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Dear Document Control Office (7407):

In compliance with the National Toxicology Program's (NTP) mission to keep our colleagues informed of the current NTP findings during ongoing studies, a copy of the Pathology Working Group (PWG) report and the Summary Pathology Tables for the chronic Gavage study on TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE) (TEFDIOXINMIX) are enclosed for your review.

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

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

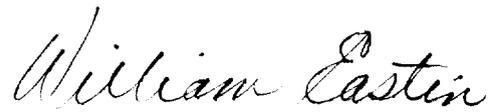
A wide variety of NTP information is also available in electronic format on the world-wide web, for example, the NTP Annual Plan, abstracts of NTP Reports, study data, and the status of all NTP studies. To view this information requires access to the internet and a Web browser such as Netscape Navigator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

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



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

Sincerely,

A handwritten signature in black ink that reads "William Eastin". The signature is written in a cursive, flowing style.

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

Encls: PWG Report and Pathology Summary Tables for Female Harlan SD Rats
cc: Central Data Management

NATIONAL TOXICOLOGY PROGRAM

TR-526 --2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN (TCDD), 2,3,4,7,8-PENTACHLORODIBENZOFURAN (PCDF) and 3,3,4,4,5-PENTACHLOROBIPHENYL (PCB 126) (DIOXIN MIXTURE)

Pathology Tables – Female Rats Scheduled Sacrifice 14 wk

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

Pathology Tables – Female Rats Scheduled Sacrifice 31 wk

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

Pathology Tables – Female Rats Scheduled Sacrifice 53 wk

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

Pathology Tables – Female Rats Core Study

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

PATHOLOGY WORKING GROUP CHAIRPERSON'S REPORT

Chronic gavage study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF), and 3,3',4,4',5-Pentachlorobiphenyl (PCB 126) (Dioxin Mixture) in female Harlan Sprague-Dawley rats

Participants: Drs. M. Jokinen (PAI - PWG Chairperson), A. Brix (EPL-QAP), K.Cimon (EPL), G. Flake (NIEHS), J. Hailey (NIEHS), R. Herbert (NIEHS), R. Maronpot (NIEHS), J. Nold (GlaxoSmithKline), A. Nyska (NIEHS), D. Sells (Battelle Columbus-SP), and Y. Tani (NIEHS - Observer)

Date: October 10, 2002

Site: NIEHS, Research Triangle Park, NC

The PWG was convened to evaluate selected slides from the two year gavage study of the tertiary mixture of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,3,4,7,8-pentachlorodibenzofuran (PeCDF), and 3,3',4,4',5-pentachlorobiphenyl (PCB 126) in female Harlan Sprague-Dawley rats. A preliminary Special PWG had been held on September 5, 2001 to standardize terminology to be used during the QA review and for future studies.

After reviewing approximately one half of the liver slides and finding there was excellent agreement among the PWG members concerning the findings, the PWG recommended, due to the large total number of liver slides to be reviewed, that the remaining liver slides be reviewed later by a smaller group of pathologists rather than all being reviewed by the complete PWG. Consequently, the remaining liver slides were reviewed by Drs. Nyska, Brix, and Sells immediately after the other PWG members had left and their findings are included in this report. In addition, a number of disagreements over minor miscellaneous lesions were reviewed and resolved by Drs. Jokinen and Nyska immediately following review of the remaining liver slides, and those findings are also included in this report.

Animals were sacrificed for interim evaluation at 14 weeks, 31 weeks, and 53 weeks after the beginning of the study, and the remaining animals were sacrificed at study termination at two years. Dose levels in TEQ (toxic equivalents) and numbers of animals examined microscopically per dose group at each interim sacrifice and at the two year terminal sacrifice were as follows:

	TEQ=0	TEQ=10	TEQ=22	TEQ=46	TEQ=100
14-Wk	10	10	10	10	10
31-Wk	10	10	10	10	10
53-Wk	8	8	8	8	8
2-Yr	53	53	53	53	53

The study was conducted at Battelle Columbus. The Study Pathologist (SP) was Dr. D. Sells and the Quality Assessment Pathologist (QAP) was Dr. A. Brix of EPL.

A number of organs were considered to be potential target organs and were reviewed by the QAP for all diagnoses, neoplastic and nonneoplastic. All neoplasms from all organs from all animals were also reviewed. The following were considered potential target organs and were reviewed from **all sacrifices** (14, 31, and 53 week and terminal sacrifices):

Liver
Lung
Pancreas
Adrenal Cortex

The following organs were reviewed from all animals from **all sacrifices** (14, 31, and 53 week and terminal sacrifice) for the specific diagnosis listed:

Thymus – Atrophy
Uterus – Metaplasia, Squamous

The following organs were reviewed from all animals from the **14-week and 31-week interim sacrifices** for the specific diagnosis listed:

Ovary, Corpus Luteum -- Atrophy

The following organs were reviewed from all animals from the **terminal sacrifice** for the specific diagnoses listed:

Mesentery, Artery – Inflammation, Chronic Active
Oral Mucosa, Gingival – Squamous Cell Carcinoma
Oral Mucosa, Gingival – Hyperplasia, Squamous
Tooth, Periodontal Tissue -- Inflammation
Heart – Cardiomyopathy
Thyroid Gland, Follicle – Atrophy
Ovary – Inflammation, Chronic Active
Bone Marrow -- Hyperplasia
Kidney – Nephropathy
Urinary Bladder, Transitional Epithelium -- Hyperplasia

The following organs were reviewed from animals from the **terminal sacrifice** when the specific diagnoses listed were present:

Brain, Corpus Callosum – Edema
Brain, Corpus Callosum, Cerebrum – Edema
Brain – Gliosis
Brain – Necrosis

Brain, Cerebrum – Necrosis
Nose – Inflammation
Nose, Turbinate -- Inflammation
Nose, Respiratory Epithelium -- Hyperplasia
Nose, Septum, Respiratory Epithelium – Hyperplasia
Nose, Turbinate – Hyperplasia
Nose, Turbinate, Goblet Cell – Hyperplasia
Nose, Turbinate, Respiratory Epithelium – Hyperplasia
Kidney – Casts, Protein
Kidney, Renal Tubule -- Hyperplasia
Kidney, Papilla, Transitional Epithelium – Hyperplasia
Kidney, Pelvis, Transitional Epithelium – Hyperplasia
Pituitary Gland -- Angiectasis
Pituitary Gland – Cyst
Pituitary Gland – Cytoplasmic Alteration
Pituitary Gland – Vacuolization, Cytoplasmic
Uterus – Hyperplasia, Adenomatous

SUMMARY OF PWG FINDINGS

Liver

Cholangiocarcinoma and Cholangiocarcinoma, Multiple occurred with moderate combined incidences in the TEQ=100 and TEQ=46 groups and with a few in the TEQ=22 group.

Incidences of several nonneoplastic liver lesions were increased in treated groups as compared with controls, with the greatest increases generally being in the TEQ=100 group. These lesions included **Cholangiofibrosis, Eosinophilic and Mixed Cell Focus, Fatty Change, Inflammation, Necrosis, Pigmentation, Regeneration, Bile Duct Cyst, Bile Duct Hyperplasia, Oval Cell Hyperplasia, Multinucleated Hepatocytes, Hepatocyte Hypertrophy, and Portal Fibrosis.**

Lung

Cystic Keratinizing Epithelioma and Cystic Keratinizing Epithelioma, Multiple occurred in numerous animals in the TEQ=100 group and a few animals in the TEQ=46 group.

Squamous Metaplasia occurred with modestly increased incidence in the TEQ=46 and TEQ=100 groups.

Bronchiolar Metaplasia of the alveolar epithelium occurred with moderate to moderately high incidence in all treated groups. **Alveolar Epithelium Hyperplasia** occurred with higher incidence in control and lower dose groups than in the higher dose groups.

Acinar Pancreas

Carcinoma or **Adenoma** occurred in a few animals in the TEQ=10, TEQ=22, and TEQ=46 groups.

Incidences of **Atrophy, Chronic Active Inflammation** (generally seen in association with atrophy), **Cytoplasmic Vacuolization**, and **Artery, Chronic Active Inflammation** were increased in treated groups, particularly in the TEQ=100 group, as compared with controls.

Adrenal Cortex

Adenoma or **Carcinoma** occurred in a few animals from treated groups only.

The incidences of **Atrophy, Hyperplasia, Cystic Degeneration**, and **Cytoplasmic Vacuolization** of the adrenal cortex were increased in treated groups as compared with controls.

Uterus

Incidences of **Squamous Metaplasia** were increased in all treated groups as compared with controls.

Squamous Cell Carcinoma of the uterus or cervix occurred in a small number of animals in some of the treated groups.

Gingival Oral Mucosa

Squamous Hyperplasia occurred with increased incidences in all treated groups as compared with controls, and was often associated with inflammation of the periodontal tissue. **Squamous Cell Carcinoma** occurred with very low incidence in some groups, including controls.

Tooth Peridontal Tissue

The incidence and average severity of **Inflammation** was increased in the TEQ=46 and TEQ=100 groups as compared with other groups. Foreign bodies (hair shafts) were often seen with the inflammation.

Kidney

The incidence and average severity of **Nephropathy** was increased in all treated groups as compared with controls.

Heart

The incidence of slight **Cardiomyopathy** was prominently increased in all treated groups as compared with controls.

Thyroid Gland

Follicular Cell Hypertrophy occurred with increased incidences in the interim and terminal sacrifice treated groups, as compared with controls. The incidence was greatest in the TEQ=100 group.

Mesentery

Artery Chronic Active Inflammation occurred in one or more animals in the TEQ=10, TEQ=46, and TEQ=100 groups. The incidence was highest in the TEQ=100 group.

Thymus

Atrophy occurred with greater incidence and average severity, as compared with controls, in all the treated interim sacrifice and terminal sacrifice groups.

Ovary

Atrophy was observed with greater incidence in the TEQ=100 at the 14-week interim sacrifice as compared with the other treated groups and controls. The incidence of **Chronic Active Inflammation** was marginally increased in all treated groups as compared with controls, and the incidence was highest in the TEQ=100 group.

Bone Marrow

Hyperplasia occurred with greater incidence and/or severity in the treated groups as compared with controls.

Brain

Necrosis or **Edema** occurred in a few animals in the TEQ=46 and TEQ=100 groups. One animal with Necrosis in the TEQ=100 group also had **Artery Degeneration** in the affected area.

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

LIVER

The SP diagnosed increased incidences of a number of neoplastic and nonneoplastic lesions in treated groups. These lesions generally occurred with

greatest incidence in the TEQ=100 group but many also occurred, generally with lower incidences, in other treated groups. Neoplastic lesions included **Cholangiocarcinoma** and **Multiple Cholangiocarcinoma**. Nonneoplastic lesions included **Cholangiofibrosis**, **Eosinophilic and Mixed Cell Focus**, **Fatty Change**, **Inflammation**, **Necrosis**, **Pigmentation**, **Regeneration**, **Bile Duct Cyst**, **Bile Duct Hyperplasia**, **Oval Cell Hyperplasia**, **Multinucleated Hepatocytes**, **Hepatocyte Hypertrophy**, and **Portal Fibrosis**. In addition, at the direction of the special preliminary PWG, the QAP added diagnoses of **Toxic Hepatopathy** and **Regeneration**, which were confirmed by the PWG Chair.

The SP had diagnosed increased incidences of Adenoma and Multiple Adenoma in treated groups. The PWG examined all diagnosed hepatocellular neoplasms and in all cases considered the lesion diagnosed as adenoma to represent either an area of regeneration or, less commonly, a focus. The PWG also reviewed examples of cholangiocarcinoma, and various nonneoplastic lesions and confirmed the diagnoses. The microscopic appearances of the various liver lesions are described below. Hepatocellular adenoma is included for the sake of completeness and to describe the criteria used to determine whether a lesion was an adenoma.

Cholangiocarcinoma consisted of an irregular, relatively large, non-circumscribed lesion that replaced normal liver parenchyma. The lesion consisted of fibrous connective tissue stroma containing numerous atypical bile ducts, which frequently contained mucinous material and cellular debris. The epithelium forming the atypical bile ducts was often discontinuous, consisted usually of large atypical cells, and displayed degenerative changes. Mitotic figures and localized invasion of adjacent liver parenchyma were also observed. **Cholangiofibrosis** appeared similar to cholangiocarcinoma but was a much smaller, well demarcated lesion which did not show evidence of localized invasion.

Hepatocellular Adenoma was a nodular mass that usually was larger than a focus, had a distinct border, and produced compression of surrounding normal parenchyma. Adenoma was composed of a rather uniform population of mildly to moderately pleomorphic hepatocytes that generally were normal size or slightly larger than normal hepatocytes and were arranged in abnormal lobular patterns. The hepatic cords within an adenoma usually intersected the surrounding normal hepatic cords at an oblique angle or sometimes even at a right angle. The presence of bile ducts, proliferating oval cells, portal areas, or blood vessels was not considered to be characteristic of hepatocellular adenoma.

Eosinophilic Focus was characterized by a focus of hepatocytes with altered tinctorial properties. Eosinophilic Focus was composed principally of cells with eosinophilic cytoplasm. To be classified as an Eosinophilic Focus at least 80% of the cells within the focus had to be eosinophilic cells, otherwise the focus was classified as a **Mixed Cell Focus**. Mixed cell focus was composed of a mixture of cells with different staining properties, generally a mixture of eosinophilic cells

and cells with clear cytoplasm (clear cells). The margins of the focus were distinct, but the hepatic cords often merged imperceptibly with the surrounding hepatic cords. Some foci had a more definite border and the cords within the focus were not always smoothly continuous with those in the surrounding parenchyma. In addition, some larger foci caused variable degrees of compression of the surrounding hepatic parenchyma. Hepatocytes within foci were generally somewhat larger than normal but appeared otherwise normal. The cells were arranged in a relatively normal lobular pattern and foci sometimes contained blood vessels and/or portal areas. The presence of proliferating bile ducts or oval cells, however, was not considered characteristic of a focus.

Regeneration was characterized by areas of focal hypertrophy and hyperplasia of hepatocytes and was considered to be due to the presence of a proliferative stimulus. Areas of regeneration varied in size with some regenerative areas being quite large while others were smaller and were the size of large foci. Regeneration was seen most commonly in this study in the higher dose groups in which prominent toxic changes were present. However, a lesser degree of regeneration was sometimes seen in lower dose animals in which toxic changes were minimal to inapparent, suggesting the presence of an hepatocellular proliferative stimulus that may have been independent of the toxic changes.

