituitary Gland	(48)	(47)	(43)	(48)
Pars Distalis, Adenoma	1 (2%)	3 (6%)		1 (2%)
Thyroid Gland	(49)	(49)	(48)	(49)
Bilateral, Follicular Cell, Adenoma		1 (2%)		
Follicular Cell, Carcinoma				1 (2%)
GENERAL BODY SYSTEM				
Peritoneum		(1)		(1)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (100%)		
GENITAL SYSTEM				
Clitoral Gland	(50)	(49)	(50)	(48)
Ovary	(47)	(49)	(50)	(49)
Cystadenoma		2 (4%)	1 (2%)	3 (6%)
Granulosa Cell Tumor Benign			1 (2%)	
Hemangioma		2 (4%)	1 (2%)	1 (2%)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)			
Luteoma				1 (2%)
Osteosarcoma, Metastatic, Bone			1 (2%)	
Teratoma Benign		1 (2%)		
Uterus	(50)	(50)	(50)	(50)
Leiomyosarcoma			1 (2%)	
Polyp Stromal		3 (6%)		1 (2%)

E 13

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)		
Lymph Node	(7)	(7)	(8)	(4)
Mediastinal, Hepatocholangiocarcinoma, Metastatic, Liver	1 (14%)	1 (14%)		
Mediastinal, Sarcoma, Metastatic, Skin	1 (14%)			
Lymph Node, Mandibular	(47)	(46)	(48)	(48)
Lymph Node, Mesenteric	(50)	(49)	(47)	(49)
Spleen	(49)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)	2 (4%)	
Thymus	(46)	(47)	(44)	(46)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)			
Thymoma Benign	1 (2%)			
INTEGUMENTARY SYSTEM				
Skin	(50)	(50)	(50)	(50)
Subcutaneous Tissue, Fibrosarcoma		5 (10%)	1 (2%)	2 (4%)
Subcutaneous Tissue, Hemangiosarcoma	1 (2%)			
Subcutaneous Tissue, Sarcoma	1 (2%)			
Subcutaneous Tissue, Schwannoma Malignant				2 (4%)
Subcutaneous Tissue, Pinna, Fibroma				1 (2%)
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Femur, Osteosarcoma			1 (2%)	
Vertebra, Osteosarcoma				1 (2%)
Skeletal Muscle	(3)	(2)	(1)	(3)
Carcinoma, Metastatic, Islets, Pancreatic		1 (50%)		
Hepatocholangiocarcinoma, Metastatic, Liver	1 (33%)			
Osteosarcoma, Metastatic, Bone			1 (100%)	
NERVOUS SYSTEM				
Brain	(50)	(50)	(49)	(50)
Spinal Cord				(2)
Meninges, Meningioma Malignant				1 (50%)

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	1 (2%)	4 (8%)	2 (4%)	5 (10%)
Alveolar/Bronchiolar Adenoma, Multiple			1 (2%)	
Alveolar/Bronchiolar Carcinoma		3 (6%)	2 (4%)	1 (2%)
Carcinoma, Metastatic, Uncertain Primary Site		1 (2%)		
Fibrosarcoma, Metastatic, Skin		2 (4%)	1 (2%)	
Hepatocellular Carcinoma, Metastatic, Liver	1 (2%)		1 (2%)	1 (2%)
Hepatocholangiocarcinoma, Metastatic, Liver	1 (2%)	1 (2%)		
Osteosarcoma, Metastatic, Bone			1 (2%)	1 (2%)
Sarcoma, Metastatic, Skin	1 (2%)			
Schwannoma Malignant, Metastatic, Skin				1 (2%)
SPECIAL SENSES SYSTEM				
Harderian Gland		(1)	(1)	(2)
Adenoma		1 (100%)		2 (100%)
Carcinoma			1 (100%)	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Fibrosarcoma, Metastatic, Skin			1 (2%)	
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
Urinary Bladder	(50)	(50)	(50)	(50)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Lymphoma Malignant	7 (14%)	10 (20%)	8 (16%)	6 (12%)

* Number of animals with any tissue examined microscopically

F01

B6C3F1 MICE FEMALE	0.0%	0.075%	0.15%	0.30%
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	21	32	31	32
Total Primary Neoplasms	25	49	36	41
Total Animals with Benign Neoplasms	13	22	14	20
Total Benign Neoplasms	13	25	14	24
Total Animals with Malignant Neoplasms	12	20	19	17
Total Malignant Neoplasms	12	24	22	17
Total Animals with Metastatic Neoplasms	3	6	4	3
Total Metastatic Neoplasm	11	15	13	4
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

F 02

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	3	2	3	1
Natural Death	8	3	5	10
Survivors				
Terminal Sacrifice	39	45	42	39
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Intestine Small, Duodenum	(49)	(50)	(48)	(49)
Carcinoma		1 (2%)		
Carcinoma, Metastatic, Intestine Small, Jejunum			1 (2%)	
Polyp Adenomatous	2 (4%)	4 (8%)	3 (6%)	
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Carcinoma	5 (10%)	1 (2%)	1 (2%)	
Leiomyosarcoma			1 (2%)	
Polyp Adenomatous				1 (2%)
Liver	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (2%)
Carcinoma, Metastatic, Islets, Pancreatic		1 (2%)		
Cholangiocarcinoma				1 (2%)
Hemangiosarcoma	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Hemangiosarcoma, Metastatic, Spleen	2 (4%)			
Hepatoblastoma	5 (10%)	1 (2%)	2 (4%)	
Hepatocellular Carcinoma	9 (18%)	10 (20%)	6 (12%)	6 (12%)
Hepatocellular Carcinoma, Multiple				3 (6%)
Hepatocellular Adenoma	10 (20%)	15 (30%)	8 (16%)	13 (26%)
Hepatocellular Adenoma, Multiple	9 (18%)	2 (4%)	5 (10%)	5 (10%)
Sarcoma			1 (2%)	
Mesentery	(7)	(6)	(7)	(5)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (20%)
Cholangiocarcinoma, Metastatic, Liver				1 (20%)
Hepatoblastoma, Metastatic, Liver			1 (14%)	
Sarcoma, Metastatic, Liver			1 (14%)	
Pancreas	(49)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (2%)
Cholangiocarcinoma, Metastatic, Liver				1 (2%)
Hepatoblastoma, Metastatic, Liver	1 (2%)			

F03

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - cont				
Salivary Glands	(50)	(50)	(50)	(50)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma	1 (2%)	1 (2%)		1 (2%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Sarcoma, Metastatic, Liver			1 (2%)	
Tooth	(5)	(5)	(4)	(1)
Odontoma		2 (40%)	1 (25%)	
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (2%)
Fibrosarcoma, Metastatic, Uncertain Primary Site		1 (2%)		
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Cholangiocarcinoma, Metastatic, Liver				1 (2%)
Islets, Pancreatic	(50)	(50)	(50)	(50
Adenoma	3 (6%)	2 (4%)	2 (4%)	
Carcinoma		1 (2%)		
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Prostate	(50)	(50)	(49)	(50)
Cholangiocarcinoma, Metastatic, Liver				1 (2%)
Seminal Vesicle	(50)	(50)	(50)	(50)
Cholangiocarcinoma, Metastatic, Liver				1 (2%)
Testes	(50)	(50)	(50)	(50)
Hemangiosarcoma, Metastatic, Liver				1 (2%)
Interstitial Cell, Adenoma		2 (4%)		

F 04

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(49)	(50)
Hemangiosarcoma	2 (4%)			
Lymph Node	(1)	(1)	(3)	(5)
Mediastinal, Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (20%)
Pancreatic, Cholangiocarcinoma, Metastatic, Liver				1 (20%)
Renal, Cholangiocarcinoma, Metastatic, Liver				1 (20%)
Lymph Node, Mandibular	(47)	(50)	(47)	(48)
Carcinoma, Metastatic, Harderian Gland			1 (2%)	
Lymph Node, Mesenteric	(49)	(49)	(48)	(49)
Hemangiosarcoma, Metastatic, Liver				1 (2%)
Spleen	(50)	(50)	(50)	(50)
Hemangiosarcoma	3 (6%)		2 (4%)	
Hemangiosarcoma, Metastatic, Bone Marrow	1 (2%)			
Hemangiosarcoma, Metastatic, Liver			1 (2%)	1 (2%)
Hemangiosarcoma, Metastatic, Skin	1 (2%)			
Thymus	(37)	(39)	(38)	(42)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				1 (2%)
INTEGUMENTARY SYSTEM				
Skin	(50)	(50)	(50)	(50)
Subcutaneous Tissue, Hemangiosarcoma	1 (2%)			
Subcutaneous Tissue, Sarcoma, Metastatic, Brain	1 (2%)			
Subcutaneous Tissue, Pinna, Melanoma Malignant				1 (2%)
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Sarcoma	1 (2%)			

F 05

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	10 (20%)	5 (10%)	8 (16%)	10 (20%)
Alveolar/Bronchiolar Adenoma, Multiple			1 (2%)	
Alveolar/Bronchiolar Carcinoma	4 (8%)	1 (2%)	3 (6%)	7 (14%)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung			1 (2%)	1 (2%)
Carcinoma, Metastatic, Harderian Gland			1 (2%)	
Carcinoma, Metastatic, Intestine Small, Jejunum	1 (2%)			
Cholangiocarcinoma, Metastatic, Liver				1 (2%)
Fibrosarcoma, Metastatic, Uncertain Primary Site		1 (2%)		
Hemangiosarcoma, Metastatic, Liver	1 (2%)			
Hepatoblastoma, Metastatic, Liver	2 (4%)			
Hepatocellular Carcinoma, Metastatic, Liver	3 (6%)	2 (4%)	2 (4%)	2 (4%)
Hepatocholangiocarcinoma, Metastatic, Liver		1 (2%)		
Sarcoma, Metastatic, Brain	1 (2%)			
Sarcoma, Metastatic, Liver			1 (2%)	
Mediastinum, Alveolar/Bronchiolar Carcinoma, Metastatic, Lung	1 (2%)			2 (4%)
Mediastinum, Fibrosarcoma, Metastatic, Uncertain Primary Site		1 (2%)		
Mediastinum, Hemangiosarcoma, Metastatic, Bone Marrow	1 (2%)			
Mediastinum, Sarcoma, Metastatic, Brain	1 (2%)			
SPECIAL SENSES SYSTEM				
Harderian Gland	(5)	(4)	(6)	(1)
Adenoma	4 (80%)	3 (75%)	4 (67%)	1 (100%)
Carcinoma			2 (33%)	
Sarcoma, Metastatic, Brain	1 (20%)			
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Carcinoma, Metastatic, Lung				2 (4%)
Renal Tubule, Adenoma		1 (2%)		

F 06

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Lymphoma Malignant	1 (2%)	1 (2%)	4 (8%)	1 (2%)

* Number of animals with any tissue examined microscopically

E07

B6C3F1 MICE MALE	0.0%	0.075%	0.15%	0.30%
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	40	35	36	38
Total Primary Neoplasms	72	55	58	52
Total Animals with Benign Neoplasms	28	28	26	29
Total Benign Neoplasms	39	37	32	31
Total Animals with Malignant Neoplasms	27	15	20	20
Total Malignant Neoplasms	33	18	23	21
Total Animals with Metastatic Neoplasms	13	4	7	7
Total Metastatic Neoplasm	18	7	11	24
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

F00

END OF REPORT

2 YEAR CHRONIC MICE

REASONS FOR REMOVAL: ALL

REMOVAL DATE RANGE: ALL

TREATMENT GROUPS: INCLUDE ALL

NTP
LAB: Battelle Columbus

STATISTICAL ANALYSIS OF PRIMARY TUMORS
SODIUM NITRITE

REPORT: PEIRPT08
DATE: 05/13/99

TIME: 09:40:55

EXPERIMENT: 88007 TEST: 06
TEST TYPE: CHRONIC
CONT: NO1-ES-55384
PATHOLOGIST: TOFT, JOHN

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED WATER

NTP C#: C88007
CAS: 7632-00-0

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

NTP
LAB: Battelle Columbus
EXPERIMENT: 88007 TEST: 06
TEST TYPE: CHRONIC
CONT: NO1-ES-55384
PATHOLOGIST: TOFT, JOHN

STATISTICAL ANALYSIS OF PRIMARY TUMORS
SODIUM NITRITE

CAGES FROM 0000 TO LAST CAGE
ROUTE: DOSED WATER

REPORT: PEIRPT06
DATE: 05/13/99
TIME: 09:40:55

NTP C#: C88007
CAS: 7632-00-0

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

Male Mice

Organ	Morphology
Intestine Small: Jejunum	Carcinoma
Intestine Small: Site Unspecified	Carcinoma
Liver	Hepatoblastoma
	Hepatocellular Carcinoma or Hepatocellular Adenoma
	Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma
Lung	Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma
All Organs	Malignant Tumors