Regeneration was characterized by multiple, small to large, nodular foci generally composed of hepatocytes that were considerably larger than normal hepatocytes (hepatocyte hypertrophy) sometimes mixed with areas of increased numbers of small hepatocytes (hepatocyte hyperplasia). The cells within regeneration generally were very large, larger than cells seen within adenomas and usually larger than cells seen within foci, with abundant eosinophilic cytoplasm and often with variable degrees of cytoplasmic vacuolization. In a few areas of regeneration, however, the cells were of more normal size or sometimes slightly smaller than normal. The cells appeared to be arranged in normal cords, but the cells often were so large as to obscure the sinusoids between the cords giving the appearance of solid sheets of hepatocytes. Bile duct hyperplasia, indicative of a proliferative response, and portal areas were usually present within regeneration. Blood vessels and/or central veins were also sometimes seen within areas of regeneration, usually when hepatocytes were not so hypertrophic as to obscure completely the normal architecture. The presence of hypertrophic, vacuolated hepatocytes together with portal areas and/or proliferating bile ducts, and possibly with central veins and/or blood vessels were considered to be characteristic of regeneration, and were considered the hallmarks that differentiated regeneration from adenoma. In those cases in which the hepatocytes were more normal sized, the presence of portal areas and/or proliferating bile ducts served to differentiate regeneration from focus or adenoma. Areas of regeneration often blended with the surrounding parenchyma. However, large, focal to multifocal areas of regeneration were sometimes seen that caused compression of surrounding tissue, and/or bulging of the capsular surface. The opinion of the PWG was that since this lesion is included as part of toxic hepatopathy, which is graded, there

was no need to grade the severity of regeneration. Therefore, this change was not graded but rather just recorded as being present.

The QAP had changed a number of diagnoses of foci made by the SP to regeneration. The PWG Chair concurred with the QAP. In addition, the PWG Chair noted a number of additional cases of regeneration that had been diagnosed as foci by the SP but had not been changed by the QAP. The PWG Chair showed a number of these to the PWG which agreed with the PWG Chair's diagnoses of regeneration. Consequently, in the remaining cases in which the PWG Chair diagnosed regeneration instead of focus, the diagnosis should be changed from focus to regeneration.

Hepatocyte Hypertrophy was characterized by enlarged hepatocytes with increased amounts of cytoplasm. In hypertrophy of minimal severity periportal hepatocytes often had deeply eosinophilic cytoplasm while centrilobular hepatocytes had clearer, paler cytoplasm. In more severe hypertrophy hepatocytes were diffusely enlarged with abundant eosinophilic cytoplasm. The SP had diagnosed the hypertrophy using the diagnosis **Hepatocyte, Periportal – Hypertrophy**. However, the PWG for TCDD had recommended that the diagnosis of Hepatocyte, Periportal -- Hypertrophy be replaced with the more general diagnosis **Hepatocyte – Hypertrophy** in all of the studies in this group. Therefore, the diagnosis of Hepatocyte, Periportal – Hypertrophy was changed in all animals to Hepatocyte – Hypertrophy.

Multinucleated Hepatocytes was characterized by scattered hepatocytes that were enlarged and contained multiple (more than 2 and often 4-6) nuclei. The presence of binucleated hepatocytes was not sufficient to make this diagnosis. This lesion had been called Cellular Atypia by the SP but at the special preliminary PWG it was decided that the diagnosis of Multinucleated Hepatocytes was more appropriate.

Inflammation was generally a minor change consisting of accumulation of mononuclear cells (predominantly lymphocytes and plasma cells, with occasional macrophages) most often within portal areas but also sometimes randomly scattered throughout the liver.

Bile Duct Hyperplasia consisted of increased numbers of portal bile ducts.

Oval Cell Hyperplasia consisted of small ovoid cells with basophilic cytoplasm and a round to ovoid nucleus that were arranged in single or double rows and located predominantly in the portal areas.

Pigmentation consisted of light brown to golden pigment present within macrophages and occasionally hepatocytes. The pigmented macrophages were often seen in portal areas but were also seen scattered randomly within the liver.

Toxic Hepatopathy was a diagnosis added by the QA pathologist during the QA review that included all nonneoplastic liver changes under one overall term. The severity of the toxic hepatopathy was graded in order to give one overall severity grade for the degree of toxicity in a liver. The purpose of this was to allow for easier comparison of the degree of toxic change among different dose groups than would be possible if the severities of all the individual nonneoplastic changes had to be compared among the different groups. This diagnosis was used in addition to, not instead of, any of the nonneoplastic diagnoses already made. The changes included under the diagnosis included focal cellular alteration, multinucleated hepatocytes, cystic degeneration, fatty change, inflammation, necrosis, pigmentation, regeneration; bile duct cysts, bile duct hyperplasia, hepatocyte degeneration, hepatocyte hypertrophy, oval cell hyperplasia, and portal fibrosis. Some treated animals occasionally had just a few of these changes present but this was not considered to be sufficient liver involvement to warrant a diagnosis of toxic hepatopathy.

Bile Duct Cyst was characterized by either single or multiple dilated bile ducts that were lined by attenuated epithelium.

Portal Fibrosis consisted of fibrous connective tissue accumulation that extended between adjacent portal areas.

Necrosis consisted of scattered necrotic areas of hepatic parenchyma that were often randomly distributed, but occasionally, in more severe cases, were distributed more diffusely.

Focal or Diffuse Fatty Change was generally a minor change consisting of discrete clear vacuoles (consistent with lipid) in the cytoplasm of hepatocytes and involving either foci of hepatocytes (focal fatty change) or scattered diffusely throughout the liver (diffuse fatty change).

LUNG

Cystic Keratinizing Epithelioma and Cystic Keratinizing Epithelioma, Multiple occurred in several animals in the TEQ=100 group and in a few animals in the TEQ=46 group. **Cystic keratinizing epithelioma** occurred either singly or as multiple lesions within the same lung. They ranged from relatively small lesions to large lesions that replaced a substantial amount of the normal lung parenchyma. They consisted of cystic structures composed of a highly irregular wall of highly keratinized stratified squamous epithelium and a center filled with keratin. The outer portion of the lesion grew by expansion into the adjacent lung but evidence of invasion was not observed. The SP had diagnosed these lesions as Squamous Cell Carcinoma but during the preliminary PWG it was decided these lesions represented Cystic Keratinizing Epithelioma rather than Squamous Cell Carcinoma.

Squamous Metaplasia occurred in a few animals in the TEQ=46 and TEQ=100 groups. It was generally a minor change consisting of one or more small, irregular foci of keratinizing stratified squamous epithelium that had replaced the normal alveolar epithelium.

Bronchiolar Metaplasia of the alveolar epithelium occurred with moderate to moderately high incidence in all treated groups. The lesion often diffusely affected the epithelium located near the terminal bronchioles at the bronchiolar-alveolar junction and the adjacent alveoli, although in cases of lesser severity it consisted of a multifocal rather than diffuse change. Bronchiolar metaplasia consisted of replacement of the normal alveolar epithelium by cuboidal to columnar, sometimes ciliated cells, and was often accompanied by prominent mucus production in the affected areas. Aggregates of large alveolar macrophages were sometimes present in the areas of bronchiolar metaplasia. Bronchiolar Metaplasia had been diagnosed as Alveolar Epithelium Hyperplasia by the SP, but during the special preliminary PWG it was decided that the term Bronchiolar Metaplasia was more appropriate. The QAP had retained a number of the SP's diagnoses of Alveolar Epithelial Hyperplasia that were considered by the PWG Chair to represent Bronchiolar Metaplasia. The PWG examined some representative examples and concurred with the PWG Chair's diagnoses. Consequently, in the remaining cases in which the PWG Chair diagnosed bronchiolar metaplasia instead of alveolar epithelium hyperplasia, the diagnosis should be changed from alveolar epithelial hyperplasia to bronchiolar metaplasia.

A number of animals in each of the groups, including controls, had a lung change that had some similarities to bronchiolar metaplasia, and which had also been diagnosed as **Alveolar Epithelium Hyperplasia** by the SP. This change in controls was also characterized by extension of cuboidal bronchiolar epithelial cells into adjacent alveoli. However, unlike bronchiolar metaplasia, prominent mucus production was not observed and a very prominent inflammatory cell infiltrate, consisting of large aggregates of alveolar macrophages commonly mixed with focal aggregates of neutrophils, was generally associated with the affected areas. Representative lungs from treated and control animals were examined by the TCDD special PWG. After careful examination the PWG found that the Bronchiolar Metaplasia and Alveolar Epithelium Hyperplasia could be separated by the prominent inflammatory component seen with Alveolar Epithelium Hyperplasia, and the prominent mucus production seen with Bronchiolar Metaplasia. Consequently, the PWG concluded it was most appropriate to retain the SP's diagnoses of **Alveolar Epithelium Hyperplasia** in cases with prominent inflammation and lack of mucus production.

(NOTE -- As a post-PWG action item the TCDD special PWG recommended staining the lungs from TCDD study animals with Alcian Blue and Periodic Acid Schiff (PAS) stains to detect the presence of mucus. These slides were examined by Drs. A. Nyska of NIEHS and M. Jokinen, the PWG Chair, who both found that, overall, the amount of mucus in the treated lungs was greater than that seen in the control lungs, thus confirming the observation of the special PWG participants.)

Aggregates of large, clear alveolar histiocytes, a change diagnosed as **Hyperplasia, Histiocytic** by the SP, were often present in lungs of animals from all groups, including controls. The TCDD PWG examined an example of histiocytic hyperplasia diagnosed by the SP and considered the diagnosis **Infiltrate Cellular, Histiocyte** to be more appropriate. The PWG recommended that the term Hyperplasia, Histiocytic be replaced with Infiltrate Cellular, Histiocyte in all of the studies in this group. Therefore, all diagnosis of Hyperplasia, Histiocytic in this study were replaced by the diagnosis Infiltrate Cellular, Histiocytic.

The PWG examined examples of cystic keratinizing epithelioma, squamous metaplasia, and bronchiolar metaplasia and in each case confirmed the diagnosis.

ACINAR PANCREAS

Adenoma and **Carcinoma** of the acinar cells occurred in a few animals in the TEQ=10, TEQ=22, and TEQ=46 groups. Incidences of **Atrophy, Chronic Active Inflammation** (generally seen in association with atrophy), **Cytoplasmic Vacuolization**, and **Artery Chronic Active Inflammation** were increased in treated groups, particularly in the TEQ=100 group, as compared with controls.

Adenoma was characterized microscopically by a discrete mass consisting of tubular and acinar structures composed of small acinar cells with brightly eosinophilic cytoplasm and lacking zymogen granules. In contrast, **Carcinoma** was a large lesion, usually with moderate amounts of dense fibrous stroma. **Carcinomas** were composed of densely packed clusters of poorly formed acinar structures consisting of small acinar cells with prominent vesicular nuclei and small amounts of eosinophilic cytoplasm with indistinct borders. Scattered solid areas composed of densely packed, highly pleomorphic, round to ovoid acinar cells with large vesicular nuclei and scant cytoplasm were also seen.

Atrophy was a focal to multifocal to diffuse change consisting of a reduction in the amount of acinar tissue with an associated increase in stromal fibrous connective tissue. **Chronic Active Inflammation** usually was seen in association with **Atrophy** and consisted of an infiltrate of mononuclear cells and a few neutrophils within the stroma. **Cytoplasmic Vacuolization** consisted of small, clear, discrete intracytoplasmic vacuoles within pancreatic acinar cells. Sometimes these vacuoles coalesced to form larger single vacuoles. The severity of the change was determined by the degree of vacuolization per cell and the amount of tissue involved. **Artery Chronic Active Inflammation** was a focal to multifocal change characterized by a thick mantle of macrophages, lymphocytes and plasma cells around the arteries, with infiltration into the muscular layers of the artery. There was often fibrinoid necrosis of the vessel, and the tunica intima was frequently thickened. Endothelial cells were swollen, or decreased in number. This inflammatory reaction often extended into the surrounding parenchyma.

There was very good agreement among the SP, QAP, and PWG Chair concerning the presence of the above changes in the acinar pancreas. All of the acinar pancreatic neoplasms were reviewed and the diagnoses confirmed. A few cases of minimal cytoplasmic vacuolation, a case of minimal atrophy, and a case of acinar cell hyperplasia were reviewed and the diagnoses confirmed.

ADRENAL CORTEX

Adenoma and Carcinoma of the adrenal cortex occurred in a small number of animals in treated groups. Incidences of **Atrophy, Hyperplasia, Cystic Degeneration, and Cytoplasmic Vacuolization** of the adrenal cortex were increased in treated groups as compared with controls. **Hypertrophy** occurred relatively frequently in all dose groups, including controls. The PWG examined some representative examples and also examined slides in which there was a difference of opinion as to whether a lesion represented cortical neoplasm.

Cortical Adenoma was a large, discrete lesion that replaced glandular parenchyma and caused compression of the remaining normal tissue. Adenoma was distinguished from hypertrophy or hyperplasia by the fact that adenoma consisted of somewhat atypical cortical cells that were arranged in abnormal patterns, rather than consisting of normal appearing cells arranged in the normal cord pattern as was the case with hypertrophy and hyperplasia. Large adenomas replaced much of the gland and caused enlargement of the gland. In contrast, **Cortical Carcinoma** was larger than adenoma, consisted of highly atypical cells arranged in highly abnormal patterns. Invasion through the capsule into adjacent tissue was also present. Carcinomas replaced much of the gland and caused enlargement of the gland.

Cortical Atrophy was a locally extensive to diffuse change characterized by loss of cortical epithelial cells within the zona fasciculata and zona reticularis with a subsequent reduction in cortical thickness. The zona glomerulosa was spared. The remaining cells were sometimes vacuolated, especially in the more severe lesions. In severe cases the entire cortex was considerably reduced in thickness resulting in a smaller gland that often was surrounded by thickened capsule.

Cortical Hyperplasia was a focal to multifocal change, generally located in the zona fasciculata, consisting of a discrete area containing increased numbers of cortical cells. The hyperplastic cells were the same size or somewhat smaller than surrounding normal cortical cells, and often had slightly basophilic cytoplasm. In some cases, especially with large lesions, there was compression of the surrounding tissue. However, these lesions were distinguishable as hyperplasia by the fact that the cells still formed normal cords, particularly in the upper zona fasciculata. Cortical hypertrophy and hyperplasia frequently occurred in the same gland.

Cortical Hypertrophy was a focal to multifocal lesion consisting of discrete foci of enlarged cortical epithelial cells within the zona fasciculata and, in more severe cases, extending into the zona reticularis. Large lesions sometimes compressed adjacent parenchyma. However, these lesions were distinguishable as hypertrophy due to the fact that the cells still formed normal cords, particularly in the upper zona fasciculata. Cortical hypertrophy and hyperplasia frequently occurred in the same gland.

Cortical Cytoplasmic Vacuolization was a focal to multifocal to diffuse change consisting of small, discrete, clear intracytoplasmic vacuoles. Sometimes the cytoplasm contained a large single vacuole that displaced the nucleus. The changes were morphologically consistent with the accumulation of lipid. Cytoplasmic vacuolization occurred most commonly within foci of hypertrophy, and for that reason the QAP had recommended deleting most of the SP's diagnoses of vacuolization. However, the PWG Chair considered it to be a legitimate change that warranted diagnosis.

Cortical Cystic Degeneration was a focal to multifocal, unilateral to bilateral lesion consisting of variably sized endothelial-lined spaces, usually containing blood and occasionally thrombi, that were located in the zona fasciculata and reticularis. Larger lesions compressed or replaced adjacent parenchyma.

UTERUS

Incidences of **Squamous Metaplasia** were increased in all treated groups as compared with controls. A few cases were examined and the diagnoses confirmed. Squamous metaplasia was generally a minimal to mild, multifocal change consisting of tubular structures within the endometrium that were lined by stratified squamous epithelium.

Squamous Cell Carcinoma occurred in the uterus or cervix of a small number of animals in various treated groups. Squamous cell carcinoma had the typical morphological appearance associated with this lesion and was characterized by irregular cords and clusters of atypical stratified squamous epithelial cells that invaded the underlying tissues.

GINGIVAL ORAL MUCOSA

Squamous Hyperplasia occurred with increased incidences in all treated groups as compared with controls, and was often associated with inflammation of the periodontal tissue. Hyperplasia was a localized lesion that occurred in the stratified squamous epithelium of the gingival oral mucosa adjacent to the incisor teeth in nasal section III. It consisted of varying degrees of thickening of the epithelium, often with the formation of epithelial rete pegs that extended a short distance into the underlying connective tissue. Ends of hair shafts and/or some degree of inflammation were often present in the areas, suggesting the possibility that the hyperplasia was related to the inflammation and hair shafts.

Squamous Cell Carcinoma occurred in a small number of animals in various groups including the controls. Squamous cell carcinoma occurred within the oral mucosa of the palate and was located adjacent to the incisor tooth in nasal section III. Squamous cell carcinoma was characterized by irregular cords and clusters of stratified squamous epithelial cells that invaded deep into the underlying connective tissue and often invaded the bone of the maxilla.

The PWG examined a few lesions in which there was a question as to whether the lesion represented squamous hyperplasia or squamous cell carcinoma; the PWG consensus for these lesions can be found on the Slide Review Worksheets attached to this report. It was unclear whether there was an association between squamous hyperplasia and squamous cell carcinoma.

TOOTH PERIODONTAL TISSUE

The incidence and average severity of **Inflammation** was increased in the TEQ=46 and TEQ=100 groups as compared with controls. The inflammation occurred in the periodontal tissue around the incisor teeth in nasal section III and consisted of an infiltrate of small to moderate numbers of mixed inflammatory cells, mainly lymphocytes mixed with a few neutrophils. Hair shafts often were present between the periodontal tissue on the tooth suggesting the inflammation may have been related to the presence of the hair shafts.

KIDNEY

The incidence and average severity of **Nephropathy** was increased in all treated groups as compared with controls. Nephropathy was generally a minimal to mild change, although sometimes moderate to marked nephropathy was seen. It had the typical appearance of this lesion as seen in aging rats, and was similar to that observed in Fischer rats. Nephropathy was characterized by scattered foci of regenerative tubules lined by basophilic epithelium and sometimes surrounded by increased basement membrane, dilated tubules filled with proteinaceous casts and surrounded by fibrous connective tissue, and scattered foci of mixed inflammatory cells. Severity was graded based upon the number and extent of changes described above. Minimal nephropathy was characterized by small numbers of scattered affected tubules, usually involving less than 10% of the renal tubules. On the other extreme, marked nephropathy involved approximately 50-60% or more of the tubules. Since there was very good agreement among the SP, QAP, and PWG Chair concerning the presence of nephropathy the PWG opted not to review any examples.

Transitional Epithelium Hyperplasia occurred with low and similar incidences across groups, including controls. The presence of transitional epithelium hyperplasia did not appear to correlate with increased severity of nephropathy since the animals with hyperplasia often had minimal nephropathy. In some cases the hyperplasia was present in kidneys with inflammation or renal pelvic calculi and the hyperplasia appeared to be secondary to those lesions. The SP

had diagnosed the transitional cell hyperplasia under two different sites, Pelvis Transitional Epithelium Hyperplasia, and Papilla Transitional Epithelium Hyperplasia. It was decided during the special preliminary PWG that it was most appropriate to combine these two under the one diagnosis of Transitional Epithelium Hyperplasia. Transitional Epithelium Hyperplasia was sometimes focal to multifocal, but generally a diffuse, usually minimal to mild change consisting of varying degrees of thickening of the renal pelvic or papillary epithelium up to approximately 1.5-2 times normal thickness.

HEART

The incidence of slight **Cardiomyopathy** was prominently increased in all treated groups as compared with controls. Cardiomyopathy had the typical microscopic appearance of this lesion as seen in aging rats, and appeared similar to cardiomyopathy seen in aging Fischer rats. It was a multifocal, generally minimal lesion consisting of hypereosinophilic myofibers that lacked cross striations, infiltrates of mononuclear cells, separation of myofibers by myxomatous material (bluish material on H&E stain), and eventual replacement of myofibers by fibrous connective tissue. The severity was graded based upon the number and extent of foci of myocardial degeneration. Minimal cardiomyopathy consisted of a few scattered affected foci of myocardial fibers. Cardiomyopathy of greater severity consisted of a greater number of lesions more diffusely scattered within the myocardium. A few cases in which there was a question as to whether or not cardiomyopathy was present were reviewed.

THYROID GLAND

The SP had diagnosed **Follicle – Atrophy** in the treated and control groups of terminal sacrifice animals. The incidence of this change was increased in treated groups as compared with controls, primarily in the TEQ=100 group, as compared with the incidence in controls. This was a localized to diffuse change, characterized by follicles that were decreased in size and contained decreased amounts of colloid in which aggregates of amphophilic, flocculant appearing material were sometimes present. The affected follicles were lined by large, prominent cuboidal follicular epithelial cells that ranged from approximately one and a half to four times normal size, usually with abundant pale cytoplasm sometimes containing small, clear, resorption vacuoles. Since some degree of this change commonly occurs spontaneously, the SP only diagnosed this change when at least half of the thyroid follicles in the glands were affected. A severity grade of minimal was recorded when 50-60% of the follicles were involved, mild severity when 60-75% of the follicles were involved, moderate when 75-90% of the follicles were involved, and marked when over 90% of the follicles were involved. The severity was minimal to mild in nearly all affected animals in all groups, including the control and treated groups.

The presence of the change was confirmed by the QA/PWG review. However, the same change had occurred in the TCDD study and the PWG for TCDD had concluded, after reviewing representative slides, that the change represented follicular cell hypertrophy rather than atrophy. Since in this study the QAP had

agreed with the SP's diagnoses of atrophy, some examples were shown to the PWG which agreed a minimal change was present but was unable to conclude decisively whether it was hypertrophy. Consequently, as a post-PWG action item, additional thyroid slides were reviewed by Drs. Flake, Hailey, Herbert, Maronpot, and Nyska, who concurred that the change was appropriately diagnosed as hypertrophy. Consequently, it was recommended that all diagnoses of Follicle – Atrophy made by the SP be changed to Follicular Cell – Hypertrophy.

Thyroid follicular cell hypertrophy in rats resulting from treatment with goitrogens has been described (Capen et al., 2002; Johnson et al., 1993; McClain, 1995). The hypertrophy was characterized by a decrease in follicular luminal size (secondary to increased secretion of colloid from the lumen) and an increase in the size of the follicular cells, and these findings are consistent with the findings of this study. In addition, TCDD and PCB126 are known to have goitrogenic activity, and thyroid follicular cell hypertrophy and hyperplasia have been reported to occur in rats treated with TCDD (Sewall et al., 1995). Sustained, excessive TSH stimulation of the thyroid gland in rats leads to hypertrophy and to hyperplasia, and if the stimulation is sufficiently excessive and prolonged it can eventually lead to neoplasia (McClain, 1995). TSH levels in this study were found to be elevated in treated interim sacrifice animals and this was considered to be the cause of the hypertrophy. However, the hypertrophy was not considered to be a preneoplastic change since only one follicular cell hyperplasia was seen and this was in a control animal, plus only a few follicular cells adenomas were observed and these were scattered across groups with no apparent relationship to treatment. Thus, there was no indication of progression to thyroid gland neoplasia.

Since TSH levels had been found to be elevated in the treated interim sacrifice animals, indicative of the presence of a goitrogenic effect, and no follicular hypertrophy (atrophy) had been diagnosed in the interim sacrifice animals, the PWG Chair was directed by NTP to review the thyroid glands from all interim sacrifice animals as part of the preparation for the PWG to see if this change was present but had not been noted previously. During this review the PWG Chair noted the presence of **Follicular Cell – Hypertrophy** in treated animals in the 14, 31, and 53 week interim sacrifice groups, and diagnosed it and graded the severity using the same criteria as used by the SP in the terminal sacrifice animals. The PWG Chair's findings were recorded on the Slide Review Worksheets, and the PWG Chair's diagnoses of Follicular Cell – Hypertrophy in the interim sacrifice animals will be added to the pathology findings for this study.

MESENTERY

Artery Chronic Active Inflammation occurred in a few treated animals, in the TEQ=10, TEQ=46, and TEQ=100 groups. This change in the mesentery appeared similar microscopically to that seen in the pancreas. Often the affected mesenteric vessels were dilated to two to three times normal size. Thrombosis was sometimes seen in areas of more severe inflammation and appeared to be secondary to damage to the vessel wall caused by the inflammation. The PWG reviewed one case and confirmed the diagnosis.

THYMUS

Atrophy occurred with greater incidence and average severity, as compared with controls, in the treated interim sacrifice and treated terminal sacrifice groups.

Atrophy consisted of varying degrees of loss of lymphoid cells from the cortex resulting in reduction of cortical thickness. There was very good agreement among the SP, QAP, and PWG Chair concerning the presence of thymus atrophy. A few slides of thymus atrophy that had been diagnosed by the PWG Chair were reviewed and the PWG Chair's diagnoses confirmed.

OVARY

Corpus Luteum Atrophy was diagnosed by the SP with higher incidence in the TEQ=100 group of 14-week interim sacrifice animals, as compared with controls and other treated groups of 14-week interim sacrifice animals. This finding was confirmed by the QA/PWG review. This change was characterized by absence of ovarian structures, primarily corpora lutea, but also lack of follicles in some cases.

The PWG noted that this same change had occurred in ovaries in the PCB126 study. Representative slides from that study were examined by Dr. Barbara Davis of NIEHS, an expert in ovarian pathology. Dr. Davis noted the atrophy was characterized by overall reduction in ovarian size, and a preponderance of interstitial tissue with few or no follicles and corpora lutea, and recommended the diagnosis **Ovary – Atrophy** be used as it was a more appropriate diagnosis for this change. Since the diagnoses of Ovary, Corpus Luteum – Atrophy in the PCB126 study were all changed to Ovary – Atrophy, in accordance with Dr. Davis's recommendation, and since the same situation was present in this study, all diagnoses of Ovary, Corpus Luteum -- Atrophy made by the SP in this study were changed to Ovary – Atrophy.

The PWG Chair diagnosed Ovary – Atrophy in one 14-week interim sacrifice animal in which it had not been diagnosed previously; this slide was examined and the PWG Chair's diagnosis was confirmed. In addition, ovary had not been examined by the SP or QAP in animals from the 53-week interim sacrifice. The ovary slides from this sacrifice were present in the PWG set and the PWG Chair noted atrophy was present in control and treated animals and diagnosed it for the sake of complete evaluation of all groups. A representative example was examined and the presence of Atrophy was confirmed. Consequently, it was suggested the PWG Chair's diagnoses be added for the sake of completeness.

The incidence of **Chronic Active Inflammation** was marginally increased in all treated groups as compared with controls, and the incidence was highest in the TEQ=100 group. A representative example was examined and the diagnosis confirmed. Microscopically, affected ovaries had been nearly or completely replaced by large aggregates of neutrophils and debris surrounded by a layer of fibrous tissue that was infiltrated with macrophages. Essentially, Chronic Active Inflammation consisted of an encapsulated abscess. In some cases the inflammation extended into the adjacent adipose tissue.

BONE MARROW

The SP diagnosed greater incidences of **Hyperplasia** in treated groups of terminal sacrifice animals as compared with controls. Hyperplasia was characterized by a diffuse increase in myeloid hematopoietic cells with varying degrees of replacement of medullary adipose tissue. In some animals the bone marrow hyperplasia occurred in animals with neoplasms, so it is possible the hyperplasia was secondary to inflammation associated with the neoplasm. However, in many cases there was no apparent cause for the presence of bone marrow hyperplasia. Consequently, the significance of the increased bone marrow hyperplasia in treated groups was unclear.