Female Mice

Organ	Morphology
Lung	Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma
Skin	Fibrosarcoma
	Schwannoma Malignant
Stomach, Forestomach	Squamous Cell Carcinoma
	Squamous Cell Carcinoma or Papilloma Squamous
All Organs	Benign Tumors
	Malignant Tumors
	Malignant and Benign Tumors

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Bone Marrow								
Hemangiosarcoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	0/50 (0%)	0/49 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.3%	0.0%	0.0%	0.0%	0.0%	2.2%	0.0%	0.0%
TERMINAL (d)	1/39 (3%)	0/45 (0%)	0/41 (0%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	661	---	---	---	---	605	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.117N	P=0.222N	P=0.232N	P=0.245N	P=0.568N	P=0.517	(e)	(e)
POLY 3	P=0.114N	P=0.234N	P=0.239N	P=0.245N	P=0.564N	P=0.502	(e)	(e)
POLY 1.5	P=0.114N	P=0.236N	P=0.240N	P=0.242N	P=0.565N	P=0.501	(e)	(e)
POLY 6	P=0.114N	P=0.231N	P=0.239N	P=0.248N	P=0.564N	P=0.499	(e)	(e)
LOGISTIC REGRESSION	P=0.111N	P=0.242N	P=0.254N	P=0.230N	P=0.523N	P=0.441	(e)	(e)
COCH-ARM / FISHERS	P=0.116N	P=0.247N	P=0.253N	P=0.247N	P=0.567N	P=0.500	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Harderian Gland								
Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	4/50 (8%)	3/50 (6%)	4/50 (8%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/50 (4%)
POLY-3 ADJUSTED (b)	8.5%	6.2%	8.4%	2.2%	0.0%	2.2%	0.0%	4.3%
TERMINAL (d)	2/39 (5%)	2/45 (4%)	4/42 (10%)	1/39 (3%)	0/40 (0%)	1/34 (3%)	0/37 (0%)	2/41 (5%)
FIRST INCIDENCE	661	612	727 (T)	727 (T)	---	728 (T)	---	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.171N	P=0.446N	P=0.606N	P=0.188N	P=0.157	P=0.468	(e)	P=0.244
POLY 3	P=0.173N	P=0.488N	P=0.637N	P=0.190N	P=0.142	P=0.500	(e)	P=0.241
POLY 1.5	P=0.167N	P=0.494N	P=0.639N	P=0.186N	P=0.141	P=0.500	(e)	P=0.239
POLY 6	P=0.181N	P=0.478N	P=0.637N	P=0.195N	P=0.145	P=0.496	(e)	P=0.244
LOGISTIC REGRESSION	P=0.159N	P=0.510N	P=0.635N	P=0.185N	(e)	P=0.468	(e)	P=0.244
COCH-ARM / FISHERS	P=0.157N	P=0.500N	P=0.643N	P=0.181N	P=0.140	P=0.500	(e)	P=0.247

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Harderian Gland Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	4.2%	0.0%	0.0%	0.0%	2.1%	0.0%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	2/42 (5%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	1/37 (3%)	0/41 (0%)
FIRST INCIDENCE	---	---	727 (T)	---	---	---	728 (T)	---
STATISTICAL TESTS								
LIFE TABLE	P=0.588	(e)	P=0.255	(e)	P=0.698	(e)	P=0.484	(e)
POLY 3	P=0.574	(e)	P=0.241	(e)	P=0.700	(e)	P=0.504	(e)
POLY 1.5	P=0.582	(e)	P=0.240	(e)	P=0.696	(e)	P=0.503	(e)
POLY 6	P=0.564	(e)	P=0.242	(e)	P=0.708	(e)	P=0.506	(e)
LOGISTIC REGRESSION	(e)	(e)	P=0.255	(e)	(e)	(e)	P=0.484	(e)
COCH-ARM / FISHERS	P=0.595	(e)	P=0.247	(e)	P=0.694	(e)	P=0.500	(e)

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Harderian Gland Carcinoma or Adenoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	4/50 (8%)	3/50 (6%)	5/50 (10%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	2/50 (4%)
POLY-3 ADJUSTED (b)	8.5%	6.2%	10.5%	2.2	0.0%	2.2%	2.1%	4.3%
TERMINAL (d)	2/39 (5%)	2/45 (4%)	5/42 (12%)	1/39 (3%)	0/40 (0%)	1/34 (3%)	1/37 (3%)	2/41 (5%)
FIRST INCIDENCE	661	612	727 (T)	727 (T)	---	728 (T)	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.194N	P=0.446N	P=0.540	P=0.188N	P=0.173	P=0.468	P=0.484	P=0.244
POLY 3	P=0.198N	P=0.488N	P=0.506	P=0.190N	P=0.158	P=0.500	P=0.504	P=0.241
POLY 1.5	P=0.190N	P=0.494N	P=0.504	P=0.186N	P=0.156	P=0.500	P=0.503	P=0.239
POLY 6	P=0.207N	P=0.478N	P=0.507	P=0.195N	P=0.162	P=0.496	P=0.506	P=0.244
LOGISTIC REGRESSION	P=0.183N	P=0.510N	P=0.512	P=0.185N	(e)	P=0.468	P=0.484	P=0.244
COCH-ARM / FISHERS	P=0.178N	P=0.500N	P=0.500	P=0.181N	P=0.153	P=0.500	P=0.500	P=0.247

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Intestine Small: Duodenum Polyp Adenomatous								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	4/50 (8%)	3/50 (6%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.3%	8.4%	6.3%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	2/39 (5%)	4/45 (9%)	3/42 (7%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	727 (T)	727 (T)	727 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.141N	P=0.405	P=0.534	P=0.238N	(e)	(e)	(e)	(e)
POLY 3	P=0.146N	P=0.347	P=0.508	P=0.244N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.142N	P=0.342	P=0.505	P=0.241N	(e)	(e)	(e)	(e)
POLY 6	P=0.150N	P=0.355	P=0.511	P=0.246N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.141N	P=0.405	P=0.534	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.137N	P=0.339	P=0.500	P=0.247N	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Intestine Small: Jejunum Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	5/50 (10%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	10.6%	2.1%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	4/39 (10%)	1/45 (2%)	1/42 (2%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	643	727 (T)	727 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.016N*	P=0.081N	P=0.092N	P=0.036N*	(e)	(e)	(e)	(e)
POLY 3	P=0.016N*	P=0.098N	P=0.099N	P=0.034N*	(e)	(e)	(e)	(e)
POLY 1.5	P=0.015N*	P=0.100N	P=0.100N	P=0.033N*	(e)	(e)	(e)	(e)
POLY 6	P=0.016N*	P=0.095N	P=0.098N	P=0.035N*	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.016N*	P=0.102N	P=0.101N	P=0.035N*	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.016N*	P=0.102N	P=0.102N	P=0.028N*	(e)	(e)	(e)	(e)

G 01

Statistical Analysis of Primary Tumors in Mice(B6C3F1) SODIUM NITRITE

Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Intestine Small: Site Unspecified Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	5/50 (10%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	10.6%	4.2%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	4/39 (10%)	2/45 (4%)	1/42 (2%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	643	727 (T)	727 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.014N*	P=0.173N	P=0.092N	P=0.036N*	(e)	(e)	(e)	(e)
POLY 3	P=0.014N*	P=0.211N	P=0.099N	P=0.034N*	(e)	(e)	(e)	(e)
POLY 1.5	P=0.014N*	P=0.214N	P=0.100N	P=0.033N*	(e)	(e)	(e)	(e)
POLY 6	P=0.015N*	P=0.206N	P=0.098N	P=0.035N*	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.015N*	P=0.211N	P=0.101N	P=0.035N*	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.014N*	P=0.218N	P=0.102N	P=0.028N*	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Intestine Small: Site Unspecified Polyp Adenomatous								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	2/50 (4%)	4/50 (8%)	3/50 (6%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	4.3%	8.4%	6.3%	2.2%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	2/39 (5%)	4/45 (9%)	3/42 (7%)	1/39 (3%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	727 (T)	727 (T)	727 (T)	727 (T)	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.305N	P=0.405	P=0.534	P=0.500N	(e)	(e)	(e)	(e)
POLY 3	P=0.307N	P=0.347	P=0.508	P=0.510N	(e)	(e)	(e)	(e)
POLY 1.5	P=0.301N	P=0.342	P=0.505	P=0.506N	(e)	(e)	(e)	(e)
POLY 6	P=0.313N	P=0.355	P=0.511	P=0.514N	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.305N	P=0.405	P=0.534	P=0.500N	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.292N	P=0.339	P=0.500	P=0.500N	(e)	(e)	(e)	(e)

Statistical Analysis of Primary Tumors in Mice(B6C3F1) SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Islets, Pancreatic Adenoma								
TUMOR RATES								
OVERALL (a)	3/50 (6%)	2/50 (4%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	3/50 (6%)	0/50 (0%)
POLY-3 ADJUSTED (b)	6.4%	4.2%	4.2%	0.0%	0.0%	0.0%	6.4%	0.0%
TERMINAL (d)	1/39 (3%)	2/45 (4%)	2/42 (5%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	2/37 (5%)	0/41 (0%)
FIRST INCIDENCE	652	727 (T)	727 (T)	---	---	---	716	---
STATISTICAL TESTS								
LIFE TABLE	P=0.092N	P=0.457N	P=0.480N	P=0.131N	P=0.555	(e)	P=0.114	(e)
POLY 3	P=0.093N	P=0.495N	P=0.497N	P=0.126N	P=0.550	(e)	P=0.123	(e)
POLY 1.5	P=0.090N	P=0.497N	P=0.497N	P=0.123N	P=0.542	(e)	P=0.121	(e)
POLY 6	P=0.096N	P=0.490N	P=0.497N	P=0.129N	P=0.562	(e)	P=0.125	(e)
LOGISTIC REGRESSION	P=0.086N	P=0.505N	P=0.511N	P=0.111N	P=0.556	(e)	P=0.125	(e)
COCH-ARM / FISHERS	P=0.086N	P=0.500N	P=0.500N	P=0.121N	P=0.539	(e)	P=0.121	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Islets, Pancreatic Carcinoma or Adenoma								
TUMOR RATES								
OVERALL (a)	3/50 (6%)	3/50 (6%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	3/50 (6%)	0/50 (0%)
POLY-3 ADJUSTED (b)	6.4%	6.3%	4.2%	0.0%	0.0%	2.2%	6.4%	0.0%
TERMINAL (d)	1/39 (3%)	3/45 (7%)	2/42 (5%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	2/37 (5%)	0/41 (0%)
FIRST INCIDENCE	652	727 (T)	727 (T)	---	---	664	716	---
STATISTICAL TESTS								
LIFE TABLE	P=0.077N	P=0.613N	P=0.480N	P=0.131N	P=0.609N	P=0.500	P=0.114	(e)
POLY 3	P=0.078N	P=0.657N	P=0.497N	P=0.126N	P=0.627N	P=0.501	P=0.123	(e)
POLY 1.5	P=0.075N	P=0.659N	P=0.497N	P=0.123N	P=0.631N	P=0.501	P=0.121	(e)
POLY 6	P=0.081N	P=0.652N	P=0.497N	P=0.129N	P=0.618N	P=0.498	P=0.125	(e)
LOGISTIC REGRESSION	P=0.073N	P=0.661	P=0.511N	P=0.111N	P=0.632N	P=0.483	P=0.125	(e)
COCH-ARM / FISHERS	P=0.072N	P=0.661N	P=0.500N	P=0.121N	P=0.634	P=0.500	P=0.121	(e)