BRAIN

Necrosis and/or **Edema** occurred in a small number of animals in the TEQ=46 and TEQ=100 dose groups. Microscopically, the lesions were generally of minimal to mild severity, focal or multifocal, and present in the cerebral cortex and/or the corpus callosum. Edema was characterized by an area of pale staining neuropil. In the corpus callosum separation of adjacent nerve bundles was also present. Necrosis consisted of scattered neurons with shrunken, deeply basophilic, pyknotic nuclei. One animal (animal number 440 in the TEQ=100 group) had both necrosis and edema. In addition, animal number 440 had **Gliosis** in the affected area of necrosis and edema. The Gliosis was characterized by a modestly increased number of glial cells, mainly astrocytes, within the affected area and was considered to be a reaction to the necrosis and edema. Moreover, animal number 440 also had fibrinoid degeneration (diagnosed as **Artery Degeneration**) of a small meningeal artery in the affected area of cerebrum. The affected vessel had a thick, diffusely homogeneous eosinophilic wall with a markedly narrowed lumen. A small arteriole within the neuropil adjacent to the affected vessel, apparently a branch of the affected artery, was similarly affected. This finding suggests the necrosis and edema in these brains may have been secondary to degenerative vascular changes.

MISCELLANEOUS

An unusual lesion in the kidney of a terminal sacrifice TEQ=100 animal (animal number 448) that had been diagnosed as **Renal Papilla Carcinoma** by the SP was examined by the PWG. This lesion was composed of two localized but separated areas in the renal medulla with each area consisting of a sheet of homogeneous, eosinophilic material, resembling amyloid, within which were embedded scattered cuboidal epithelial cells. Some of the PWG members noted the lesion resembled a **Yolk Sac Carcinoma** of the ovary. The PWG concluded the lesion was most likely a **Developmental Malformation**, although they recommended performing a Congo Red stain on the kidney to rule out amyloid. The Congo Red stain was performed on the tissue and was negative for amyloid. Consequently, the lesion was diagnosed as **Development Malformation**.

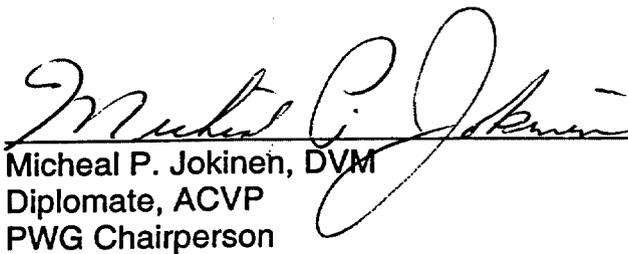
In previous studies Squamous Hyperplasia of the forestomach epithelium, sometimes with associated inflammation, was seen with somewhat increased

incidence in treated groups as compared with controls. Similar findings had not been diagnosed in this study by the SP. The QAP was directed by NTP to review forestomachs from 20 control and 20 high dose terminal sacrifice animals to confirm that no treatment related findings were present. The QAP review confirmed the absence of treatment related forestomach lesions in this study. None of the forestomachs were examined by the PWG Chair.

POST-PWG ACTION ITEMS

Stain the kidney lesion from animal number 448 with a Congo Red stain to rule out amyloidosis. This was performed and the staining was negative for amyloid. This was discussed under the section on miscellaneous lesions above.

Review additional slides of thyroid gland from control and high dose animals to confirm the presence of follicular cell hypertrophy. This review was performed by NTP pathologists and the presence of follicular cell hypertrophy was confirmed. This was discussed in the thyroid gland section above.



Michael P. Jokinen, DVM
Diplomate, ACVP
PWG Chairperson

2/20/03

Date

References:

Capen CC, DeLellis RA, Yarrington JT (2002). Endocrine System. In Haschek WM, Rousseaux CG, Wallig MA (eds.) Handbook of Toxicologic Pathology, 2nd Edition. Pages 681—783, Academic Press, San Diego.

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McClain MR (1995). Mechanistic consideration for the relevance of animal data on thyroid neoplasia to human risk assessment. Mutat. Res. 333:131-142.

Sewall CH, Flagler N, Vanden Heuvel JP, Clark GC, Tritscher AM, Maronpot RM, Lucier GW (1995). Alterations in thyroid function in female Sprague-Dawley rats following chronic treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Toxicol. and Appl. Pharmacol. 132:237-244.

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
Date: 04/22/03
Time: 10:22:30

14 WEEK SSAC

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 09/17/98 - 09/18/98

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:22:30

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)	(10)
Clear Cell Focus				1 (10%)	1 (10%)
Fatty Change, Diffuse	10 (100%)	10 (100%)	10 (100%)	10 (100%)	8 (80%)
Inflammation				1 (10%)	1 (10%)
Mixed Cell Focus, Multiple		1 (10%)	3 (30%)	5 (50%)	8 (80%)
Hepatocyte, Hypertrophy	(10)	(10)	(10)	(10)	(10)
Pancreas				2 (20%)	1 (10%)
Basophilic Focus					1 (10%)
Inflammation, Chronic Active					1 (10%)
Acinus, Atrophy	(10)				
Stomach, Fore stomach	1 (10%)				
Hyperkeratosis	1 (10%)				
Hyperplasia, Squamous	1 (10%)				
Inflammation	1 (10%)				
Stomach, Glandular	(10)				1 (10%)
Cyst					1 (10%)

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)	(10)
Hyperplasia					1 (10%)
Hypertrophy	1 (10%)				
Thyroid Gland	(10)	(10)	(10)	(10)	(10)
Follicular Cell, Hypertrophy		3 (30%)	7 (70%)	10 (100%)	7 (70%)

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:22:30

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)	(10)
Atrophy		1 (10%)	2 (20%)	3 (30%)	4 (40%)
Uterus	(10)	(10)	(10)	(10)	(10)
Metaplasia, Squamous		1 (10%)	1 (10%)		2 (20%)
Endometrium, Hyperplasia, Cystic	2 (20%)				2 (20%)

HEMATOPOIETIC SYSTEM

Spleen	(10)	(10)	(10)	(10)	(10)
Pigmentation	10 (100%)	(10)	(10)	(10)	10 (100%)
Thymus	(10)	2 (20%)	3 (30%)	4 (40%)	7 (70%)
Atrophy					

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)	(10)
Hemorrhage			1 (10%)	1 (10%)	
Infiltration Cellular, Histiocyte			1 (10%)	1 (10%)	
Inflammation, Chronic Active					1 (10%)

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
Date: 04/22/03
Time: 10:22:30

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX
CONTROL

TERT. MIX
TEQ=10

TERT. MIX
TEQ=22

TERT. MIX
TEQ=46

TERT. MIX
TEQ=100

RESPIRATORY SYSTEM - CONT
Alveolar Epithelium, Hyperplasia

1 (10%)

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
Route: GAVAGE

Report: PETRPT05
Date: 04/22/03
Time: 10:23:03

14 WEEK SSAC

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 09/17/98 - 09/18/98

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:23:03

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially in Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
Route: GAVAGE

Report: PIRP05
Date: 04/22/03
Time: 10:23:03

SPRAGUE-DAWLEY RATS FEMALE
TERT. MIX TERT. MIX TERT. MIX TERT. MIX TERT. MIX
CONTROL TEQ=10 TEQ=22 TEQ=46 TEQ=100

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES(b)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
Date: 04/22/03
Time: 10:28:55

14 WEEK SSAC

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 scheduled sacrifice

Removal Date Range: 09/17/98 - 09/18/98

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:28:55

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)	(10)
Clear Cell Focus				1 [1.0]	1
Fatty Change, Diffuse	10 [1.0]	10 [1.0]	10 [1.0]	10 [1.0]	8 [1.0]
Inflammation				5 [1.2]	1 [1.4]
Mixed Cell Focus, Multiple		1 [1.0]			8 [1.4]
Hepatocyte, Hypertrophy	(10)	(10)	(10)	(10)	(10)
Pancreas				2 [1.0]	1
Basophilic Focus					1 [1.0]
Inflammation, Chronic Active	(10)				(10)
Acinus, Atrophy					
Stomach, Forestomach					
Hyperkeratosis	1 [2.0]				
Hyperplasia, Squamous	1 [3.0]				
Inflammation	1 [2.0]				
Stomach, Glandular					
Cyst	(10)				(10)

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)	(10)
Hyperplasia					1 [1.0]
Hypertrophy	1 [2.0]				
Thyroid Gland	(10)	(10)	(10)	(10)	(10)
Follicular Cell, Hypertrophy		3 [1.0]		7 [1.0]	7 [1.4]

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:28:55

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)	(10)
Atrophy		1 [3.0]	2 [3.0]	3 [2.7]	4 [3.5]
Uterus	(10)	(10)	(10)	(10)	(10)
Metaplasia, Squamous		1 [1.0]	1 [1.0]	1 [1.0]	2 [1.5]
Endometrium, Hyperplasia, Cystic	2 [3.0]				2 [3.0]

HEMATOPOIETIC SYSTEM

Spleen	(10)	(10)	(10)	(10)	(10)
Pigmentation	10 [1.2]	(10)	(10)	(10)	10 [1.0]
Thymus	(10)	2 [1.0]	3 [1.0]	4 [1.0]	(10)
Atrophy					7 [1.1]

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)	(10)
Hemorrhage			1 [1.0]	1 [1.0]	
Infiltration Cellular, Histiocyte			1 [1.0]	1 [1.0]	
Inflammation, Chronic Active					1 [1.0]

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES (b)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
Date: 04/22/03
Time: 10:28:55

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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RESPIRATORY SYSTEM - CONT
Alveolar Epithelium, Hyperplasia

1 [3.0]

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
Date: 04/22/03
Time: 10:29:25

31 WEEK SSAC/FINAL#1

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 01/13/99 - 01/14/99

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:29:25

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)	(10)
Clear Cell Focus					1 (10%)
Eosinophilic Focus					1 (10%)
Fatty Change, Diffuse					10 (100%)
Inflammation	8 (80%)	10 (100%)	10 (100%)	10 (100%)	10 (100%)
Mixed Cell Focus	3 (30%)	2 (20%)	1 (10%)	4 (40%)	2 (20%)
Pigmentation	3 (30%)	2 (20%)	4 (40%)	4 (40%)	6 (60%)
Hepatocyte, Hypertrophy		4 (40%)	9 (90%)	10 (100%)	10 (100%)
Hepatocyte, Multinucleated		3 (30%)	5 (50%)	9 (90%)	10 (100%)
Pancreas	(10)	(10)	(10)	(10)	8 (80%)
Inflammation, Chronic Active	1 (10%)				1 (10%)
Acinus, Atrophy	1 (10%)	1 (10%)	2 (20%)		5 (50%)
Stomach, Glandular					(10)
Glands, Ectasia	(10)				2 (20%)

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)	(10)
Degeneration, Cystic	1 (10%)				2 (20%)
Hyperplasia	1 (10%)				3 (30%)
Hypertrophy	5 (50%)	1 (10%)	1 (10%)	1 (10%)	
Vacuolization Cytoplasmic	1 (10%)				(10)
Pituitary Gland	(10)				

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:29:25

SPRAGUE-DAWLEY RATS FEMALE

	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46	TERT.MIX TEQ=100
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ENDOCRINE SYSTEM - CONT

Hyperplasia	1 (10%)				1 (10%)
Hypertrophy	(10)	(10)	(10)	(10)	(10)
Thyroid Gland	1 (10%)				1 (10%)
G-Cell, Hyperplasia	1 (10%)	5 (50%)			3 (30%)
Follicular Cell, Hypertrophy			1 (10%)	4 (40%)	

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)	(10)
Atrophy	10 (100%)	9 (90%)	9 (90%)	8 (80%)	9 (90%)
Uterus	(10)	(10)	(10)	(10)	(10)
Inflammation, Suppurative	4 (40%)		1 (10%)		2 (20%)
Metaplasia, Squamous	8 (80%)	9 (90%)	8 (80%)	8 (80%)	8 (80%)
Endometrium, Hyperplasia, Cystic	2 (20%)		1 (10%)		2 (20%)

HEMATOPOIETIC SYSTEM

Lymph Node			(1)		
Metaplasia, Squamous			1 (100%)		
Spleen	(10)				(10)
Pigmentation	10 (100%)	(10)	(10)	(10)	10 (100%)
Thymus	(10)		3 (30%)		7 (78%)
Atrophy				7 (70%)	

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PTRPT03
Date: 04/22/03
Time: 10:29:25

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)	(10)
Hemorrhage				1 (10%)	
Infiltration Cellular, Histiocyte	1 (10%)	1 (10%)	1 (10%)		1 (10%)

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

Kidney	(1)
Inflammation, Chronic Active	1 (100%)

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
Route: GAVAGE

Report: PRRP05
Date: 04/22/03
Time: 10:32:45

31 WEEK SSAC/FINAL#1

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 01/13/99 - 01/14/99

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: BEIRPT05
 Date: 04/22/03
 Time: 10:32:45

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially in Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:32:45

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
SPRAGUE-DAWLEY RATS FEMALE					
INTEGUMENTARY SYSTEM					
Mammary Gland	(10)	(2)			(10)
Fibroadenoma		2 (100%)			
MUSCULOSKELETAL SYSTEM					
None					
NERVOUS SYSTEM					
None					
RESPIRATORY SYSTEM					
None					
SPECIAL SENSES SYSTEM					
None					
URINARY SYSTEM					
None					

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:32:45

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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TUMOR SUMMARY

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

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES (b)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

31 WEEK SSAC/FINAL#1

Report: PEIRPT18
Date: 04/22/03
Time: 10:36:36

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: A11

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 01/13/99 - 01/14/99

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:36:36

SPRAGUE-DAWLEY RATS FEMALE

CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	16	16	16	16	16
Early Deaths					
Survivors					
Animals Examined Microscopically	10	10	10	10	10

ALIMENTARY SYSTEM

Liver	(10)	(10)	(10)	(10)	(10)
Clear Cell Focus			1		1
Eosinophilic Focus					1 [1.0]
Fatty Change, Diffuse					10 [1.6]
Inflammation	8 [1.0]	10 [1.0]	10 [1.1]	10 [1.3]	2
Mixed Cell Focus	3	2	1	4	6
Pigmentation	3	4 [1.0]	4	10 [1.6]	10 [1.4]
Hepatocyte, Hypertrophy		3 [1.0]	5 [1.0]	1 [1.0]	8 [1.1]
Hepatocyte, Multinucleated	(10)	(10)	(10)	(10)	(10)
Pancreas	1 [1.0]				1 [1.0]
Inflammation, Chronic Active	1 [1.0]	1 [1.0]	2 [1.0]		5 [1.0]
Acinus, Atrophy					(10)
Acinus, Vacuolization					2 [1.5]
Stomach, Glandular					
Glands, Ectasia	(10)				