G 03

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver								
Hemangiosarcoma								
TUMOR RATES								
OVERALL (a)	2/50 (4%)	2/50 (4%)	1/50 (2%)	2/50 (4%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
POLY 3 ADJUSTED (b)	4.3%	4.2%	2.1%	4.3%	0.0%	0.0%	2.1%	0.0%
TERMINAL (d)	1/39 (3%)	2/45 (4%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	1/37 (3%)	0/41 (0%)
FIRST INCIDENCE	705	727 (T)	664	549	---	---	728 (T)	---
STATISTICAL TESTS								
LIFE TABLE	P=0.595N	P=0.646N	P=0.481N	P=0.683	P=0.698	(e)	P=0.484	(e)
POLY 3	P=0.582N	P=0.687N	P=0.493N	P=0.688	P=0.700	(e)	P=0.504	(e)
POLY 1.5	P=0.580N	P=0.690N	P=0.496N	P=0.690	P=0.696	(e)	P=0.503	(e)
POLY 6	P=0.583N	P=0.681N	P=0.490N	P=0.687	P=0.708	(e)	P=0.506	(e)
LOGISTIC REGRESSION	P=0.538N	P=0.681N	P=0.516N	P=0.657N	(e)	(e)	P=0.484	(e)
COCH-ARM / FISHERS	P=0.577N	P=0.691N	P=0.500N	P=0.691N	P=0.694	(e)	P=0.500	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver								
Hepatoblastoma								
TUMOR RATES								
OVERALL (a)	5/50 (10%)	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)	10.6%	2.1%	4.2%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	3/39 (8%)	1/45 (2%)	2/42 (5%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	617	727 (T)	727 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.027N*	P=0.085N	P=0.199N	P=0.039N*	(e)	(e)	(e)	(e)
POLY 3	P=0.027N*	P=0.099N	P=0.214N	P=0.034N*	(e)	(e)	(e)	(e)
POLY 1.5	P=0.026N*	P=0.101N	P=0.215N	P=0.033N*	(e)	(e)	(e)	(e)
POLY 6	P=0.028N*	P=0.097N	P=0.214N	P=0.036N*	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	P=0.025N*	P=0.105N	P=0.220N	P=0.032N*	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.025N*	P=0.102N	P=0.218N	P=0.028N*	(e)	(e)	(e)	(e)

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Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver Hepatocellular Adenoma								
TUMOR RATES								
OVERALL (a)	19/50 (38%)	17/50 (34%)	13/50 (26%)	18/50 (36%)	9/50 (18%)	7/50 (14%)	3/50 (6%)	6/50 (12%)
POLY-3 ADJUSTED (b)	40.1%	35.4%	27.3%	38.5%	19.5%	15.2%	6.4%	12.9%
TERMINAL (d)	16/39 (41%)	16/45 (36%)	12/42 (31%)	14/39 (36%)	8/40 (20%)	5/34 (15%)	3/37 (8%)	6/41 (15%)
FIRST INCIDENCE	643	637	727 (T)	472	586	667	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.514N	P=0.247N	P=0.095N	P=0.513N	P=0.171N	P=0.506N	P=0.079N	P=0.271N
POLY 3	P=0.473N	P=0.395N	P=0.134N	P=0.521N	P=0.197N	P=0.394N	P=0.057N	P=0.283N
POLY 1.5	P=0.463N	P=0.406N	P=0.136N	P=0.513N	P=0.201N	P=0.392N	P=0.058N	P=0.287N
POLY 6	P=0.486N	P=0.377N	P=0.135N	P=0.528N	P=0.190N	P=0.406N	P=0.055N	P=0.276N
LOGISTIC REGRESSION	P=0.504N	P=0.374N	P=0.118N	P=0.534N	P=0.184N	P=0.394N	P=0.056N	P=0.270N
COCH-ARM / FISHERS	P=0.450N	P=0.418N	P=0.142N	P=0.500N	P=0.203N	P=0.393N	P=0.061N	P=0.288N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver Hepatocellular Carcinoma								
TUMOR RATES								
OVERALL (a)	9/50 (18%)	10/50 (20%)	6/50 (12%)	9/50 (18%)	2/50 (4%)	2/50 (4%)	4/50 (8%)	1/50 (2%)
POLY-3 ADJUSTED (b)	19.1%	20.6%	12.5%	19.3%	4.4%	4.4%	8.5%	2.2%
TERMINAL (d)	8/39 (21%)	8/45 (18%)	5/42 (12%)	5/39 (13%)	2/40 (5%)	1/34 (3%)	3/37 (8%)	1/41 (2%)
FIRST INCIDENCE	617	601	596	583	728 (T)	673	691	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.519N	P=0.585N	P=0.245N	P=0.588	P=0.399N	P=0.645	P=0.312	P=0.491N
POLY 3	P=0.490N	P=0.527	P=0.275N	P=0.591	P=0.422N	P=0.693N	P=0.349	P=0.494N
POLY 1.5	P=0.485N	P=0.514	P=0.280N	P=0.594	P=0.428N	P=0.692N	P=0.344	P=0.498N
POLY 6	P=0.493N	P=0.548	P=0.269N	P=0.594	P=0.411N	P=0.690	P=0.354	P=0.489N
LOGISTIC REGRESSION	P=0.458N	P=0.499	P=0.287N	P=0.602N	P=0.417N	P=0.692	P=0.351	P=0.491N
COCH-ARM / FISHERS	P=0.475N	P=0.500	P=0.288N	P=0.602N	P=0.431N	P=0.691N	P=0.339	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver								
Hepatocellular Carcinoma or Hepatoblastoma								
TUMOR RATES								
OVERALL (a)	12/50 (24%)	11/50 (22%)	7/50 (14%)	9/50 (18%)	2/50 (4%)	2/50 (4%)	4/50 (8%)	1/50 (2%)
POLY-3 ADJUSTED (b)	25.4%	22.7%	14.6%	19.3%	4.4%	4.4%	8.5%	2.2%
TERMINAL (d)	10/39 (26%)	9/45 (20%)	6/42 (14%)	5/39 (13%)	2/40 (5%)	1/34 (3%)	3/37 (8%)	1/41 (2%)
FIRST INCIDENCE	617	601	596	583	728 (T)	673	691	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.267N	P=0.374N	P=0.124N	P=0.332N	P=0.399N	P=0.645	P=0.312	P=0.491N
POLY 3	P=0.239N	P=0.472N	P=0.143N	P=0.325N	P=0.422N	P=0.693N	P=0.349	P=0.494N
POLY 1.5	P=0.235N	P=0.486N	P=0.147N	P=0.321N	P=0.428N	P=0.692N	P=0.344	P=0.498N
POLY 6	P=0.243N	P=0.451N	P=0.139N	P=0.324N	P=0.411N	P=0.690	P=0.354	P=0.489N
LOGISTIC REGRESSION	P=0.219N	P=0.497N	P=0.150N	P=0.316N	P=0.417N	P=0.692	P=0.351	P=0.491N
COCH-ARM / FISHERS	P=0.225N	P=0.500N	P=0.154N	P=0.312N	P=0.431N	P=0.691N	P=0.339	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Liver								
Hepatocellular Carcinoma or Hepatocellular Adenoma								
TUMOR RATES								
OVERALL (a)	24/50 (48%)	24/50 (48%)	16/50 (32%)	25/50 (50%)	10/50 (20%)	8/50 (16%)	7/50 (14%)	7/50 (14%)
POLY-3 ADJUSTED (b)	50.2%	49.2%	33.3%	52.4%	21.6%	17.3%	14.9%	15.1%
TERMINAL (d)	20/39 (51%)	21/45 (47%)	15/42 (36%)	18/39 (46%)	9/40 (23%)	6/34 (18%)	6/37 (16%)	7/41 (17%)
FIRST INCIDENCE	617	601	596	472	586	667	691	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.447	P=0.354N	P=0.048N*	P=0.482	P=0.212N	P=0.523N	P=0.349N	P=0.278N
POLY 3	P=0.516	P=0.539N	P=0.068N	P=0.499	P=0.250N	P=0.399N	P=0.285N	P=0.292N
POLY 1.5	P=0.521	P=0.558N	P=0.070N	P=0.498	P=0.256N	P=0.396N	P=0.290N	P=0.296N
POLY 6	P=0.513	P=0.508N	P=0.067N	P=0.508	P=0.239N	P=0.412N	P=0.280N	P=0.284N
LOGISTIC REGRESSION	P=0.506	P=0.560N	P=0.066N	P=0.479	P=0.229N	P=0.402N	P=0.277N	P=0.276N
COCH-ARM / FISHERS	P=0.529	P=0.579N	P=0.076N	P=0.500	P=0.257N	P=0.398N	P=0.298N	P=0.298N

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Liver Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma								
TUMOR RATES								
OVERALL (a)	26/50 (52%)	25/50 (50%)	17/50 (34%)	25/50 (50%)	10/50 (20%)	8/50 (16%)	7/50 (14%)	7/50 (14%)
POLY-3 ADJUSTED (b)	54.3%	51.2%	35.4%	52.4%	21.6%	17.3%	14.9%	15.1%
TERMINAL (d)	21/39 (54%)	22/45 (49%)	16/42 (38%)	18/39 (46%)	9/40 (23%)	6/34 (18%)	6/37 (16%)	7/41 (17%)
FIRST INCIDENCE	617	601	596	472	586	667	691	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.484N	P=0.279N	P=0.033N*	P=0.520N	P=0.212N	P=0.523N	P=0.349N	P=0.278N
POLY 3	P=0.410N	P=0.460N	P=0.046N*	P=0.506N	P=0.250N	P=0.399N	P=0.285N	P=0.292N
POLY 1.5	P=0.404N	P=0.479N	P=0.048N*	P=0.505N	P=0.256N	P=0.396N	P=0.290N	P=0.296N
POLY 6	P=0.415N	P=0.430N	P=0.046N*	P=0.501N	P=0.239N	P=0.412N	P=0.280N	P=0.284N
LOGISTIC REGRESSION	P=0.422N	P=0.478N	P=0.044N*	P=0.524N	P=0.229N	P=0.402N	P=0.277N	P=0.276N
COCH-ARM / FISHERS	P=0.396N	P=0.500N	P=0.053N	P=0.500N	P=0.257N	P=0.398N	P=0.298N	P=0.298N

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Lung Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	10/50 (20%)	5/50 (10%)	9/50 (18%)	10/50 (20%)	1/50 (2%)	4/50 (8%)	3/50 (6%)	5/50 (10%)
POLY-3 ADJUSTED (b)	21.2%	10.4%	18.9%	22.0%	1.2%	8.7%	6.4%	10.8%
TERMINAL (d)	9/39 (23%)	4/45 (9%)	8/42 (19%)	10/39 (26%)	1/40 (3%)	2/34 (6%)	3/37 (8%)	5/41 (12%)
FIRST INCIDENCE	617	644	707	727 (T)	728 (T)	659	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.333	P=0.087N	P=0.433N	P=0.596	P=0.142	P=0.154	P=0.278	P=0.109
POLY 3	P=0.335	P=0.121N	P=0.490N	P=0.562	P=0.118	P=0.181	P=0.313	P=0.105
POLY 1.5	P=0.352	P=0.126N	P=0.494N	P=0.576	P=0.115	P=0.181	P=0.310	P=0.103
POLY 6	P=0.315	P=0.114N	P=0.487N	P=0.546	P=0.123	P=0.178	P=0.316	P=0.108
LOGISTIC REGRESSION	P=0.327	P=0.127N	P=0.477N	P=0.558	P=0.122	P=0.179	P=0.278	P=0.109
COCH-ARM / FISHERS	P=0.375	P=0.131N	P=0.500N	P=0.598N	P=0.113	P=0.181	P=0.309	P=0.102