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Adrenal Cortex	(10)	(10)	(10)	(10)	(10)
Degeneration, Cystic	1 [2.0]				2 [2.0]
Hyperplasia	1 [2.0]				3 [1.0]
Hypertrophy	5 [1.4]	1 [1.0]	1 [1.0]	1 [1.0]	
Vacuolization	1 [1.0]				
Cytoplasmic					
Pituitary Gland	(10)				(10)

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES(b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:36:36

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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ENDOCRINE SYSTEM - CONT	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
Hyperplasia	1 [2.0]				
Hypertrophy					1 [1.0]
Thyroid Gland	(10)	(10)	(10)	(10)	(10)
C-Cell, Hyperplasia	1 [2.0]				
Follicular Cell, Hypertrophy	1 [1.0]	5 [1.8]	1 [1.0]	4 [2.0]	3 [1.0]

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(10)	(10)	(10)	(10)	(10)
Atrophy	10 [3.8]	9 [3.8]	9 [4.0]	8 [3.8]	9 [3.9]
Uterus	(10)	(10)	(10)	(10)	(10)
Inflammation, Suppurative	4 [1.3]	1 [2.0]	1 [2.0]	2 [1.0]	2 [1.0]
Metaplasia, Squamous	8 [1.9]	9 [1.4]	8 [1.9]	8 [1.9]	8 [1.8]
Endometrium, Hyperplasia, Cystic	2 [3.5]		1 [4.0]		2 [4.0]

HEMATOPOIETIC SYSTEM

Lymph Node			(1)		
Metaplasia, Squamous			1 [1.0]		
Spleen	(10)				(10)
Pigmentation	10 [1.4]				10 [1.4]
Thymus	(10)		(10)	(10)	(9)
Atrophy		(10)	3 [1.3]	7 [1.9]	7 [2.1]

INTEGUMENTARY SYSTEM

None

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:36:36

	SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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None

RESPIRATORY SYSTEM

Lung	(10)	(10)	(10)	(10)	(10)	(10)
Hemorrhage	1 [1.0]	1 [1.0]	1 [1.0]	1 [1.0]	1 [2.0]	1 [1.0]
Infiltration Cellular, Histiocyte						

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

Kidney	(1)					
Inflammation, Chronic Active	1 [3.0]					

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
Date: 04/22/03
Time: 10:39:38

53 WEEK SSAC/FINAL#1

Facility: Battelle Columbus Laboratory
Chemical CAS #: TEPDIOXINMIX
Lock Date: 09/12/01
Cage Range: All
Reasons For Removal: 25017 Scheduled Sacrifice
Removal Date Range: 06/16/99 - 06/19/99
Treatment Groups:
Include 001 TERT.MIXCONTROL
Include 002 TERT.MIXTEQ=10
Include 003 TERT.MIXTEQ=22
Include 004 TERT.MIXTEQ=46
Include 005 TERT.MIXTEQ=100

a Number of animals examined microscopically at site and number of animals with lesion
Page 1

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:39:38

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL TERT. MIX TEQ=10 TERT. MIX TEQ=22 TERT. MIX TEQ=46 TERT. MIX TEQ=100

DISPOSITION SUMMARY

Disposition	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	13	13	13	13	13
Early Deaths					
Survivors					
Animals Examined Microscopically	8	8	8	8	8

ALIMENTARY SYSTEM

Liver	(8)	(8)	(8)	(8)	(8)
Basophilic Focus	1 (13%)			2 (25%)	1 (13%)
Cholangiofibrosis					1 (13%)
Clear Cell Focus	1 (13%)	1 (13%)			1 (13%)
Eosinophilic Focus				1 (13%)	
Eosinophilic Focus, Multiple		1 (13%)			2 (25%)
Fatty Change, Diffuse					1 (13%)
Fatty Change, Focal					2 (25%)
Inflammation	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)
Mixed Cell Focus	2 (25%)	2 (25%)	4 (50%)	1 (13%)	4 (50%)
Mixed Cell Focus, Multiple	1 (13%)	2 (25%)	3 (38%)	5 (63%)	7 (88%)
Pigmentation		4 (50%)	8 (100%)	8 (100%)	8 (100%)
Regeneration					1 (13%)
Toxic Hepatopathy				3 (38%)	8 (100%)
Bile Duct, Fibrosis					1 (13%)
Bile Duct, Hyperplasia					1 (13%)
Bile Duct, Inflammation, Chronic Active		5 (63%)	7 (88%)	1 (13%)	6 (75%)
Hepatocyte, Hypertrophy			3 (38%)	8 (100%)	1 (13%)
Hepatocyte, Multinucleated	(8)	(8)			8 (100%)
Pancreas					
Basophilic Focus					1 (13%)
Inflammation, Chronic Active					1 (13%)
Acinus, Atrophy					1 (13%)
Acinus, Vacuolization Cytoplasmic	(8)				2 (25%)
Stomach, Glandular					7 (88%)
Cyst, Squamous					1 (13%)
Developmental Malformation	1 (13%)				1 (100%)

CARDIOVASCULAR SYSTEM

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:39:38

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
SPRAGUE-DAWLEY RATS FEMALE					
None					
ENDOCRINE SYSTEM					
Adrenal Cortex	(8)	(8)	(8)	(8)	(8)
Degeneration, Cystic	1 (13%)		2 (25%)	1 (13%)	2 (25%)
Hyperplasia	3 (38%)	7 (88%)	5 (63%)	3 (38%)	5 (63%)
Hypertrophy					1 (13%)
Vacuolization Cytoplasmic					(8)
Thyroid Gland	(8)	(8)	(8)	(8)	(8)
C-Cell, Hyperplasia			1 (13%)		
Follicular Cell, Hypertrophy	2 (25%)	2 (25%)	3 (38%)	3 (38%)	4 (50%)
GENERAL BODY SYSTEM					
None					
GENITAL SYSTEM					
Ovary	(8)	(8)	(8)	(8)	(8)
Atrophy	8 (100%)	8 (100%)	8 (100%)	6 (75%)	8 (100%)
Cyst				1 (13%)	
Inflammation, Suppurative	1 (13%)	(8)	(8)	(8)	(8)
Uterus	(8)	(8)	(8)	(8)	(8)
Inflammation, Suppurative	1 (13%)				7 (88%)
Metaplasia, Squamous	8 (100%)	8 (100%)	8 (100%)	6 (75%)	7 (88%)
Endometrium, Hyperplasia, Cystic	6 (75%)				2 (25%)
HEMATOPOIETIC SYSTEM					
Spleen	(8)				(8)
Pigmentation	8 (100%)	(8)	(8)	(8)	8 (100%)
Thymus	(8)	(8)	(8)	(8)	(6)
Atrophy	3 (38%)	7 (88%)	8 (100%)	8 (100%)	6 (100%)
INTEGUMENTARY SYSTEM					
Mammary Gland	(8)	(1)	(1)	(1)	(8)
Cyst	3 (38%)				

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/22/03
 Time: 10:39:38

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
SPRAGUE-DAWLEY RATS FEMALE					

INTEGUMENTARY SYSTEM - CONT					
Hyperplasia	1 (13%)				1 (13%)
Skin Ulcer			1 (100%)		

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung					
Infiltration Cellular, Histiocyte	(8) 6 (75%)	(8) 5 (63%)	(8) 5 (63%)	(8) 4 (50%)	(8) 6 (75%)
Inflammation		1 (13%)		1 (13%)	
Inflammation, Chronic Active			2 (25%)	4 (50%)	
Alveolar Epithelium, Metaplasia, Bronchiolar		1 (13%)			6 (75%)

SPECIAL SENSERS SYSTEM

None

URINARY SYSTEM

Kidney					
Inflammation, Chronic Active			1 (100%)	1 (100%)	
Nephropathy			1 (100%)		

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
Route: GAVAGE

Report: PEIRPT05
Date: 04/22/03
Time: 10:42:39

53 WEEK SSAC/FINAL#1

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 06/16/99 - 06/19/99

Treatment Groups: Include 001 TERT.MIXCONTROL
 Include 002 TERT.MIXTEQ=10
 Include 003 TERT.MIXTEQ=22
 Include 004 TERT.MIXTEQ=46
 Include 005 TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a) Report: PEIRPT05
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE) Date: 04/22/03
 Route: GAVAGE Time: 10:42:39

SPRAGUE-DAWLEY RATS FEMALE TERT. MIX TERT. MIX TERT. MIX TERT. MIX TERT. MIX
 CONTROL TEQ=10 TEQ=22 TEQ=46 TEQ=100

DISPOSITION SUMMARY

Animals Initially in Study	98	98	98	98	98
Scheduled Sacrifice	13	13	13	13	13
Early Deaths					
Survivors					
Animals Examined Microscopically	8	8	8	8	8

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

Thyroid Gland	(8)	(8)	(8)	(8)	(8)
C-Cell, Adenoma	2 (25%)				

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:42:39

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46	TERT. MIX TEO=100
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INTEGUMENTARY SYSTEM

Mammary Gland	(8)	(1)	(1)	(1)	(8)
Fibroadenoma		1 (100%)	1 (100%)	1 (100%)	2 (25%)
Skin		(1)	(1)		
Subcutaneous Tissue, Fibrosarcoma		1 (100%)	1 (100%)		

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:42:39

SPRAGUE-DAWLEY RATS FEMALE TERT. MIX TERT. MIX TERT. MIX TERT. MIX TERT. MIX
 CONTROL TEQ=10 TEQ=22 TEQ=46 TEQ=100

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	2	1	2	1	2
Total Primary Neoplasms	2	1	2	1	2
Total Animals with Benign Neoplasms	2	1	1	1	2
Total Benign Neoplasms	2	1	1	1	2
Total Animals with Malignant Neoplasms			1		
Total Malignant Neoplasms			1		
Total Animals with Metastatic Neoplasms					
Total Metastatic Neoplasms					
Total Animals with Malignant Neoplasms Uncertain Primary Site					
Total Animals with Neoplasms Uncertain Benign or Malignant					
Total Uncertain Neoplasms					

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

53 WEEK SSAC/FINAL#1

Report: PEIRPT18
Date: 04/22/03
Time: 10:47:09

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEFDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25017 Scheduled Sacrifice

Removal Date Range: 06/16/99 - 06/19/99

Treatment Groups:

Include 001	TERT.MIXCONTROL
Include 002	TERT.MIXTEQ=10
Include 003	TERT.MIXTEQ=22
Include 004	TERT.MIXTEQ=46
Include 005	TERT.MIXTEQ=100

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES(1b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:47:09

SPRAGUE-DAWLEY RATS FEMALE

DISPOSITION SUMMARY

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
Animals Initially In Study	98	98	98	98	98
Scheduled Sacrifice	13	13	13	13	13
Early Deaths					
Survivors					
Animals Examined Microscopically	8	8	8	8	8

ALIMENTARY SYSTEM

Liver	(8)	(8)	(8)	(8)	(8)
Basophilic Focus	1				1
Cholangiofibrosis					1 [1.0]
Clear Cell Focus	1	1		2 [1.0]	1 [1.0]
Eosinophilic Focus			1		1
Eosinophilic Focus, Multiple					2 [1.0]
Fatty Change, Diffuse					4 [1.3]
Fatty Change, Focal					8 [2.0]
Inflammation	8 [1.0]	8 [1.0]	8 [1.1]	3 [1.0]	4 [1.3]
Mixed Cell Focus	2	2	4	8 [1.4]	8 [1.9]
Mixed Cell Focus, Multiple	1	2	3	5	7
Pigmentation		4 [1.0]	8 [1.3]	8 [1.0]	8 [2.0]
Regeneration					1
Toxic Hepatopathy					8 [1.6]
Bile Duct, Fibrosis					1 [1.0]
Bile Duct, Hyperplasia					6 [1.0]
Bile Duct, Inflammation, Chronic Active					1 [1.0]
Hepatocyte, Hypertrophy		5 [1.2]	7 [1.4]	1 [1.0]	8 [2.5]
Hepatocyte, Multinucleated			3 [1.0]	8 [1.5]	8 [1.8]
Pancreas	(8)	(8)	(8)	(8)	(8)
Basophilic Focus					1
Inflammation, Chronic Active					1 [1.0]
Acinus, Atrophy					1 [2.0]
Acinus, Vacuolization Cytoplasmic					7 [1.0]
Stomach, Glandular	(8)				7 [1.6]
Cyst, Squamous	1 [1.0]				(8)
Developmental Malformation				1 [2.0]	

CARDIOVASCULAR SYSTEM

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/22/03
 Time: 10:47:09

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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None

ENDOCRINE SYSTEM

Adrenal Cortex	(8)	(8)	(8)	(8)
Degeneration, Cystic	1 [2.0]			2 [1.5]
Hyperplasia			2 [2.0]	2 [2.0]
Hypertrophy	3 [1.7]	7 [1.0]	5 [1.0]	3 [1.0]
Vacuolization Cytoplasmic				5 [1.6]
Thyroid Gland	(8)	(8)	(8)	1 [1.0]
C-Cell, Hyperplasia			1 [1.0]	(8)
Follicular Cell, Hypertrophy	2 [1.0]	2 [1.5]	3 [1.0]	3 [1.7]
				4 [2.3]

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(8)	(8)	(8)	(8)	(8)
Atrophy	8 [3.9]	8 [4.0]	8 [4.0]	6 [4.0]	8 [3.8]
Cyst				1 [2.0]	
Inflammation, Suppurative	1 [3.0]	(8)	(8)	(8)	(8)
Uterus	(8)	(8)	(8)	(8)	(8)
Inflammation, Suppurative	1 [1.0]				7 [2.1]
Metaplasia, Squamous	8 [2.1]	8 [2.1]	8 [2.1]	6 [2.5]	2 [4.0]
Endometrium, Hyperplasia, Cystic	6 [1.7]				

HEMATOPOIETIC SYSTEM

Spleen	(8)	(8)	(8)	(8)	(8)
Pigmentation	8 [1.6]	(8)	(8)	(8)	8 [2.1]
Thymus	(8)	7 [1.7]	8 [2.0]	8 [3.4]	(6)
Atrophy	3 [2.0]				6 [3.7]

INTEGUMENTARY SYSTEM

Mammary Gland	(8)	(1)	(1)	(1)	(8)
Cyst	3 [1.0]				

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES[b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PRTPT18
 Date: 04/22/03
 Time: 10:47:09

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX
 CONTROL

TERT. MIX
 TEQ=10

TERT. MIX
 TEQ=22

TERT. MIX
 TEQ=46

TERT. MIX
 TEQ=100

INTEGUMENTARY SYSTEM - CONT

Skin
 Hyperplasia
 Ulcer

1 [1.0]

(1)
 1 [2.0]

1 [1.0]

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

Lung
 Infiltration Cellular, Histocyte
 Inflammation
 Inflammation, Chronic Active
 Alveolar Epithelium, Metaplasia, Bronchiolar

(8)
 6 [1.2]

(8)
 5 [1.0]
 1 [1.0]

1 [1.0]

(8)
 5 [1.0]

2 [1.5]

(8)
 4 [1.0]
 1 [1.0]
 4 [1.0]

(8)
 6 [1.0]
 6 [1.3]

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

Kidney
 Inflammation, Chronic Active
 Nephropathy

(1)
 1 [2.0]
 1 [1.0]

(1)
 1 [3.0]

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

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
Date: 04/24/03
Time: 08:07:42

FINAL#1/RATS

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25018 Dosing Accident
25020 Natural Death

25019 Moribund Sacrifice
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL TERT. MIX TEQ=10 TERT. MIX TEQ=22 TERT. MIX TEQ=46 TERT. MIX TEQ=100

DISPOSITION SUMMARY

Disposition	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
Animals Initially In Study	98	98	98	98	98
Early Deaths	26	25	22	25	33
Moribund Sacrifice	11	5	6	4	10
Natural Death			1	1	2
Dosing Accident					
Survivors	16	23	24	23	8
Terminal Sacrifice					
Animals Examined Microscopically	53	53	53	53	53

ALIMENTARY SYSTEM

Esophagus	(53)	(53)	(53)	(53)	(53)
Muscularis, Inflammation	2 (4%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Intestine Large, Colon	(53)	(52)	(53)	(53)	(51)
Parasite Metazoan			1 (2%)		
Intestine Large, Rectum	(52)	(53)	(53)	(53)	(52)
Parasite Metazoan	2 (4%)	4 (8%)	5 (9%)	1 (2%)	2 (4%)
Artery, Inflammation, Chronic Active					
Serosa, Inflammation	(51)	(53)	(53)	(53)	(53)
Intestine Large, Cecum					
Artery, Inflammation, Chronic Active	(52)	(53)	(53)	(53)	(53)
Intestine Small, Duodenum					
Serosa, Inflammation, Chronic Active	(53)	(53)	(53)	(53)	(53)
Liver					
Angiectasis	3 (6%)	2 (4%)	10 (19%)	5 (9%)	3 (6%)
Basophilic Focus	9 (17%)	14 (26%)	3 (6%)	7 (13%)	8 (16%)
Basophilic Focus, Multiple	15 (28%)	12 (23%)	3 (6%)	4 (8%)	17 (33%)
Cholangiofibrosis					
Clear Cell Focus	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Clear Cell Focus, Multiple	1 (2%)				
Degeneration, Cystic	4 (8%)	2 (4%)	5 (9%)	1 (2%)	2 (4%)
Eosinophilic Focus	1 (2%)	7 (13%)	6 (11%)	15 (28%)	19 (37%)
Eosinophilic Focus, Multiple	3 (6%)	5 (9%)	14 (26%)	34 (64%)	36 (71%)
Fatty Change, Diffuse	3 (6%)	4 (8%)	7 (13%)	2 (4%)	1 (2%)
Fatty Change, Focal	16 (30%)	18 (34%)	19 (36%)	8 (15%)	9 (18%)
Hematopoietic Cell Proliferation					
Hepatodiphagmatic Nodule	36 (68%)	50 (94%)	45 (85%)	50 (94%)	50 (98%)
Inflammation					
Karyomegaly	4 (8%)	5 (9%)	5 (9%)	1 (2%)	
Mixed Cell Focus					

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

	TERT. MIX CONTROL		TERT. MIX TEQ=10		TERT. MIX TEQ=22		TERT. MIX TEQ=46		TERT. MIX TEQ=100	
ALIMENTARY SYSTEM - CONT										
Mixed Cell Focus, Multiple	17 (32%)	28 (53%)	30 (57%)	37 (70%)	17 (33%)					
Necrosis	3 (6%)	1 (2%)	9 (17%)	3 (6%)	15 (29%)					
Pigmentation	4 (8%)	35 (66%)	41 (77%)	48 (91%)	51 (100%)					
Regeneration		1 (2%)	3 (6%)	10 (19%)	38 (75%)					
Toxic Hepatopathy		5 (9%)	14 (26%)	38 (72%)	47 (92%)					
Bile Duct, Cyst	1 (2%)	3 (6%)	3 (6%)	4 (8%)	9 (18%)					
Bile Duct, Dilatation	1 (2%)				1 (2%)					
Bile Duct, Fibrosis	3 (6%)	2 (4%)	1 (2%)	5 (9%)	1 (2%)					
Bile Duct, Hyperplasia	2 (4%)	3 (6%)	5 (9%)	25 (47%)	42 (82%)					
Centrilobular, Degeneration	3 (6%)	2 (4%)	1 (2%)	1 (2%)	6 (12%)					
Centrilobular, Fibrosis					1 (2%)					
Hepatocyte, Hypertrophy	1 (2%)	27 (51%)	34 (64%)	46 (87%)	50 (98%)					
Hepatocyte, Multinucleated		12 (23%)	10 (19%)	39 (74%)	51 (100%)					
Oval Cell, Hyperplasia		1 (2%)	1 (2%)	26 (49%)	42 (82%)					
Portal, Fibrosis					11 (22%)					
Serosa, Fibrosis					1 (2%)					
Serosa, Inflammation, Chronic	1 (2%)	(1)	(2)	(6)	(8)					
Mesentery					2 (25%)					
Inflammation, Chronic Active										
Necrosis					1 (50%)					
Artery, Inflammation, Chronic Active		1 (100%)	1 (50%)	3 (50%)	6 (75%)					
Fat, Necrosis	(10)	(18)	(19)	2 (33%)	(31)					
Oral Mucosa	8 (80%)	17 (94%)	18 (95%)	26 (90%)	30 (97%)					
Gingival, Hyperplasia, Squamous	(52)	(53)	(53)	(53)	(51)					
Pancreas	1 (2%)									
Degeneration	3 (6%)	1 (2%)	6 (11%)	7 (13%)	16 (31%)					
Inflammation, Chronic Active	3 (6%)	2 (4%)	7 (13%)	1 (2%)	20 (39%)					
Inflammation, Granulomatous	2 (4%)		1 (2%)	7 (13%)						
Acinus, Atrophy	1 (2%)		3 (6%)	15 (28%)	30 (59%)					
Acinus, Hyperplasia	1 (2%)		3 (6%)	8 (15%)	14 (27%)					
Acinus, Vacuolization		6 (11%)	1 (2%)							
Artery, Inflammation, Chronic Active										
Duct, Cyst										
Duct, Dilatation										
Duct, Inflammation, Chronic Active										
Salivary Glands	(53)	(53)	(53)	(53)	(53)					
Atrophy	1 (2%)									
Inflammation	2 (4%)									
Mineralization										
Stomach, Fore stomach	(53)	(53)	(53)	(53)	(53)					
Cyst										
Diverticulum										
Edema	1 (2%)		1 (2%)	1 (2%)						

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX
CONTROL

TERT. MIX
TEQ=10

TERT. MIX
TEQ=22

TERT. MIX
TEQ=46

TERT. MIX
TEQ=100

ALIMENTARY SYSTEM - CONT

Lesion	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
Erosion					
Hyperkeratosis	5 (9%)	1 (2%)	1 (2%)	2 (4%)	6 (12%)
Hyperplasia, Squamous	2 (4%)		4 (8%)	9 (17%)	3 (6%)
Inflammation	1 (2%)		2 (4%)	1 (2%)	2 (4%)
Mineralization	3 (6%)		4 (8%)	2 (4%)	1 (2%)
Ulcer			2 (4%)	2 (4%)	1 (2%)
Artery, Inflammation, Chronic Active			(53)	(53)	(52)
Stomach, Glandular	(53)				
Erosion	1 (2%)		4 (8%)	3 (6%)	1 (2%)
Mineralization	2 (4%)				2 (4%)
Artery, Inflammation, Chronic Active	(1)				(1)
Tongue					(1)
Infiltration Cellular	(24)	(23)	(27)	(37)	(30)
Tooth	23 (96%)	21 (91%)	22 (81%)	34 (92%)	30 (100%)
Periodontal Tissue, Inflammation					

CARDIOVASCULAR SYSTEM

Blood Vessel	(53)	(53)	(53)	(52)	(53)
Aorta, Mineralization				1 (2%)	3 (6%)
Heart	(53)	(53)	(53)	(52)	(53)
Cardiomyopathy	11 (21%)	26 (49%)	31 (58%)	30 (58%)	32 (60%)
Inflammation, Suppurative	1 (2%)			1 (2%)	1 (2%)
Mineralization				1 (2%)	1 (2%)
Necrosis				1 (2%)	1 (2%)
Thrombosis	1 (2%)			1 (2%)	1 (2%)
Artery, Degeneration				1 (2%)	1 (2%)
Artery, Inflammation, Chronic Active				1 (2%)	1 (2%)

ENDOCRINE SYSTEM

Adrenal Cortex	(52)	(53)	(53)	(53)	(51)
Angiectasis	15 (29%)	20 (38%)	18 (34%)	17 (32%)	8 (16%)
Atrophy		3 (6%)			18 (35%)
Degeneration, Cystic	9 (17%)	15 (28%)	19 (36%)	25 (47%)	16 (31%)
Hematopoietic Cell Proliferation			1 (2%)		1 (2%)
Hyperplasia	12 (23%)	26 (49%)	23 (43%)	25 (47%)	21 (41%)
Hypertrophy	44 (85%)	45 (85%)	47 (89%)	46 (87%)	45 (88%)
Inflammation				1 (2%)	
Mineralization		1 (2%)	2 (4%)		1 (2%)
Necrosis					2 (4%)

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE

ENDOCRINE SYSTEM - CONT	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
Thrombosis					
Vacuolization Cytoplasmic Capsule, Inflammation	6 (12%)	1 (2%)	11 (21%)	7 (13%)	15 (29%)
Adrenal Medulla	(52)	(53)	(53)	1 (2%)	1 (2%)
Hyperplasia	10 (19%)	21 (40%)	12 (23%)	15 (28%)	(51)
Islets, Pancreatic	(52)	(53)	(53)	(53)	9 (18%)
Hyperplasia			1 (2%)	2 (4%)	(51)
Pituitary Gland	(53)	(53)	(53)	(53)	(53)
Angiectasis	6 (11%)		1 (2%)	2 (4%)	3 (6%)
Cyst	1 (2%)		1 (2%)	2 (4%)	
Cytoplasmic Alteration		3 (6%)			
Hemorrhage	1 (2%)				
Vacuolization Cytoplasmic Pars Distalis, Hyperplasia	18 (34%)	1 (2%)	2 (4%)	3 (6%)	1 (2%)
Pars Intermedia, Cyst	(53)	19 (36%)	24 (45%)	20 (38%)	19 (36%)
Thyroid Gland			1 (2%)		
C-Cell, Hyperplasia	24 (45%)	(53)	(51)	(52)	(51)
Follicular Cell, Hyperplasia	1 (2%)	24 (45%)	20 (39%)	18 (35%)	14 (27%)
Follicular Cell, Hypertrophy	4 (8%)	13 (25%)	12 (24%)	18 (35%)	23 (45%)

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Clitoral Gland	(51)	(53)	(53)	(51)	(50)
Hyperplasia, Squamous Inflammation	42 (82%)	40 (75%)	37 (70%)	1 (2%)	29 (58%)
Duct, Cyst	39 (76%)	41 (77%)	44 (83%)	39 (76%)	44 (88%)
Ovary	(52)	(52)	(53)	(53)	(51)
Atrophy	44 (85%)	44 (85%)	43 (81%)	49 (92%)	40 (78%)
Cyst	8 (15%)	16 (31%)	20 (38%)	14 (26%)	7 (14%)
Fibrosis		1 (2%)			
Hemorrhage					
Inflammation, Chronic Active Artery, Inflammation, Chronic Active		2 (4%)	1 (2%)	2 (4%)	1 (2%)
Oviduct		(2)		(2)	(5)
Cyst		2 (100%)			1 (20%)
Inflammation, Chronic Active	(52)	(53)	(53)	(53)	4 (80%)
Uterus					(51)

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRP03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
GENITAL SYSTEM - CONT					
Adenomyosis		1 (2%)	1 (2%)	2 (4%)	1 (2%)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Inflammation, Suppurative	6 (12%)	5 (9%)	9 (17%)	13 (25%)	3 (6%)
Metaplasia, Squamous	21 (40%)	32 (60%)	32 (60%)	35 (66%)	6 (12%)
Thrombosis				1 (2%)	30 (59%)
Ulcer		1 (2%)		1 (2%)	
Cervix, Hyperplasia, Stromal	1 (2%)				1 (2%)
Endometrium, Fibrosis	37 (71%)	35 (66%)	34 (64%)	33 (62%)	23 (45%)
Endometrium, Hyperplasia, Cystic	1 (2%)				
Epithelium, Necrosis					

HEMATOPOIETIC SYSTEM

Bone Marrow	(53)	(53)	(53)	(53)	(53)
Hyperplasia	36 (68%)	36 (68%)	34 (64%)	41 (77%)	48 (91%)
Lymph Node	(4)	(1)	(2)	(9)	(11)
Lumbar, Ectasia					
Lumbar, Hemorrhage					
Lumbar, Hyperplasia, Lymphoid					
Lumbar, Hyperplasia, Plasma Cell	1 (25%)	1 (100%)	1 (50%)	3 (33%)	1 (9%)
Mediastinal, Ectasia					
Mediastinal, Fibrosis					
Mediastinal, Hemorrhage					
Mediastinal, Hyperplasia, Histiocytic					
Mediastinal, Hyperplasia, Lymphoid					
Mediastinal, Hyperplasia, Plasma Cell					
Pancreatic, Ectasia	1 (25%)				
Pancreatic, Hyperplasia, Histiocytic					
Popliteal, Hyperplasia, Plasma Cell					
Renal, Hyperplasia, Histiocytic	1 (25%)	(53)	(53)	(53)	(53)
Lymph Node, Mandibular	(53)	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Ectasia					
Hemorrhage					
Hyperplasia, Plasma Cell	31 (58%)	42 (79%)	30 (57%)	22 (42%)	27 (51%)
Necrosis, Focal					
Lymph Node, Mesenteric	(52)	(53)	(53)	(53)	(50)
Ectasia	1 (2%)				
Hemorrhage	1 (2%)				
Hyperplasia, Histiocytic					
Hyperplasia, Lymphoid					
Pigmentation					