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Lung Alveolar/Bronchiolar Carcinoma								
TUMOR RATES								
OVERALL (a)	4/50 (8%)	1/50 (2%)	3/50 (6%)	7/50 (14%)	0/50 (0%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
POLY-3 ADJUSTED (b)	8.4%	2.1%	6.3%	15.1%	0.0%	6.6%	4.3%	2.2%
TERMINAL (d)	3/39 (8%)	1/45 (2%)	3/42 (7%)	5/39 (13%)	0/40 (0%)	3/34 (9%)	2/37 (5%)	1/41 (2%)
FIRST INCIDENCE	526	727 (T)	727 (T)	502	---	728 (T)	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.070	P=0.149N	P=0.464N	P=0.262	P=0.580	P=0.094	P=0.221	P=0.505
POLY 3	P=0.074	P=0.177N	P=0.498N	P=0.249	P=0.566	P=0.118	P=0.242	P=0.503
POLY 1.5	P=0.076	P=0.178N	P=0.499N	P=0.254	P=0.560	P=0.119	P=0.240	P=0.501
POLY 6	P=0.071	P=0.173N	P=0.497N	P=0.246	P=0.575	P=0.115	P=0.244	P=0.506
LOGISTIC REGRESSION	P=0.098	P=0.185N	P=0.525N	P=0.304	(e)	P=0.094	P=0.221	P=0.505
COCH-ARM / FISHERS	P=0.080	P=0.181N	P=0.500N	P=0.262	P=0.556	P=0.121	P=0.247	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Lung Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma								
TUMOR RATES								
OVERALL (a)	13/50 (26%)	6/50 (12%)	12/50 (24%)	17/50 (34%)	1/50 (2%)	6/50 (12%)	5/50 (10%)	6/50 (12%)
POLY-3 ADJUSTED (b)	27.2%	12.5%	25.2%	36.6%	2.2%	13.0%	10.7%	12.9%
TERMINAL (d)	11/39 (28%)	5/45 (11%)	11/42 (26%)	15/39 (39%)	1/40 (3%)	4/34 (12%)	5/37 (14%)	6/41 (15%)
FIRST INCIDENCE	526	644	707	502	723 (T)	659	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.056	P=0.037N*	P=0.422N	P=0.253	P=0.136	P=0.044 *	P=0.086	P=0.062
POLY 3	P=0.057	P=0.059N	P=0.503N	P=0.223	P=0.110	P=0.057	P=0.106	P=0.059
POLY 1.5	P=0.063	P=0.061N	P=0.501N	P=0.236	P=0.107	P=0.057	P=0.105	P=0.057
POLY 6	P=0.051	P=0.055N	P=0.506N	P=0.211	P=0.116	P=0.055	P=0.108	P=0.061
LOGISTIC REGRESSION	P=0.066	P=0.065N	P=0.490N	P=0.248	P=0.120	P=0.058	P=0.086	P=0.062
COCH-ARM / FISHERS	P=0.073	P=0.062N	P=0.500N	P=0.257	P=0.105	P=0.056	P=0.102	P=0.056

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Ovary								
Cystadenoma								
TUMOR RATES								
OVERALL (a)					0/47 (0%)	2/49 (4%)	1/50 (2%)	3/49 (6%)
POLY-3 ADJUSTED (b)					0.0%	4.5%	2.1%	6.6%
TERMINAL (d)					0/37 (0%)	2/33 (6%)	1/37 (3%)	3/40 (8%)
FIRST INCIDENCE					---	728 (T)	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE					P=0.130	P=0.213	P=0.500	P=0.135
POLY 3					P=0.113	P=0.247	P=0.518	P=0.130
POLY 1.5					P=0.111	P=0.248	P=0.516	P=0.128
POLY 6					P=0.117	P=0.243	P=0.520	P=0.133
LOGISTIC REGRESSION					(e)	P=0.213	P=0.500	P=0.135
COCH-ARM / FISHERS					P=0.108	P=0.258	P=0.515	P=0.129

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Ovary								
Hemangioma								
TUMOR RATES								
OVERALL (a)					0/47 (0%)	2/49 (4%)	1/50 (2%)	1/49 (2%)
POLY-3 ADJUSTED (b)					0.0%	4.5%	2.1%	2.2%
TERMINAL (d)					0/37 (0%)	2/33 (6%)	1/37 (3%)	1/40 (3%)
FIRST INCIDENCE					---	728 (T)	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE					P=0.535	P=0.213	P=0.500	P=0.516
POLY 3					P=0.520	P=0.247	P=0.518	P=0.512
POLY 1.5					P=0.515	P=0.248	P=0.516	P=0.510
POLY 6					P=0.528	P=0.243	P=0.520	P=0.516
LOGISTIC REGRESSION					(e)	P=0.213	P=0.500	P=0.516
COCH-ARM / FISHERS					P=0.511	P=0.258	P=0.515	P=0.510

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Pituitary Gland: Pars Distalis or Unspecified Site								
Adenoma								
TUMOR RATES								
OVERALL (a)	0/49 (0%)	0/49 (0%)	0/47 (0%)	0/47 (0%)	1/48 (2%)	3/47 (6%)	0/43 (0%)	1/48 (2%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	2.3%	6.9%	0.0%	2.2%
TERMINAL (d)	0/38 (0%)	0/44 (0%)	0/40 (0%)	0/37 (0%)	1/38 (3%)	2/32 (6%)	0/33 (0%)	1/40 (3%)
FIRST INCIDENCE	---	---	---	---	728 (T)	643	---	728 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.384N	P=0.273	P=0.528N	P=0.750N
POLY 3	(e)	(e)	(e)	(e)	P=0.401N	P=0.305	P=0.515N	P=0.754N
POLY 1.5	(e)	(e)	(e)	(e)	P=0.406N	P=0.303	P=0.518N	P=0.757N
POLY 6	(e)	(e)	(e)	(e)	P=0.396N	P=0.301	P=0.513N	P=0.749N
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.408N	P=0.299	(e)	P=0.750N
COCH ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.412N	P=0.301	P=0.527N	P=0.753N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
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%)	1/50 (2%)	5/50 (10%)	1/50 (2%)	3/50 (6%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	2.2%	10.7%	2.1%	6.4%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	1/34 (3%)	0/37 (0%)	2/41 (5%)
FIRST INCIDENCE	---	---	---	---	586	451	477	705
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.491	P=0.103	P=0.753N	P=0.317
POLY 3	(e)	(e)	(e)	(e)	P=0.462	P=0.103	P=0.755N	P=0.308
POLY 1.5	(e)	(e)	(e)	(e)	P=0.459	P=0.103	P=0.757N	P=0.306
POLY 6	(e)	(e)	(e)	(e)	P=0.468	P=0.101	P=0.753N	P=0.312
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.474	P=0.081	P=0.741	P=0.303
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.456	P=0.102	P=0.753N	P=0.309

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Fibrosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	5/50 (10%)	1/50 (2%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	0.0%	10.7%	2.1%	4.3%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	1/34 (3%)	0/37 (0%)	1/41 (2%)
FIRST INCIDENCE	---	---	---	---	---	651	477	705
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.534	P=0.032 *	P=0.504	P=0.248
POLY 3	(e)	(e)	(e)	(e)	P=0.514	P=0.032 *	P=0.507	P=0.241
POLY 1.5	(e)	(e)	(e)	(e)	P=0.507	P=0.032 *	P=0.505	P=0.239
POLY 6	(e)	(e)	(e)	(e)	P=0.524	P=0.032 *	P=0.510	P=0.245
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.517	P=0.029 *	P=0.405	P=0.241
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.500	P=0.028 *	P=0.500	P=0.247

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin Fibrosarcoma, Sarcoma, Myxosarcoma, or Fibrous Histiocytoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)	5/50 (10%)	1/50 (2%)	2/50 (4%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	2.2%	10.7%	2.1%	4.3%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	1/34 (3%)	0/37 (0%)	1/41 (2%)
FIRST INCIDENCE	---	---	---	---	586	651	477	705
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.491N	P=0.103	P=0.753N	P=0.508
POLY 3	(e)	(e)	(e)	(e)	P=0.517N	P=0.103	P=0.755N	P=0.503
POLY 1.5	(e)	(e)	(e)	(e)	P=0.520N	P=0.103	P=0.757N	P=0.501
POLY 6	(e)	(e)	(e)	(e)	P=0.512N	P=0.101	P=0.753N	P=0.506
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.498N	P=0.081	P=0.741	P=0.501
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.523N	P=0.102	P=0.753N	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Skin								
Schwannoma Malignant								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	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%	4.2%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	1/41 (2%)
FIRST INCIDENCE	---	---	---	---	---	---	---	520
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.051	(e)	(e)	P=0.240
POLY 3	(e)	(e)	(e)	(e)	P=0.047 *	(e)	(e)	P=0.244
POLY 1.5	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.241
POLY 6	(e)	(e)	(e)	(e)	P=0.048 *	(e)	(e)	P=0.249
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	P=0.060	(e)	(e)	P=0.249
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.247

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Spleen								
Hemangiosarcoma								
TUMOR RATES								
OVERALL (a)	3/50 (6%)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/49 (0%)	1/50 (2%)	2/50 (4%)	0/50 (0%)
POLY-3 ADJUSTED (b)	6.4%	0.0%	4.2%	0.0%	0.0%	2.2%	4.3%	0.0%
TERMINAL (d)	2/39 (5%)	0/45 (0%)	1/42 (2%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	2/37 (5%)	0/41 (0%)
FIRST INCIDENCE	661	---	707	---	---	605	728 (T)	---
STATISTICAL TESTS								
LIFE TABLE	P=0.131N	P=0.105N	P=0.472N	P=0.126N	P=0.602N	P=0.517	P=0.221	(e)
POLY 3	P=0.131N	P=0.116N	P=0.494N	P=0.125N	P=0.610N	P=0.503	P=0.244	(e)
POLY 1.5	P=0.128N	P=0.118N	P=0.496N	P=0.123N	P=0.612N	P=0.504	P=0.243	(e)
POLY 6	P=0.135N	P=0.114N	P=0.492N	P=0.128N	P=0.605N	P=0.500	P=0.245	(e)
LOGISTIC REGRESSION	P=0.125N	P=0.122N	P=0.501N	P=0.121N	P=0.607N	P=0.459	P=0.221	(e)
COCH-ARM / FISHERS	P=0.125N	P=0.121N	P=0.500N	P=0.121N	P=0.612N	P=0.505	P=0.253	(e)

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Stomach, Forestomach Squamous Cell Carcinoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	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%	4.3%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	2/41 (5%)
FIRST INCIDENCE	---	---	---	---	---	---	---	728 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.055	(e)	(e)	P=0.244
POLY 3	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.241
POLY 1.5	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.239
POLY 6	(e)	(e)	(e)	(e)	P=0.047 *	(e)	(e)	P=0.244
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	(e)	(e)	(e)	P=0.244
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.046 *	(e)	(e)	P=0.247

Dose	Males 0.0%	Males 0.075%	Males 0.15%	Males 0.30%	Females 0.0%	Females 0.075%	Females 0.15%	Females 0.30%
Stomach, Forestomach Squamous Cell Carcinoma or Papilloma Squamous								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	5/50 (10%)
POLY-3 ADJUSTED (b)	2.1%	2.1%	0.0%	2.2%	2.2%	0.0%	2.1%	10.7%
TERMINAL (d)	1/39 (3%)	1/45 (2%)	0/42 (0%)	1/39 (3%)	1/40 (3%)	0/34 (0%)	1/37 (3%)	4/41 (10%)
FIRST INCIDENCE	727 (T)	727 (T)	---	727 (T)	728 (T)	---	728 (T)	708
STATISTICAL TESTS								
LIFE TABLE	P=0.629N	P=0.730N	P=0.485N	P=0.762	P=0.016 *	P=0.532N	P=0.744	P=0.111
POLY 3	P=0.616N	P=0.756N	P=0.497N	P=0.754	P=0.011 *	P=0.500N	P=0.756N	P=0.106
POLY 1.5	P=0.616N	P=0.758N	P=0.498N	P=0.756	P=0.011 *	P=0.500N	P=0.758N	P=0.104
POLY 6	P=0.617N	P=0.752N	P=0.495N	P=0.752	P=0.012 *	P=0.504N	P=0.754N	P=0.109
LOGISTIC REGRESSION	P=0.629N	P=0.730N	(e)	P=0.762	P=0.014 *	(e)	P=0.744	P=0.112
COCH-ARM / FISHERS	P=0.616N	P=0.753N	P=0.500N	P=0.753N	P=0.011 *	P=0.500N	P=0.753N	P=0.102

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Stomach, Forestomach Squamous Cell Papilloma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	1/50 (2%)	0/50 (0%)	1/50 (2%)	3/50 (6%)
POLY-3 ADJUSTED (b)	2.1%	2.1%	0.0%	2.2%	2.2%	0.0%	2.1%	6.4%
TERMINAL (d)	1/39 (3%)	1/45 (2%)	0/42 (0%)	1/39 (3%)	1/40 (3%)	0/34 (0%)	1/37 (3%)	2/41 (5%)
FIRST INCIDENCE	727 (T)	727 (T)	---	727 (T)	728 (T)	---	728 (T)	708
STATISTICAL TESTS								
LIFE TABLE	P=0.629N	P=0.730N	P=0.485N	P=0.762	P=0.114	P=0.532N	P=0.744	P=0.316
POLY 3	P=0.616N	P=0.756N	P=0.497N	P=0.754	P=0.099	P=0.500N	P=0.756N	P=0.312
POLY 1.5	P=0.616N	P=0.753N	P=0.498N	P=0.756	P=0.097	P=0.500N	P=0.758N	P=0.308
POLY 6	P=0.617N	P=0.752N	P=0.495N	P=0.752	P=0.103	P=0.504N	P=0.754N	P=0.318
LOGISTIC REGRESSION	P=0.629N	P=0.730N	(e)	P=0.762	P=0.108	(e)	P=0.744	P=0.317
COCH-ARM / FISHERS	P=0.616N	P=0.753N	P=0.500N	P=0.753N	P=0.097	P=0.500N	P=0.753N	P=0.309

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Testes Adenoma								
TUMOR RATES								
OVERALL (a)	0/50 (0%)	2/50 (4%)	0/50 (0%)	0/50 (0%)				
POLY-3 ADJUSTED (b)	0.0%	4.2%	0.0%	0.0%				
TERMINAL (d)	0/39 (0%)	2/45 (4%)	0/42 (0%)	0/39 (0%)				
FIRST INCIDENCE	---	727 (T)	---	---				
STATISTICAL TESTS								
LIFE TABLE	P=0.412N	P=0.270	(e)	(e)				
POLY 3	P=0.405N	P=0.242	(e)	(e)				
POLY 1.5	P=0.405N	P=0.240	(e)	(e)				
POLY 6	P=0.404N	P=0.246	(e)	(e)				
LOGISTIC REGRESSION	(e)	P=0.270	(e)	(e)				
COCH-ARM / FISHERS	P=0.405N	P=0.247	(e)	(e)				

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Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Tooth								
Odontoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	2/50 (4%)	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
POLY-3 ADJUSTED (b)	0.0%	4.2%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%
TERMINAL (d)	0/39 (0%)	2/45 (4%)	1/42 (2%)	0/39 (0%)	0/40 (0%)	0/34 (0%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE	---	727 (T)	727 (T)	---	---	---	---	---
STATISTICAL TESTS								
LIFE TABLE	P=0.471N	P=0.270	P=0.515	(e)	(e)	(e)	(e)	(e)
POLY 3	P=0.469N	P=0.242	P=0.503	(e)	(e)	(e)	(e)	(e)
POLY 1.5	P=0.466N	P=0.240	P=0.502	(e)	(e)	(e)	(e)	(e)
POLY 6	P=0.471N	P=0.246	P=0.505	(e)	(e)	(e)	(e)	(e)
LOGISTIC REGRESSION	(e)	P=0.270	P=0.515	(e)	(e)	(e)	(e)	(e)
COCH-ARM / FISHERS	P=0.461N	P=0.247	P=0.500	(e)	(e)	(e)	(e)	(e)

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
Uterus								
Polyp Stromal								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)					0/50 (0%)	3/50 (6%)	0/50 (0%)	1/50 (2%)
POLY-3 ADJUSTED (b)					0.0%	6.5%	0.0%	2.1%
TERMINAL (d)					0/40 (0%)	1/34 (3%)	0/37 (0%)	0/41 (0%)
FIRST INCIDENCE					---	664	---	659
STATISTICAL TESTS								
LIFE TABLE					P=0.607N	P=0.107	(e)	P=0.516
POLY 3					P=0.627N	P=0.120	(e)	P=0.5
POLY 1.5					P=0.631N	P=0.120	(e)	P=0.5
POLY 6					P=0.624N	P=0.117	(e)	P=0.5
LOGISTIC REGRESSION					P=0.633N	P=0.120	(e)	P=0.5
COCH-ARM / FISHERS					P=0.634	P=0.121	(e)	P=0.5

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE
Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Hemangioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)	1/50 (2%)	1/50 (2%)
POLY-3 ADJUSTED (b)	0.0%	0.0%	0.0%	0.0%	0.0%	4.4%	2.1%	2.2%
TERMINAL (d)	0/39 (0%)	0/45 (0%)	0/42 (0%)	0/39 (0%)	0/40 (0%)	2/34 (6%)	1/37 (3%)	1/41 (2%)
FIRST INCIDENCE	---	---	---	---	---	728 (T)	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	(e)	(e)	(e)	(e)	P=0.521	P=0.203	P=0.484	P=0.505
POLY 3	(e)	(e)	(e)	(e)	P=0.508	P=0.237	P=0.504	P=0.503
POLY 1.5	(e)	(e)	(e)	(e)	P=0.503	P=0.238	P=0.503	P=0.501
POLY 6	(e)	(e)	(e)	(e)	P=0.515	P=0.233	P=0.506	P=0.506
LOGISTIC REGRESSION	(e)	(e)	(e)	(e)	(e)	P=0.203	P=0.484	P=0.505
COCH-ARM / FISHERS	(e)	(e)	(e)	(e)	P=0.500	P=0.247	P=0.500	P=0.500

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Hemangiosarcoma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	7/50 (14%)	2/50 (4%)	3/50 (6%)	2/50 (4%)	1/50 (2%)	1/50 (2%)	3/50 (6%)	0/50 (0%)
POLY-3 ADJUSTED (b)	14.9%	4.2%	6.3%	4.3%	2.2%	2.2%	6.4%	0.0%
TERMINAL (d)	5/39 (13%)	2/45 (4%)	1/42 (2%)	0/39 (0%)	1/40 (3%)	0/34 (0%)	3/37 (8%)	0/41 (0%)
FIRST INCIDENCE	661	727 (T)	664	549	728 (T)	605	728 (T)	---
STATISTICAL TESTS								
LIFE TABLE	P=0.091N	P=0.059N	P=0.142N	P=0.092N	P=0.393N	P=0.752	P=0.278	P=0.495N
POLY 3	P=0.083N	P=0.076N	P=0.151N	P=0.084N	P=0.402N	P=0.759N	P=0.313	P=0.497N
POLY 1.5	P=0.082N	P=0.078N	P=0.154N	P=0.083N	P=0.407N	P=0.755N	P=0.310	P=0.499N
POLY 6	P=0.085N	P=0.073N	P=0.148N	P=0.086N	P=0.393N	P=0.760	P=0.316	P=0.494N
LOGISTIC REGRESSION	P=0.073N	P=0.076N	P=0.159N	P=0.073N	P=0.410N	P=0.748	P=0.278	(e)
COCH-ARM / FISHERS	P=0.080N	P=0.080N	P=0.159N	P=0.080N	P=0.409N	P=0.753N	P=0.309	P=0.500N

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Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Hemangiosarcoma or Hemangioma								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	7/50 (14%)	2/50 (4%)	3/50 (6%)	2/50 (4%)	1/50 (2%)	3/50 (6%)	4/50 (8%)	1/50 (2%)
POLY 3 ADJUSTED (b)	14.9%	4.2%	6.3%	4.3%	2.2%	6.5%	8.6%	2.2%
TERMINAL (d)	5/39 (13%)	2/45 (4%)	1/42 (2%)	0/39 (0%)	1/40 (3%)	2/34 (6%)	4/37 (11%)	1/41 (2%)
FIRST INCIDENCE	661	727 (T)	664	549	728 (T)	605	728 (T)	728 (T)
STATISTICAL TESTS								
LIFE TABLE	P=0.091N	P=0.059N	P=0.142N	P=0.092N	P=0.494N	P=0.272	P=0.156	P=0.156N
POLY 3	P=0.083N	P=0.076N	P=0.151N	P=0.084N	P=0.513N	P=0.308	P=0.185	P=0.787N
POLY 1.5	P=0.082N	P=0.078N	P=0.154N	P=0.083N	P=0.519N	P=0.308	P=0.183	P=0.759N
POLY 6	P=0.085N	P=0.073N	P=0.148N	P=0.086N	P=0.502N	P=0.304	P=0.188	P=0.754N
LOGISTIC REGRESSION	P=0.073N	P=0.076N	P=0.159N	P=0.073N	P=0.514N	P=0.303	P=0.156	P=0.756N
COCH-ARM / FISHERS	P=0.080N	P=0.080N	P=0.159N	P=0.080N	P=0.523N	P=0.309	P=0.181	P=0.753N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Malignant Lymphoma: Histiocytic, Lymphocytic, Mixed, NOS, or Undifferentiated Cell Type								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	1/50 (2%)	1/50 (2%)	4/50 (8%)	1/50 (2%)	7/50 (14%)	10/50 (20%)	8/50 (16%)	6/50 (12%)
POLY-3 ADJUSTED (b)	2.1%	2.1%	8.4%	2.2%	14.9%	21.5%	16.7%	12.8%
TERMINAL (d)	1/39 (3%)	1/45 (2%)	3/42 (7%)	0/39 (0%)	4/40 (10%)	7/34 (21%)	4/37 (11%)	4/41 (10%)
FIRST INCIDENCE	727 (T)	727 (T)	664	594	580	650	524	673
STATISTICAL TESTS								
LIFE TABLE	P=0.508	P=0.730N	P=0.203	P=0.753	P=0.295N	P=0.248	P=0.471	P=0.474N
POLY 3	P=0.508	P=0.756N	P=0.186	P=0.756	P=0.331N	P=0.288	P=0.515	P=0.502N
POLY 1.5	P=0.515	P=0.758N	P=0.183	P=0.758	P=0.335N	P=0.295	P=0.510	P=0.503N
POLY 6	P=0.501	P=0.752N	P=0.189	P=0.755	P=0.322N	P=0.272	P=0.518	P=0.498N
LOGISTIC REGRESSION	P=0.542	P=0.730N	P=0.182	P=0.734N	P=0.338	P=0.290	P=0.459	P=0.504N
COCH-ARM / FISHERS	P=0.526	P=0.753N	P=0.181	P=0.753N	P=0.334N	P=0.298	P=0.500	P=0.500N

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	28/50 (56%)	28/50 (56%)	26/50 (52%)	29/50 (58%)	13/50 (26%)	22/50 (44%)	14/50 (28%)	20/50 (40%)
POLY-3 ADJUSTED (b)	58.1%	57.4%	54.6%	62.0%	28.1%	46.6%	29.6%	42.7%
TERMINAL (d)	22/39 (56%)	25/45 (56%)	25/42 (60%)	25/39 (64%)	12/40 (30%)	15/34 (44%)	12/37 (32%)	18/41 (44%)
FIRST INCIDENCE	617	612	707	472	586	643	610	659
STATISTICAL TESTS								
LIFE TABLE	P=0.373	P=0.328N	P=0.294N	P=0.480	P=0.299	P=0.021 *	P=0.421	P=0.118
POLY 3	P=0.385	P=0.555N	P=0.444N	P=0.427	P=0.208	P=0.048 *	P=0.526	P=0.103
POLY 1.5	P=0.423	P=0.567N	P=0.430N	P=0.459	P=0.202	P=0.047 *	P=0.515	P=0.100
POLY 6	P=0.333	P=0.535N	P=0.475N	P=0.385	P=0.223	P=0.048 *	P=0.538	P=0.111
LOGISTIC REGRESSION	P=0.382	P=0.559N	P=0.372N	P=0.435	P=0.229	P=0.045 *	P=0.532	P=0.116
COCH-ARM / FISHERS	P=0.471	P=0.580N	P=0.421N	P=0.500	P=0.203	P=0.046 *	P=0.500	P=0.101