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL TERT. MIX TEO=10 TERT. MIX TEO=22 TERT. MIX TEO=46 TERT. MIX TEO=100

HEMATOPOIETIC SYSTEM - CONT

Spleen	(52)	(53)	(53)	(53)	(51)
Hematopoietic Cell Proliferation	43 (83%)	48 (91%)	42 (79%)	44 (83%)	42 (82%)
Hemorrhage					1 (2%)
Inflammation, Suppurative					1 (2%)
Necrosis	1 (2%)	50 (94%)	52 (98%)	47 (89%)	1 (2%)
Pigmentation	45 (87%)	2 (4%)	3 (6%)	2 (4%)	46 (90%)
Lymphoid Follicle, Atrophy	1 (2%)	1 (2%)	3 (6%)		3 (6%)
Red Pulp, Atrophy					
Thymus	(52)	(48)	(50)	(53)	(50)
Atrophy	32 (62%)	43 (90%)	45 (90%)	50 (94%)	48 (96%)
Cyst	2 (4%)			1 (2%)	
Ectopic Thyroid					
Hemorrhage				1 (2%)	

INTEGUMENTARY SYSTEM

Mammary Gland	(53)	(53)	(53)	(53)	(52)
Cyst		3 (6%)	1 (2%)	1 (2%)	
Hyperplasia	22 (42%)	7 (13%)	14 (26%)	12 (23%)	9 (17%)
Inflammation, Granulomatous	3 (6%)	4 (8%)	1 (2%)	3 (6%)	1 (2%)
Inflammation, Suppurative				1 (2%)	
Skin	(53)	(53)	(53)	(53)	(53)
Cyst Epithelial Inclusion		2 (4%)	1 (2%)	3 (6%)	3 (6%)
Hyperkeratosis			1 (2%)		
Inflammation, Suppurative			1 (2%)		
Ulcer				1 (2%)	
Hair Follicle, Atrophy		1 (2%)		1 (2%)	1 (2%)

MUSCULOSKELETAL SYSTEM

Bone	(53)	(53)	(53)	(53)	(53)
Mineralization			1 (2%)		

NERVOUS SYSTEM

Brain	(53)	(53)	(53)	(53)	(53)
Edema					3 (6%)
Gliosis	1 (2%)			1 (2%)	1 (2%)
Hemorrhage		1 (2%)			
Hydrocephalus	1 (2%)	4 (8%)	2 (4%)	2 (4%)	

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT03
 Date: 04/24/03
 Time: 08:07:42

	SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
NERVOUS SYSTEM - CONT						
Inflammation, Granulomatous		1 (2%)		1 (2%)		3 (6%)
Mineralization						1 (2%)
Necrosis						
Artery, Degeneration						

	RESPIRATORY SYSTEM					
Lung	(53)	(53)	(53)	(53)	(53)	(53)
Congestion			1 (2%)		1 (2%)	1 (2%)
Cyst			2 (4%)		2 (4%)	1 (2%)
Edema			1 (2%)		1 (2%)	1 (2%)
Hemorrhage	43 (81%)	50 (94%)	48 (91%)	48 (91%)	48 (91%)	50 (94%)
Infiltration Cellular, Histocyte	4 (8%)	2 (4%)	3 (6%)	3 (6%)	1 (2%)	2 (4%)
Inflammation	2 (4%)		2 (4%)		8 (15%)	11 (21%)
Metaplasia, Squamous					1 (2%)	2 (4%)
Mineralization		21 (40%)	25 (47%)	10 (19%)	1 (2%)	2 (4%)
Alveolar Epithelium, Hyperplasia			20 (38%)	33 (62%)	41 (77%)	40 (75%)
Alveolar Epithelium, Metaplasia						1 (2%)
Perivascular, Inflammation, Chronic Active	(53)	(53)	(53)	(53)	(53)	(53)
Nose	1 (2%)	2 (4%)	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Inflammation					1 (2%)	1 (2%)
Goblet Cell, Hyperplasia					1 (2%)	1 (2%)
Goblet Cell, Septum, Hyperplasia					1 (2%)	1 (2%)
Nasolacrimal Duct, Inflammation			1 (2%)		1 (2%)	1 (2%)
Respiratory Epithelium, Hyperplasia		1 (2%)			4 (8%)	4 (8%)
Turbinate, Cyst					1 (2%)	1 (2%)
Turbinate, Respiratory Epithelium, Hyperplasia						1 (2%)

	SPECIAL SENSES SYSTEM					
Eye	(53)	(53)	(53)	(53)	(53)	(53)
Anterior Chamber, Ciliary Body, Iris, Inflammation, Suppurative						1 (2%)
Cornea, Inflammation, Suppurative						1 (2%)
Lens, Degeneration	1 (2%)		1 (2%)		2 (4%)	1 (2%)
Retina, Atrophy	(53)	(53)	(52)	(52)	(53)	(53)
Harderian Gland	8 (15%)	11 (21%)	4 (8%)		5 (9%)	3 (6%)
Inflammation						8 (15%)

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PE1RPT03
 Date: 04/24/03
 Time: 08:07:42

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
URINARY SYSTEM					
Kidney	(52)	(53)	(53)	(53)	(51)
Calculus Micro Observation Only	9 (17%)	5 (9%)	8 (15%)	4 (8%)	1 (2%)
Cysts Protein			1 (2%)	1 (2%)	
Cyst		1 (2%)			
Developmental Malformation				1 (2%)	
Fibrosis					1 (2%)
Inflammation, Chronic	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Inflammation, Chronic Active	3 (6%)	2 (4%)	3 (6%)	3 (6%)	6 (12%)
Inflammation, Suppurative	41 (79%)	48 (91%)	47 (89%)	42 (79%)	35 (69%)
Mineralization	26 (50%)	41 (77%)	40 (75%)	47 (89%)	49 (96%)
Nephropathy	2 (4%)		1 (2%)	1 (2%)	1 (2%)
Pelvis, Dilatation			1 (2%)		
Pelvis, Inflammation	2 (4%)	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Renal Tubule, Hyperplasia				2 (4%)	
Renal Tubule, Necrosis	1 (2%)		1 (2%)		
Transitional Epithelium, Hyperplasia	5 (10%)	5 (9%)	8 (15%)	10 (19%)	8 (16%)
Ureter	1 (100%)		1 (100%)	1 (100%)	1 (100%)
Cyst					
Inflammation					
Metaplasia, Squamous			1 (100%)	1 (100%)	
Transitional Epithelium, Hyperplasia			1 (100%)	1 (100%)	
Urinary Bladder	(52)	(52)	(53)	(53)	(50)
Edema				1 (2%)	
Hemorrhage					
Inflammation	12 (23%)	3 (6%)	4 (8%)	8 (15%)	1 (2%)
Metaplasia, Squamous				1 (2%)	
Transitional Epithelium, Hyperplasia			1 (2%)	3 (6%)	4 (8%)

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
Route: GAVAGE

Report: PEIRPPT05
Date: 04/22/03
Time: 10:51:19

CORE STUDY/FINAL#1

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25018 Dosing Accident
25020 Natural Death

25019 Moribund Sacrifice
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

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

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:51:19

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL TERT. MIX TEO=10 TERT. MIX TEO=22 TERT. MIX TEO=46 TERT. MIX TEO=100

DISPOSITION SUMMARY

Disposition	TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46	TERT. MIX TEO=100
Animals Initially in Study	98	98	98	98	98
Early Deaths	26	25	22	25	33
Moribund Sacrifice	11	5	6	4	10
Natural Death			1	1	2
Dosing Accident					
Survivors	16	23	24	23	8
Terminal Sacrifice					
Animals Examined Microscopically	53	53	53	53	53

ALIMENTARY SYSTEM

Intestine Large, Colon	(53)	(52)	(53)	(53)	(51)
Carcinoma	1 (2%)				(52)
Intestine Large, Rectum	(52)	(53)	(53)	(53)	(52)
Polyp Adenomatous			1 (2%)		
Schwannoma Malignant, Metastatic, Uterus				1 (2%)	(51)
Intestine Large, Cecum	(51)	(53)	(53)	(53)	(52)
Intestine Small, Duodenum	(52)	(53)	(53)	(53)	(50)
Carcinoma			1 (2%)		(50)
Intestine Small, Jejunum	(52)	(53)	(53)	(53)	(50)
Leiomyosarcoma	1 (2%)	(53)	1 (2%)	(53)	(50)
Intestine Small, Ileum	(52)	(53)	(53)	(53)	(50)
Liver	(53)	(53)	(53)	(53)	(50)
Cholangiocarcinoma			2 (4%)		(51)
Cholangiocarcinoma, Multiple				5 (9%)	(51)
Histiocytic Sarcoma				2 (4%)	4 (8%)
Mesentery		(1)	(2)	(6)	1 (2%)
Histiocytic Sarcoma					(8)
Lipoma					1 (13%)
Oral Mucosa	(10)	(18)	(19)	1 (17%)	(31)
Gingival, Squamous Cell Carcinoma	1 (10%)	1 (6%)	(53)	(29)	2 (6%)
Pancreas	(52)	(53)	2 (4%)	(53)	(51)
Acinus, Adenoma					
Acinus, Carcinoma		1 (2%)	(53)	2 (4%)	(53)
Salivary Glands	(53)	(53)	(53)	(53)	(53)
Carcinoma		1 (2%)			1 (2%)
Schwannoma Malignant, Metastatic, Skin					(52)
Stomach, Forestomach	(53)	(53)	(53)	(53)	(52)
Stomach, Glandular	(53)	(53)	(53)	(53)	(52)

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
ALIMENTARY SYSTEM - cont					
Tongue	(1)				(1)
Squamous Cell Carcinoma, Metastatic, Oral	1 (100%)				
Mucosa	(24)				
Tooth	1 (4%)				
Periodontal Tissue, Fibrosarcoma		(23)	(27)	(37)	(30)

CARDIOVASCULAR SYSTEM

Blood Vessel	(53)	(53)	(53)	(52)	(53)
Aorta, Adventitia, Carcinoma, Metastatic,					
Mammary Gland	1 (2%)	(53)	(53)	(52)	(53)
Heart	(53)				
Fibrous Histiocytoma, Metastatic, Skeletal		1 (2%)			
Muscle					
Schwannoma Malignant	2 (4%)			1 (2%)	3 (6%)

ENDOCRINE SYSTEM

Adrenal Cortex	(52)	(53)	(53)	(53)	(51)
Adenoma		1 (2%)	1 (2%)	1 (2%)	
Carcinoma		1 (2%)	1 (2%)	1 (2%)	
Adrenal Medulla	(52)	(53)	(53)	(53)	(51)
Pheochromocytoma, Benign	4 (8%)	3 (6%)	4 (8%)	4 (8%)	1 (2%)
Bilateral, Pheochromocytoma Benign	1 (2%)	1 (2%)			
Islets, Pancreatic	(52)	(53)	(53)	(53)	(51)
Adenoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Carcinoma	1 (2%)				
Parathyroid Gland	(50)	(50)	(49)	(47)	(52)
Adenoma	1 (2%)				
Pituitary Gland	(53)	(53)	(53)	(53)	(53)
Carcinoma		1 (2%)	1 (2%)	1 (2%)	
Pars Distalis, Adenoma	28 (53%)	29 (55%)	22 (42%)	20 (38%)	10 (19%)
Thyroid Gland	(53)	(53)	(51)	(52)	(51)
Bilateral, C-Cell, Adenoma	2 (4%)	2 (4%)	3 (6%)	1 (2%)	
Bilateral, Follicular Cell, Carcinoma			1 (2%)		
C-Cell, Adenoma	15 (28%)	8 (15%)	15 (29%)	8 (15%)	5 (10%)
C-Cell, Carcinoma	2 (4%)			1 (2%)	1 (2%)
Follicular Cell, Adenoma					1 (2%)

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/23/03
 Time: 10:51:19

SPRAGUE-DAWLEY RATS FEMALE TERT. MIX CONTROL TERT. MIX TEO=10 TERT. MIX TEO=22 TERT. MIX TEO=46 TERT. MIX TEO=100

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

Ovary	(52)	(52)	(53)	(53)	(51)
Fibrous Histiocytoma, Metastatic, Skeletal Muscle		1 (2%)			1 (2%)
Granulosa Cell Tumor Malignant			1 (2%)	1 (2%)	(51)
Granulosa Cell Tumor Benign	(52)	(53)	(53)	2 (4%)	1 (2%)
Uterus		1 (2%)	2 (4%)		1 (2%)
Carcinoma					1 (2%)
Hemangiosarcoma			2 (4%)		
Histiocytic Sarcoma					
Leiomyoma			2 (4%)		
Leiomyosarcoma	1 (2%)	1 (2%)	2 (4%)	3 (6%)	2 (4%)
Polyp Stromal	3 (6%)		1 (2%)		
Polyp Stromal, Multiple	1 (2%)		1 (2%)		
Schwannoma Malignant	1 (2%)		1 (2%)	2 (4%)	1 (2%)
Squamous Cell Carcinoma					
Squamous Cell Papilloma	1 (2%)		1 (2%)		
Cervix, Carcinoma	1 (2%)				
Cervix, Squamous Cell Carcinoma			1 (2%)		1 (2%)
Serosa, Carcinoma, Metastatic, Uterus	1 (2%)				
Vagina				1 (1)	
Schwannoma Malignant				1 (100%)	

HEMATOPOIETIC SYSTEM

Bone Marrow	(53)	(53)	(53)	(53)	(53)
Lymph Node	(4)	(11)	(2)	(9)	(11)
Deep Cervical, Carcinoma, Metastatic, Thyroid Gland				1 (11%)	1 (9%)
Pancreatic, Histiocytic Sarcoma					1 (9%)
Renal, Histiocytic Sarcoma	(53)	(53)	(53)	(53)	(53)
Lymph Node, Mandibular	(52)	(53)	(53)	(53)	(50)
Lymph Node, Mesenteric					1 (2%)
Histiocytic Sarcoma	(52)	(53)	(53)	(53)	(51)
Spleen	(52)	(48)	(50)	(53)	(50)
Thymus					