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Malignant Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	27/50 (54%)	15/50 (30%)	20/50 (40%)	20/50 (40%)	12/50 (24%)	21/50 (42%)	19/50 (38%)	17/50 (34%)
POLY-3 ADJUSTED (b)	54.9%	30.9%	40.8%	41.1%	25.2%	43.5%	38.6%	35.1%
TERMINAL (d)	20/39 (51%)	13/45 (29%)	15/42 (36%)	11/39 (28%)	7/40 (18%)	11/34 (32%)	11/37 (30%)	12/41 (29%)
FIRST INCIDENCE	501	601	596	502	580	605	477	401
STATISTICAL TESTS								
LIFE TABLE	P=0.316N	P=0.006N**	P=0.095N	P=0.170N	P=0.465	P=0.042 *	P=0.104	P=0.235
POLY 3	P=0.234N	P=0.013N*	P=0.116N	P=0.121N	P=0.320	P=0.045 *	P=0.113	P=0.201
POLY 1.5	P=0.234N	P=0.012N*	P=0.116N	P=0.120N	P=0.312	P=0.044 *	P=0.107	P=0.196
POLY 6	P=0.229N	P=0.012N*	P=0.115N	P=0.117N	P=0.329	P=0.044 *	P=0.118	P=0.205
LOGISTIC REGRESSION	P=0.176N	P=0.014N*	P=0.131N	P=0.078N	P=0.270	P=0.039 *	P=0.069	P=0.175
COCH-ARM / FISHERS	P=0.233N	P=0.013N*	P=0.115N	P=0.115N	P=0.299	P=0.044 *	P=0.097	P=0.189

A 05

Statistical Analysis of Primary Tumors in Mice(B6C3F1) - SODIUM NITRITE

Terminal Sacrifice at 104 weeks

Dose	Males 0.0%	0.075%	0.15%	0.30%	Females 0.0%	0.075%	0.15%	0.30%
All Organs Malignant and Benign Tumors								
TUMOR RATES	#	#	#	#	#	#	#	#
OVERALL (a)	40/50 (80%)	35/50 (70%)	36/50 (72%)	38/50 (76%)	21/50 (42%)	33/50 (66%)	31/50 (62%)	32/50 (64%)
POLY-3 ADJUSTED (b)	80.5%	71.1%	73.5%	76.8%	44.0%	67.4%	63.0%	65.6%
TERMINAL (d)	30/39 (77%)	31/45 (69%)	31/42 (74%)	28/39 (72%)	16/40 (40%)	20/34 (59%)	22/37 (60%)	25/41 (61%)
FIRST INCIDENCE	501	601	596	472	580	605	477	401
STATISTICAL TESTS								
LIFE TABLE	P=0.469	P=0.063N	P=0.162N	P=0.461N	P=0.156	P=0.012 *	P=0.037 *	P=0.052
POLY 3	P=0.479N	P=0.196N	P=0.279N	P=0.423N	P=0.054	P=0.015 *	P=0.045 *	P=0.024 *
POLY 1.5	P=0.473N	P=0.192N	P=0.262N	P=0.417N	P=0.050	P=0.014 *	P=0.041 *	P=0.023 *
POLY 6	P=0.487N	P=0.193N	P=0.304N	P=0.425N	P=0.060	P=0.017 *	P=0.048 *	P=0.028 *
LOGISTIC REGRESSION	P=0.454N	P=0.181N	P=0.242N	P=0.370N	P=0.045 *	P=0.013 *	P=0.033 *	P=0.023 *
COCH-ARM / FISHERS	P=0.467N	P=0.178N	P=0.241N	P=0.405N	P=0.047 *	P=0.013 *	P=0.036 *	P=0.022 *

(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).

A 06

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
SODIUM NITRITE

FINAL #1 CORE STUDY RATS

Facility: Battelle Columbus Laboratory

Chemical CAS #: 7632-00-0

Lock Date: 03/20/98

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

A 07

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	11	6	10	15
Natural Death	6	13	4	2
Survivors				
Terminal Sacrifice	33	31	36	33
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(49)	(50)	(50)
Inflammation			1 (2%)	
Intestine Large, Colon	(50)	(48)	(50)	(50)
Parasite Metazoan		1 (2%)	1 (2%)	1 (2%)
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Inflammation, Granulomatous				1 (2%)
Parasite Metazoan	4 (8%)	1 (2%)	2 (4%)	7 (14%)
Liver	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)	3 (6%)	5 (10%)
Basophilic Focus	45 (90%)	42 (84%)	48 (96%)	45 (90%)
Clear Cell Focus	9 (18%)	6 (12%)	8 (16%)	7 (14%)
Cyst				1 (2%)
Eosinophilic Focus	9 (18%)	10 (20%)	8 (16%)	10 (20%)
Hemorrhage	1 (2%)			1 (2%)
Hepatodiaphragmatic Nodule	4 (8%)	11 (22%)	7 (14%)	8 (16%)
Inflammation, Chronic Active	23 (46%)	23 (46%)	28 (56%)	28 (56%)
Inflammation, Granulomatous			1 (2%)	1 (2%)
Mixed Cell Focus	11 (22%)	3 (6%)	7 (14%)	9 (18%)
Necrosis	5 (10%)	2 (4%)		4 (8%)
Pigmentation, Lipofuscin			1 (2%)	
Regeneration	1 (2%)			
Vacuolization Cytoplasmic	1 (2%)	5 (10%)	4 (8%)	4 (8%)
Bile Duct, Hyperplasia	8 (16%)	4 (8%)	4 (8%)	4 (8%)
Mesentery	(7)	(5)	(7)	(4)
Fat, Inflammation, Chronic Active	6 (86%)	5 (100%)	7 (100%)	4 (100%)
Fat, Necrosis	1 (14%)			
Pancreas	(50)	(50)	(49)	(50)
Atrophy				1 (2%)
Inflammation, Chronic Active			1 (2%)	
Acinus, Atrophy	6 (12%)	6 (12%)	8 (16%)	8 (16%)
Acinus, Hyperplasia	1 (2%)		1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(50)
Edema		1 (2%)	2 (4%)	2 (4%)
Erosion	1 (2%)	1 (2%)	1 (2%)	

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

A 08

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - CONT				
Hyperkeratosis	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Inflammation, Chronic Active	1 (2%)			
Ulcer	4 (8%)	2 (4%)	2 (4%)	1 (2%)
Epithelium, Hyperplasia	8 (16%)	6 (12%)	8 (16%)	40 (80%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Erosion		2 (4%)	1 (2%)	
Inflammation, Chronic Active	1 (2%)			
Mineralization	1 (2%)	3 (6%)	1 (2%)	
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(50)	(50)	(50)
Mineralization		2 (4%)		
Heart	(50)	(49)	(50)	(50)
Inflammation, Chronic Active	3 (6%)	4 (8%)	3 (6%)	3 (6%)
Mineralization		2 (4%)		
Necrosis	1 (2%)			
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Angiectasis	40 (80%)	39 (78%)	45 (90%)	45 (90%)
Degeneration	1 (2%)			
Hemorrhage	1 (2%)			
Hyperplasia	15 (30%)	11 (22%)	11 (22%)	10 (20%)
Hypertrophy	8 (16%)	7 (14%)	7 (14%)	4 (8%)
Necrosis	2 (4%)	1 (2%)		
Vacuolization Cytoplasmic	4 (8%)	5 (10%)	1 (2%)	3 (6%)
Adrenal Medulla	(50)	(50)	(45)	(49)
Hyperplasia	6 (12%)	7 (14%)	4 (9%)	5 (10%)
Bilateral, Hyperplasia			1 (2%)	
Pituitary Gland	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			
Cyst	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Hemorrhage	3 (6%)			
Pigmentation, Hemosiderin		1 (2%)		
Pars Distalis, Angiectasis	2 (4%)			
Pars Distalis, Cyst	4 (8%)	10 (20%)	5 (10%)	9 (18%)
Pars Distalis, Hemorrhage		1 (2%)		
Pars Distalis, Hyperplasia	10 (20%)	10 (20%)	19 (38%)	12 (24%)
Pars Intermedia, Cyst				1 (2%)
Thyroid Gland	(50)	(49)	(48)	(50)
Inflammation, Chronic Active			1 (2%)	
Ultimobranchial Cyst	1 (2%)		1 (2%)	4 (8%)
Vacuolization Cytoplasmic	1 (2%)			

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

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
ENDOCRINE SYSTEM - CONT				
Bilateral, C-Cell, Hyperplasia		1 (2%)		
C-Cell, Hyperplasia	24 (48%)	27 (53%)	34 (71%)	26 (52%)
Follicle, Cyst			1 (2%)	
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral Gland	(46)	(48)	(49)	(49)
Atrophy	1 (2%)			
Cyst	9 (20%)	1 (2%)	12 (24%)	3 (6%)
Hyperplasia	8 (17%)	4 (8%)	7 (14%)	7 (14%)
Inflammation, Chronic Active		1 (2%)	2 (4%)	1 (2%)
Ovary	(50)	(49)	(50)	(50)
Cyst	4 (8%)	4 (8%)	3 (6%)	5 (10%)
Inflammation, Chronic Active				1 (2%)
Follicle, Cyst	1 (2%)		2 (4%)	2 (4%)
Periovarian Tissue, Cyst	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Uterus	(50)	(50)	(50)	(50)
Cyst		2 (4%)		
Dysplasia				1 (2%)
Fibrosis	1 (2%)			
Hemorrhage		1 (2%)	2 (4%)	1 (2%)
Hydrometra	3 (6%)	4 (8%)	4 (8%)	5 (10%)
Inflammation, Chronic Active			1 (2%)	
Thrombosis			2 (4%)	1 (2%)
Cervix, Hydrometra			1 (2%)	
Cervix, Hyperplasia				1 (2%)
Cervix, Hypertrophy	1 (2%)			
Cervix, Epithelium, Cyst				1 (2%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hyperplasia			1 (2%)	
Myelofibrosis			1 (2%)	
Lymph Node	(2)	(1)	(2)	(1)
Ectasia				1 (100%)
Lymph Node, Mandibular	(49)	(49)	(50)	(50)
Hyperplasia	1 (2%)	1 (2%)		2 (4%)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Pigmentation, Lipofuscin		1 (2%)	1 (2%)	

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

A 10

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
HEMATOPOIETIC SYSTEM - CONT				
Spleen	(50)	(50)	(50)	(50)
Fibrosis	1 (2%)			
Hematopoietic Cell Proliferation	1 (2%)	1 (2%)	1 (2%)	4 (8%)
Necrosis			1 (2%)	
Pigmentation, Hemosiderin	1 (2%)	3 (6%)	1 (2%)	1 (2%)
Vacuolization Cytoplasmic	1 (2%)			
Lymphoid Follicle, Depletion Cellular				1 (2%)
Thymus	(49)	(47)	(49)	(48)
Atrophy	1 (2%)		1 (2%)	
Cyst	1 (2%)			
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(50)
Galactocele	14 (28%)	10 (20%)	12 (24%)	10 (20%)
Hyperplasia	10 (20%)	5 (10%)	3 (6%)	9 (18%)
Skin	(50)	(50)	(50)	(50)
Ulcer				2 (4%)
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteosclerosis	1 (2%)			
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)			
Hydrocephalus			1 (2%)	1 (2%)
Mineralization				1 (2%)
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Congestion		1 (2%)	2 (4%)	
Inflammation, Chronic Active	16 (32%)	13 (26%)	14 (28%)	17 (34%)
Pigmentation	1 (2%)			
Alveolar Epithelium, Hyperplasia	10 (20%)	10 (20%)	8 (16%)	3 (6%)
Bronchiole, Epithelium, Hyperplasia	1 (2%)		1 (2%)	
Nose	(50)	(49)	(50)	(50)
Inflammation, Chronic Active				3 (6%)
Olfactory Epithelium, Metaplasia	1 (2%)			

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

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
SPECIAL SENSES SYSTEM				
Eye		(1)	(1)	(3)
Inflammation, Chronic Active		1 (100%)		
Cornea, Inflammation, Chronic Active				1 (33%)
Lens, Mineralization				1 (33%)
Retina, Degeneration			1 (100%)	3 (100%)
Harderian Gland				(1)
Inflammation, Chronic Active				1 (100%)
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Accumulation, Hyaline Droplet		1 (2%)		
Casts Protein				1 (2%)
Cyst			2 (4%)	4 (8%)
Infarct	1 (2%)		1 (2%)	1 (2%)
Inflammation, Chronic Active	1 (2%)	5 (10%)	4 (8%)	5 (10%)
Mineralization	1 (2%)	1 (2%)	2 (4%)	
Necrosis	1 (2%)			
Nephropathy	14 (28%)	16 (32%)	20 (40%)	23 (46%)
Pigmentation	2 (4%)	3 (6%)	1 (2%)	
Renal Tubule, Regeneration		1 (2%)		
Urinary Bladder	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	3 (6%)	2 (4%)	2 (4%)	5 (10%)

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

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially In Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	16	4	12	8
Natural Death	5	8	2	6
Survivors				
Terminal Sacrifice	29	37	36	36
Natural Death		1		
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan	5 (10%)	4 (8%)	3 (6%)	2 (4%)
Intestine Large, Cecum	(50)	(50)	(50)	(49)
Congestion	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Angiectasis		2 (4%)	3 (6%)	1 (2%)
Basophilic Focus	31 (62%)	34 (68%)	37 (74%)	42 (84%)
Clear Cell Focus	19 (38%)	25 (50%)	26 (52%)	23 (46%)
Cyst				1 (2%)
Degeneration	1 (2%)			
Degeneration, Cystic	5 (10%)	15 (30%)	12 (24%)	4 (8%)
Eosinophilic Focus	4 (8%)	10 (20%)	11 (22%)	6 (12%)
Fibrosis	2 (4%)			
Hemorrhage	1 (2%)	1 (2%)		
Hepatodiaphragmatic Nodule	11 (22%)	6 (12%)	4 (8%)	8 (16%)
Inflammation, Chronic Active	13 (26%)	19 (38%)	25 (50%)	24 (48%)
Mixed Cell Focus	7 (14%)	7 (14%)	4 (8%)	2 (4%)
Necrosis	5 (10%)	2 (4%)	1 (2%)	4 (8%)
Regeneration	1 (2%)	1 (2%)		1 (2%)
Vacuolization Cytoplasmic	8 (16%)	5 (10%)	4 (8%)	1 (2%)
Bile Duct, Hyperplasia	41 (82%)	38 (76%)	43 (86%)	38 (76%)
Mesentery	(11)	(7)	(5)	(8)
Fat, Inflammation, Chronic Active	8 (73%)	5 (71%)	5 (100%)	6 (75%)
Fat, Mineralization	1 (9%)			
Fat, Necrosis			1 (20%)	
Oral Mucosa	(2)		(1)	
Pharyngeal, Cyst	1 (50%)			
Pancreas	(50)	(50)	(50)	(49)
Atrophy		1 (2%)		
Inflammation, Chronic Active		1 (2%)		
Acinus, Atrophy	16 (32%)	27 (54%)	22 (44%)	28 (57%)
Acinus, Hyperplasia	4 (8%)	3 (6%)	6 (12%)	8 (16%)
Salivary Glands	(50)	(50)	(50)	(50)

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

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - CONT				
Atrophy		1 (2%)		
Cyst		1 (2%)		
Inflammation, Chronic Active	1 (2%)			
Stomach, Forestomach	(50)	(50)	(50)	(50)
Edema	1 (2%)		1 (2%)	1 (2%)
Erosion	2 (4%)			
Hyperkeratosis		1 (2%)	4 (8%)	4 (8%)
Inflammation, Chronic Active	1 (2%)	1 (2%)		1 (2%)
Mineralization			1 (2%)	1 (2%)
Ulcer	4 (8%)	1 (2%)	2 (4%)	1 (2%)
Epithelium, Hyperplasia	12 (24%)	9 (18%)	10 (20%)	44 (88%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Erosion	1 (2%)		3 (6%)	1 (2%)
Thrombosis	1 (2%)			
Ulcer	2 (4%)	1 (2%)	1 (2%)	
Epithelium, Hyperplasia				1 (2%)
Tongue			(1)	
Epithelium, Hyperplasia			1 (100%)	
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	9 (18%)	15 (30%)	16 (32%)	12 (24%)
Thrombosis	1 (2%)	1 (2%)		
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Accessory Adrenal Cortical Nodule		1 (2%)		
Angiectasis	16 (32%)	21 (42%)	15 (30%)	22 (44%)
Hematopoietic Cell Proliferation	1 (2%)			
Hyperplasia	11 (22%)	15 (30%)	15 (30%)	10 (20%)
Hypertrophy	7 (14%)	7 (14%)	2 (4%)	9 (18%)
Necrosis		1 (2%)		
Vacuolization Cytoplasmic	3 (6%)	3 (6%)	8 (16%)	3 (6%)
Bilateral, Hyperplasia	1 (2%)			
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	11 (22%)	18 (36%)	16 (32%)	13 (26%)
Islets, Pancreatic	(50)	(50)	(50)	(49)
Hyperplasia		1 (2%)		1 (2%)
Pituitary Gland	(50)	(49)	(50)	(50)
Angiectasis		1 (2%)		
Cyst		2 (4%)	1 (2%)	
Hemorrhage		1 (2%)		
Pigmentation, Hemosiderin			1 (2%)	

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

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
ENDOCRINE SYSTEM - CONT				
Pars Distalis, Angiectasis		1 (2%)	1 (2%)	1 (2%)
Pars Distalis, Cyst	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Pars Distalis, Hyperplasia	9 (18%)	9 (18%)	18 (36%)	10 (20%)
Thyroid Gland	(50)	(50)	(50)	(50)
C-Cell, Hyperplasia	11 (22%)	17 (34%)	16 (32%)	13 (26%)
Follicle, Cyst		3 (6%)	1 (2%)	
GENERAL BODY SYSTEM				
Peritoneum			(1)	
Inflammation, Chronic Active			1 (100%)	
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Degeneration	1 (2%)			
Preputial Gland	(50)	(50)	(50)	(50)
Cyst	3 (6%)	1 (2%)	1 (2%)	3 (6%)
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Inflammation, Chronic Active	8 (16%)	10 (20%)	6 (12%)	1 (2%)
Inflammation, Suppurative				1 (2%)
Prostate	(50)	(50)	(50)	(50)
Inflammation, Chronic Active			1 (2%)	
Seminal Vesicle	(50)	(50)	(50)	(49)
Atrophy	34 (68%)	34 (68%)	36 (72%)	33 (67%)
Cyst			1 (2%)	
Testes	(50)	(50)	(50)	(50)
Degeneration	8 (16%)	12 (24%)	11 (22%)	11 (22%)
Mineralization	7 (14%)	1 (2%)	2 (4%)	2 (4%)
Interstitial Cell, Hyperplasia	9 (18%)	6 (12%)	9 (18%)	7 (14%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Atrophy				1 (2%)
Myelofibrosis	1 (2%)		3 (6%)	
Lymph Node	(5)	(4)	(4)	(2)
Ectasia			1 (25%)	
Pancreatic, Ectasia	1 (20%)			
Lymph Node, Mandibular	(48)	(50)	(50)	(50)
Congestion	1 (2%)			1 (2%)
Hyperplasia	1 (2%)		1 (2%)	2 (4%)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Amyloid Deposition				1 (2%)

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

B 01

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
HEMATOPOIETIC SYSTEM - CONT				
Congestion		1 (2%)	1 (2%)	
Ectasia			1 (2%)	
Hyperplasia	1 (2%)			
Pigmentation, Lipofuscin	1 (2%)	1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Accessory Spleen	1 (2%)		1 (2%)	
Congestion	2 (4%)	3 (6%)		
Fibrosis	3 (6%)	2 (4%)	3 (6%)	4 (8%)
Hematopoietic Cell Proliferation	5 (10%)		2 (4%)	1 (2%)
Hyperplasia	1 (2%)			
Hyperplasia, Histiocytic		1 (2%)		
Inflammation, Granulomatous		1 (2%)		
Necrosis	1 (2%)	1 (2%)		
Pigmentation, Hemosiderin	1 (2%)		1 (2%)	1 (2%)
Capsule, Fibrosis		1 (2%)		
Lymphoid Follicle, Depletion Cellular		1 (2%)		
Thymus	(50)	(49)	(49)	(48)
Atrophy		1 (2%)	2 (4%)	
INTEGUMENTARY SYSTEM				
Mammary Gland	(45)	(47)	(47)	(47)
Cyst		1 (2%)		
Galactocele		2 (4%)		1 (2%)
Hyperplasia	4 (9%)	6 (13%)	4 (9%)	3 (6%)
Skin	(49)	(50)	(50)	(50)
Acanthosis			1 (2%)	
Hyperkeratosis		1 (2%)	1 (2%)	
Hyperplasia, Basal Cell	1 (2%)			
Inflammation, Chronic Active				1 (2%)
Mineralization				1 (2%)
Epidermis, Cyst	1 (2%)			
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)	1 (2%)	
Hydrocephalus		1 (2%)		

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

B 02

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Congestion			1 (2%)	2 (4%)
Hemorrhage				1 (2%)
Inflammation, Chronic Active	18 (36%)	7 (14%)	11 (22%)	11 (22%)
Metaplasia, Osseous		1 (2%)		
Necrosis			1 (2%)	
Parasite Metazoan		1 (2%)		
Alveolar Epithelium, Hyperplasia	11 (22%)	11 (22%)	20 (40%)	14 (28%)
Bronchiole, Epithelium, Hyperplasia				1 (2%)
Bronchus, Inflammation, Suppurative	1 (2%)			
Interstitium, Fibrosis			1 (2%)	1 (2%)
Nose	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)	1 (2%)		
Inflammation, Granulomatous		1 (2%)		
Inflammation, Suppurative		1 (2%)		1 (2%)
SPECIAL SENSES SYSTEM				
Eye		(1)	(1)	(2)
Hemorrhage			1 (100%)	
Lens Capsule, Mineralization				1 (50%)
Retina, Degeneration				2 (100%)
Retrobulbar, Inflammation, Chronic Active			1 (100%)	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Congestion				1 (2%)
Crystals				1 (2%)
Cyst			2 (4%)	4 (8%)
Infarct	1 (2%)			
Mineralization	1 (2%)		1 (2%)	
Nephropathy	42 (84%)	45 (90%)	47 (94%)	47 (94%)
Pigmentation	1 (2%)	1 (2%)		
Renal Tubule, Degeneration				1 (2%)
Renal Tubule, Necrosis	1 (2%)			
Urinary Bladder	(49)	(50)	(50)	(50)
Inflammation, Chronic Active		1 (2%)	6 (12%)	1 (2%)

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

B03

END OF REPORT

B 04

FINAL #1 CORE STUDY RATS

Facility: Battelle Columbus Laboratory

Chemical CAS #. 7632-00-0

Lock Date: 03/20/98

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

B 05

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	11	6	10	15
Natural Death	6	13	4	2
Survivors				
Terminal Sacrifice	33	31	36	33
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Fibroma			1 (2%)	
Intestine Small, Jejunum	(50)	(44)	(49)	(50)
Leiomyoma			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Oral Mucosa	(1)	(1)		
Squamous Cell Carcinoma	1 (100%)	1 (100%)		
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma				1 (2%)
Tongue		(2)	(1)	
Squamous Cell Carcinoma		1 (50%)	1 (100%)	
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(50)	(50)	(50)
Heart	(50)	(49)	(50)	(50)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Carcinoma		1 (2%)		1 (2%)
Adrenal Medulla	(50)	(50)	(45)	(49)
Pheochromocytoma Benign	4 (8%)	2 (4%)		2 (4%)
Pituitary Gland	(50)	(50)	(50)	(50)
Pars Distalis, Adenoma	24 (48%)	25 (50%)	17 (34%)	21 (42%)
Thyroid Gland	(50)	(49)	(48)	(50)
Bilateral, C-Cell, Adenoma				1 (2%)
C-Cell, Adenoma	7 (14%)	4 (8%)	10 (21%)	6 (12%)
C-Cell, Carcinoma	2 (4%)			1 (2%)
Follicular Cell, Adenoma	1 (2%)			

B 06

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
ENDOCRINE SYSTEM - cont				
Follicular Cell, Carcinoma	1 (2%)		1 (2%)	1 (2%)
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral Gland	(46)	(48)	(49)	(49)
Adenoma	8 (17%)	8 (17%)	5 (10%)	3 (6%)
Carcinoma	2 (4%)	1 (2%)		1 (2%)
Bilateral, Adenoma		2 (4%)	1 (2%)	
Ovary	(50)	(49)	('	(50)
Granulosa Cell Tumor Benig		1 (2%)		
Schwannoma Malignant			1 (2%)	
Sertoli Cell Tumor Malignant			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Adenocarcinoma	2 (4%)			
Adenoma		1 (2%)		
Polyp Stromal	7 (14%)	3 (6%)	8 (16%)	7 (14%)
Sarcoma Stromal			1 (2%)	
Cervix, Carcinoma		1 (2%)		
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Lymph Node	(2)	(1)	(2)	(1)
Carcinoma, Metastatic, Lung			1 (50%)	
Mediastinal, Carcinoma, Metastatic, Adrenal Cortex		1 (100%)		
Lymph Node, Mandibular	(49)	(49)	(50)	(50)
Carcinoma, Metastatic, Zymbal's Gland				1 (2%)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(50)
Thymus	(49)	(47)	(49)	(48)
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)		3 (6%)
Adenoma, Multiple	1 (2%)			
Carcinoma	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Fibroadenoma	14 (28%)	14 (28%)	18 (36%)	20 (40%)

B 07

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
INTEGUMENTARY SYSTEM - cont				
Fibroadenoma, Multiple	7 (14%)	13 (26%)	13 (26%)	5 (10%)
Skin	(50)	(50)	(50)	(50)
Basal Cell Adenoma				1 (2%)
Basal Cell Carcinoma	1 (2%)			1 (2%)
Fibroma	1 (2%)		1 (2%)	1 (2%)
Fibrosarcoma				1 (2%)
Hemangiopericytoma	1 (2%)			
Lipoma			2 (4%)	
Squamous Cell Carcinoma	1 (2%)			1 (2%)
Trichoepithelioma	1 (2%)			
Pinna, Melanoma Malignant		1 (2%)		1 (2%)
Subcutaneous Tissue, Fibroma			1 (2%)	
MUSCULOSKELETAL SYSTEM				
None				
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Astrocytoma Malignant			1 (2%)	
Spinal Cord			(1)	
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	3 (6%)	2 (4%)	3 (6%)	2 (4%)
Alveolar/Bronchiolar Carcinoma			1 (2%)	
Carcinoma, Metastatic, Adrenal Cortex		1 (2%)		
Sarcoma			1 (2%)	
Nose	(50)	(49)	(50)	(50)
Squamous Cell Carcinoma, Metastatic, Skin				1 (2%)
SPECIAL SENSES SYSTEM				
Zymbal's Gland			(2)	(2)
Carcinoma			1 (50%)	1 (50%)

B 08

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Nephroblastoma			1 (2%)	
Renal Tubule, Adenoma				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Leukemia Mononuclear	15 (30%)	10 (20%)	1 (2%)	1 (2%)

* Number of animals with any tissue examined microscopically

B 09

FISCHER 344 RATS FEMALE	0.0%	0.075%	0.15%	0.30%
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	45	45	49	45
Total Primary Neoplasms	107	94	95	87
Total Animals with Benign Neoplasms	42	42	46	42
Total Benign Neoplasms	81	77	82	75
Total Animals with Malignant Neoplasms	23	16	12	12
Total Malignant Neoplasms	26	17	13	12
Total Animals with Metastatic Neoplasms		1	1	2
Total Metastatic Neoplasm		2	1	2
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

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

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
DISPOSITION SUMMARY				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	16	4	12	8
Natural Death	5	8	2	6
Survivors				
Terminal Sacrifice	29	37	36	36
Natural Death		1		
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Intestine Large, Colon	(50)	(50)	(50)	(50)
Carcinoma		1 (2%)		
Leiomyosarcoma				1 (2%)
Schwannoma Malignant, Metastatic, Heart	1 (2%)			
Intestine Large, Cecum	(50)	(50)	(50)	(49)
Intestine Small, Duodenum	(49)	(50)	(50)	(50)
Intestine Small, Jejunum	(50)	(48)	(50)	(49)
Intestine Small, Ileum	(50)	(49)	(50)	(49)
Liver	(50)	(50)	(50)	(50)
Hepatocellular Adenoma			1 (2%)	
Histiocytic Sarcoma		1 (2%)		1 (2%)
Leiomyosarcoma, Metastatic, Intestine Large, Colon				1 (2%)
Sarcoma, Metastatic, Uncertain Primary Site				1 (2%)
Schwannoma Malignant, Metastatic, Heart	1 (2%)			
Mesentery	(11)	(7)	(5)	(8)
Fat, Leiomyosarcoma, Metastatic, Intestine Large, Colon				1 (13%)
Fat, Sarcoma		1 (14%)		
Oral Mucosa	(2)		(1)	
Pharyngeal, Squamous Cell Carcinoma			1 (100%)	
Pancreas	(50)	(50)	(50)	(49)
Leiomyosarcoma, Metastatic, Intestine Large, Colon				1 (2%)
Acinus, Adenocarcinoma		2 (4%)		
Acinus, Adenoma			1 (2%)	
Acinus, Carcinoma		1 (2%)		
Stomach, Forestomach	(50)	(50)	(50)	(50)
Sarcoma, Metastatic, Uncertain Primary Site				1 (2%)
Squamous Cell Papilloma	1 (2%)		1 (2%)	
Stomach, Glandular	(50)	(50)	(50)	(50)

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
ALIMENTARY SYSTEM - cont				
Carcinoid Tumor Benign			1 (2%)	
Leiomyosarcoma	1 (2%)			
Sarcoma, Metastatic, Uncertain Primary Site				1 (2%)
Schwannoma Malignant, Metastatic, Heart	1 (2%)			
CARDIOVASCULAR SYSTEM				
Blood Vessel	(50)	(50)	(50)	(50)
Heart	(50)	(50)	(50)	(50)
Schwannoma Malignant	1 (2%)			
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma			1 (2%)	
Adrenal Medulla	(50)	(50)	(50)	(50)
Pheochromocytoma Malignant	1 (2%)	1 (2%)		1 (2%)
Pheochromocytoma Benign	5 (10%)	10 (20%)	6 (12%)	9 (18%)
Bilateral, Pheochromocytoma Benign	1 (2%)			1 (2%)
Islets, Pancreatic	(50)	(50)	(50)	(49)
Adenoma	4 (8%)			1 (2%)
Carcinoma	1 (2%)			2 (4%)
Parathyroid Gland	(45)	(48)	(49)	(48)
Adenoma			1 (2%)	
Pituitary Gland	(50)	(49)	(50)	(50)
Sarcoma NOS				1 (2%)
Pars Distalis, Adenoma	13 (26%)	13 (27%)	15 (30%)	10 (20%)
Pars Intermedia, Adenoma				1 (2%)
Thyroid Gland	(50)	(50)	(50)	(50)
C-Cell, Adenoma	12 (24%)	8 (16%)	7 (14%)	4 (8%)
C-Cell, Adenoma, Multiple				1 (2%)
C-Cell, Carcinoma	2 (4%)		2 (4%)	1 (2%)
Follicular Cell, Adenoma	1 (2%)		1 (2%)	1 (2%)
Follicular Cell, Carcinoma	1 (2%)			
GENERAL BODY SYSTEM				
None				

NTP Experiment-Test: 88007-05 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a) Report: PEIRPT05
Study Type: CHRONIC SODIUM NITRITE Date: 10/18/99
Route: DOSED WATER Time: 13:52:35

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Preputial Gland	(50)	(50)	(50)	(50)
Adenoma		3 (6%)	1 (2%)	2 (4%)
Carcinoma	5 (10%)	1 (2%)	7 (14%)	5 (10%)
Prostate	(50)	(50)	(50)	(50)
Seminal Vesicle	(50)	(50)	(50)	(49)
Testes	(50)	(50)	(50)	(50)
Bilateral, Interstitial Cell, Adenoma	37 (74%)	44 (88%)	38 (76%)	40 (80%)
Interstitial Cell, Adenoma	10 (20%)	2 (4%)	9 (18%)	6 (12%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Histiocytic Sarcoma				1 (2%)
Lymph Node	(5)	(4)	(4)	(2)
Carcinoma, Metastatic, Thyroid Gland	1 (20%)			
Deep Cervical, Histiocytic Sarcoma		1 (25%)		
Pancreatic, Sarcoma, Metastatic, Uncertain Primary Site				1 (50%)
Lymph Node, Mandibular	(48)	(50)	(50)	(50)
Histiocytic Sarcoma		1 (2%)		
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Sarcoma, Metastatic, Uncertain Primary Site				1 (2%)
Spleen	(50)	(50)	(50)	(50)
Fibroma				1 (2%)
Fibrosarcoma		1 (2%)		
Histiocytic Sarcoma				1 (2%)
Sarcoma, Metastatic, Uncertain Primary Site				1 (2%)
Thymus	(50)	(49)	(49)	(48)
Histiocytic Sarcoma		1 (2%)		
INTEGUMENTARY SYSTEM				
Mammary Gland	(45)	(47)	(47)	(47)
Carcinoma			1 (2%)	
Fibroadenoma	3 (7%)	5 (11%)	2 (4%)	
Fibroadenoma, Multiple			1 (2%)	
Skin	(49)	(50)	(50)	(50)
Basal Cell Adenoma		1 (2%)		
Basal Cell Carcinoma	1 (2%)			
Fibroma		1 (2%)	5 (10%)	3 (6%)
Fibroma, Multiple			1 (2%)	
Fibrosarcoma	1 (2%)			2 (4%)
Keratoacanthoma	2 (4%)	3 (6%)	1 (2%)	3 (6%)

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
INTEGUMENTARY SYSTEM - cont				
Keratoacanthoma, Multiple				1 (2%)
Lipoma	1 (2%)			
Sarcoma			1 (2%)	
Squamous Cell Carcinoma		1 (2%)		
Trichoepithelioma		1 (2%)		
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma				1 (2%)
Maxilla, Osteosarcoma	1 (2%)			
Skeletal Muscle	(1)			(1)
Sarcoma, Metastatic, Uncertain Primary Site				1 (100%)
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Histiocytic Sarcoma		1 (2%)		
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	2 (4%)	3 (6%)	2 (4%)	2 (4%)
Alveolar/Bronchiolar Carcinoma			1 (2%)	
Carcinoma, Metastatic, Thyroid Gland	1 (2%)			
Histiocytic Sarcoma		1 (2%)		
Leiomyosarcoma, Metastatic, Intestine Large, Colon				1 (2%)
Schwannoma Malignant, Metastatic, Heart	1 (2%)			
Trachea	(50)	(50)	(50)	(50)
SPECIAL SENSES SYSTEM				
Harderian Gland		(2)		
Histiocytic Sarcoma		1 (50%)		
Zymbal's Gland	(1)			(2)
Carcinoma	1 (100%)			2 (100%)

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Renal Tubule, Adenoma			1 (2%)	
Urinary Bladder	(49)	(50)	(50)	(50)
Transitional Epithelium, Papilloma	1 (2%)			
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Histiocytic Sarcoma		1 (2%)		1 (2%)
Leukemia Mononuclear	17 (34%)	12 (24%)	7 (14%)	3 (6%)
Lymphoma Malignant		1 (2%)		
Mesothelioma Malignant	3 (6%)	3 (6%)	4 (8%)	1 (2%)

* Number of animals with any tissue examined microscopically

C 01

FISCHER 344 RATS MALE	0.0%	0.075%	0.15%	0.30%
TUMOR SUMMARY				
Total Animals with Primary Neoplasms (b)	49	49	50	50
Total Primary Neoplasms	129	120	123	107
Total Animals with Benign Neoplasms	47	48	49	49
Total Benign Neoplasms	93	94	99	86
Total Animals with Malignant Neoplasms	30	22	21	20
Total Malignant Neoplasms	36	26	24	21
Total Animals with Metastatic Neoplasms	2			2
Total Metastatic Neoplasm	6			11
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

C 02

END OF REPORT

C 03

C 04

CERTIFICATE OF AUTHENTICITY

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Date produced 10 (Month) 18 (Day) 00 (Year)

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