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PEIRPT05
 Date: 04/22/03
 Time: 10:51:19

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
HEMATOPOIETIC SYSTEM - cont					
Fibrosarcoma, Metastatic, Skin	1 (2%)				

INTEGUMENTARY SYSTEM

Mammary Gland	(53)	(53)	(53)	(53)	(52)
Adenoacanthoma			1 (2%)		
Adenolipoma		1 (2%)	1 (2%)		
Carcinoma	5 (9%)	6 (11%)	3 (6%)	5 (9%)	1 (2%)
Carcinoma, Multiple	1 (2%)				
Fibroadenoma	21 (40%)	17 (32%)	19 (36%)	20 (38%)	15 (29%)
Fibroadenoma, Multiple	13 (25%)	10 (19%)	16 (30%)	8 (15%)	3 (6%)
Skin	(53)	(53)	(53)	(53)	(53)
Fibroma	1 (2%)	2 (4%)	2 (4%)	3 (6%)	
Fibrosarcoma	1 (2%)			1 (2%)	
Pilomatricoma				1 (2%)	
Schwannoma Malignant					1 (2%)
Schwannoma Malignant, Metastatic, Uterus					
Squamous Cell Papilloma			1 (2%)		

MUSCULOSKELETAL SYSTEM

Skeletal Muscle	(1)				
Fibrous Histiocytoma	1 (100%)				

NERVOUS SYSTEM

Brain	(53)	(53)	(53)	(53)	(53)
Carcinoma, Metastatic, Kidney	1 (2%)				
Carcinoma, Metastatic, Pituitary Gland					
Granular Cell Tumor Malignant		1 (2%)			
Medulloblastoma Mal					
Oligodendroglioma Malignant		1 (2%)			
Meninges, Meningioma Malignant		1 (2%)			
Spinal Cord	(1)	(1)			

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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RESPIRATORY SYSTEM

Lung	(53)	(53)	(53)	(53)	(53)
Alveolar/Bronchiolar Adenoma				1 (2%)	
Carcinoma, Metastatic, Mammary Gland	3 (6%)	1 (2%)	1 (2%)	2 (4%)	
Carcinoma, Metastatic, Uterus	1 (2%)				
Carcinoma, Metastatic, Adrenal Cortex			1 (2%)	2 (4%)	9 (17%)
Cystic Keratinizing Epithelioma					11 (21%)
Cystic Keratinizing Epithelioma, Multiple					
Fibrosarcoma, Metastatic, Skin	1 (2%)				
Fibrous Histicytoma, Metastatic, Skeletal Muscle		1 (2%)			
Histicytic Sarcoma					1 (2%)
Schwannoma Malignant, Metastatic, Skin					1 (2%)
Mediastinum, Carcinoma, Metastatic, Mammary Gland	1 (2%)				
Mediastinum, Fibrous Histicytoma, Metastatic, Skeletal Muscle	(53)	1 (2%)	(53)	(53)	(53)
Nose					
Schwannoma Malignant			1 (2%)		

SPECIAL SENSES SYSTEM

Harderian Gland	(53)	(53)	(52)	(53)	(53)
Histicytic Sarcoma					1 (2%)

URINARY SYSTEM

Kidney	(52)	(53)	(53)	(53)	(51)
Hemangiosarcoma			1 (2%)		
Nephroblastoma	1 (2%)				
Bilateral, Renal Tubule, Carcinoma	1 (2%)				
Renal Tubule, Carcinoma		1 (2%)			
Transitional Epithelium, Papilloma				1 (2%)	

SYSTEMIC LESIONS

Multiple Organs	* (53)	* (53)	* (53)	* (53)	* (53)
Adenolipoma			1 (2%)		

* Number of animals with any tissue examined microscopically

NTP Experiment-Test: 96007-04 INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
 Study Type: CHRONIC TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
 Route: GAVAGE

Report: PTRRPT05
 Date: 04/22/03
 Time: 10:51:19

SPRAGUE-DAWLEY RATS FEMALE

TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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SYSTEMIC LESIONS - cont

Multiple Organs	* (53)	* (53)	* (53)	* (53)
Histiocytic Sarcoma	2 (4%)	1 (2%)	1 (2%)	4 (8%)
Lymphoma Malignant				1 (2%)

SPRAGUE-DAWLEY RATS FEMALE TERT. MIX TERT. MIX TERT. MIX TERT. MIX TERT. MIX
 CONTROL TEQ=10 TEQ=10 TEQ=22 TEQ=46 TEQ=100

TUMOR SUMMARY

Total Animals with Primary Neoplasms (b)	51	46	50	50	45
Total Primary Neoplasms	115	93	117	98	84
Total Animals with Benign Neoplasms	45	43	46	43	36
Total Benign Neoplasms	92	76	96	74	57
Total Animals with Malignant Neoplasms	18	14	19	21	23
Total Malignant Neoplasms	23	17	21	23	27
Total Animals with Metastatic Neoplasms	7	2	2	4	1
Total Metastatic Neoplasms	11	5	2	5	2
Total Animals with Malignant Neoplasms Uncertain Primary Site					
Total Animals with Neoplasms Uncertain- Benign or Malignant				1	
Total Uncertain Neoplasms				1	

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

NTP
LAB: Battelle Columbus
EXPERIMENT: 96007 TEST: 04
TEST TYPE: CHRONIC
CONT: N01-ES-75411
PATHOLOGIST: SELLS, DONALD

STATISTICAL ANALYSIS OF PRIMARY TUMORS
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

REPORT: PEIRPT08
DATE: 04/22/03
TIME: 10:54:37
PAGE: 1
NTP C#: 96007B
CAS: TEFDIOXINMIX

CORE STUDY/FINAL#1

REASONS FOR REMOVAL:

25018 Dosing Accident
25019 Moribund Sacrifice
25020 Natural Death
25021 Terminal Sacrifice

REMOVAL DATE RANGE:

ALL

TREATMENT GROUPS:

INCLUDE ALL

NTP
LAB: Battelle Columbus
EXPERIMENT: 96007 TEST: 04
TEST TYPE: CHRONIC
CONT: N01-ES-75411
PATHOLOGIST: SELLS, DONALD
Rats (SPRAGUE-DAWLEY)

STATISTICAL ANALYSIS OF PRIMARY TUMORS
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

REPORT: P1RPT08
DATE: 04/22/03
TIME: 10:54:37
NTP #: 96007B
CAS: TEFDIOXINMTX

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
Heart
Islets, Pancreatic
Kidney
Liver
Lung
Nose
Ovary
Pancreas
Parathyroid Gland
Pituitary Gland
Salivary Glands
Thyroid Gland

NTP
LAB: Battelle Columbus
EXPERIMENT: 96007 TEST: 04
TEST TYPE: CHRONIC
CONT: N01-ES-75411
PATHOLOGIST: SELLS, DONALD

STATISTICAL ANALYSIS OF PRIMARY TUMORS
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)
CAGES FROM 0000 TO LAST CAGE
ROUTE: GAVAGE

REPORT: PEIRPT08
DATE: 04/22/03
TIME: 10:54:37
NTP C#: 96007B
CAS: TEPDIOXINMIX

SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS
IN THE ANALYSIS OF TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Female Rats

Organ Morphology
Liver Cholangiocarcinoma
Lung Cystic Keratinizing Epithelioma
Mammary Gland Carcinoma or Adenoma
Fibroadenoma

Pituitary Gland: Pars Distalis or Unspecified Site
Adenoma
Fibroma, Fibroadenoma or Adenoma
Fibroma, Fibroadenoma, Carcinoma, or Adenoma

Thyroid Gland: C-Cell
Adenoma
Carcinoma or Adenoma
Histiocytic Sarcoma

All Organs
Benign Tumors
Malignant Tumors
Malignant and Benign Tumors

Adrenal Medulla
 pheochromocytoma Benign

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

OVERALL (a)	5/52 (10%)	4/53 (8%)	4/53 (8%)	4/53 (8%)	1/51 (2%)
POLY-3 RATE (b)	5/35.98	4/41.21	4/42.32	4/39.85	1/32.48
POLY-3 PERCENT (g)	13.9%	9.7%	9.5%	10.0%	3.1%
TERMINAL (d)	3/16 (19%)	1/23 (4%)	1/24 (4%)	2/23 (9%)	0/8 (0%)
FIRST INCIDENCE	693	456	456	669	674

STATISTICAL TESTS

LIFE TABLE	P=0.207N	P=0.345N	P=0.305N	P=0.333N	P=0.263N
POLY 3	P=0.128N	P=0.414N	P=0.398N	P=0.435N	P=0.122N
POLY 1.5	P=0.107N	P=0.441N	P=0.437N	P=0.454N	P=0.112N
POLY 6	P=0.161N	P=0.383N	P=0.356N	P=0.411N	P=0.143N
LOGISTIC REGRESSION	P=0.109N	P=0.435N	P=0.414N	P=0.403N	P=0.180N
COCH-ARM / FISHERS	P=0.089N	P=0.488N	P=0.488N	P=0.488N	P=0.107N
ORDER RESTRICTED	P=0.118N	(e)	(e)	(e)	(e)

Heart
 Schwannoma Malignant

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

OVERALL (a)	2/53 (4%)	0/53 (0%)	0/53 (0%)	1/52 (2%)	3/53 (6%)
POLY-3 RATE (b)	2/36.88	0/39.99	0/41.29	1/40.10	3/34.73
POLY-3 PERCENT (g)	5.4%	0.0%	0.0%	2.5%	8.6%
TERMINAL (d)	1/16 (6%)	0/23 (0%)	0/24 (0%)	0/23 (0%)	0/8 (0%)
FIRST INCIDENCE	526	---	---	465	312

STATISTICAL TESTS

LIFE TABLE	P=0.080	P=0.189N	P=0.180N	P=0.441N	P=0.434
POLY 3	P=0.090	P=0.219N	P=0.212N	P=0.471N	P=0.472
POLY 1.5	P=0.098	P=0.225N	P=0.223N	P=0.483N	P=0.486
POLY 6	P=0.081	P=0.212N	P=0.201N	P=0.458N	P=0.446
LOGISTIC REGRESSION	P=0.166	P=0.237N	P=0.237N	P=0.546N	P=0.553
COCH-ARM / FISHERS	P=0.111	P=0.248N	P=0.248N	P=0.507N	P=0.500
ORDER RESTRICTED	P=0.077	(e)	(e)	(e)	(e)

Islets, Pancreatic Carcinoma or Adenoma

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
OVERALL (a)	2/52 (4%)	1/53 (2%)	1/53 (2%)	1/53 (2%)
POLY-3 RATE (b)	2/36.05	1/39.99	1/41.29	1/39.44
POLY-3 PERCENT (g)	5.6%	2.5%	2.4%	2.5%
TERMINAL (d)	1/16 (6%)	1/23 (4%)	1/24 (4%)	1/23 (4%)
FIRST INCIDENCE	655	729 (T)	729 (T)	729 (T)
STATISTICAL TESTS				
LIFE TABLE				
POLY 3	P=0.270N	P=0.402N	P=0.383N	P=0.395N
	P=0.207N	P=0.464N	P=0.453N	P=0.469N
POLY 1.5	P=0.195N	P=0.473N	P=0.473N	P=0.477N
	P=0.222N	P=0.454N	P=0.435N	P=0.460N
POLY 6	P=0.231N	P=0.445N	P=0.427N	P=0.452N
LOGISTIC REGRESSION	P=0.182N	P=0.493N	P=0.493N	P=0.493N
COCH-ARM / FISHERS	P=0.143N	(e)	(e)	(e)
ORDER RESTRICTED				

Liver Cholangiocarcinoma

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
OVERALL (a)	0/53 (0%)	0/53 (0%)	2/53 (4%)	7/53 (13%)
POLY-3 RATE (b)	0/36.25	0/39.99	2/41.51	7/40.30
POLY-3 PERCENT (g)	0.0%	0.0%	4.8%	17.4%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	1/24 (4%)	5/23 (22%)
FIRST INCIDENCE	---	---	669	521
STATISTICAL TESTS				
LIFE TABLE				
POLY 3	P<0.001 **	(e)	P=0.321	P=0.025 *
	P<0.001 **	(e)	P=0.268	P=0.011 *
POLY 1.5	P<0.001 **	(e)	P=0.254	P=0.009 **
	P<0.001 **	(e)	P=0.285	P=0.012 **
POLY 6	P<0.001 **	(e)	P=0.276	P=0.013 *
LOGISTIC REGRESSION	P<0.001 **	(e)	P=0.248	P=0.006 **
COCH-ARM / FISHERS	P<0.001 **	(e)	(e)	P=0.001 **
ORDER RESTRICTED				(e)

Lung
 Cystic Keratinizing Epithelioma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

OVERALL (a)	0/53 (0%)	0/53 (0%)	0/53 (0%)	2/53 (4%)	20/53 (38%)
POLY-3 RATE (b)	0/36.25	0/39.99	0/41.29	2/39.57	20/36.59
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	5.1%	54.7%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	0/24 (0%)	1/23 (4%)	5/8 (63%)
FIRST INCIDENCE				697	542

STATISTICAL TESTS

LIFE TABLE

P<0.001 **	(e)	(e)	(e)	P=0.300	P<0.001 **
P<0.001 **	(e)	(e)	(e)	P=0.256	P<0.001 **
P<0.001 **	(e)	(e)	(e)	P=0.249	P<0.001 **
P<0.001 **	(e)	(e)	(e)	P=0.266	P<0.001 **
P<0.001 **	(e)	(e)	(e)	P=0.271	P<0.001 **
P<0.001 **	(e)	(e)	(e)	P=0.248	P<0.001 **

LOGISTIC REGRESSION
 COCH-ARM / FISHERS
 ORDER RESTRICTED

Mammary Gland
 Carcinoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

OVERALL (a)	6/53 (11%)	6/53 (11%)	3/53 (6%)	5/53 (9%)	1/53 (2%)
POLY-3 RATE (b)	6/38.75	6/42.31	3/41.42	5/41.78	1/32.91
POLY-3 PERCENT (g)	15.5%	14.2%	7.2%	12.0%	3.0%
TERMINAL (d)	2/16 (13%)	3/23 (13%)	1/24 (4%)	2/23 (9%)	0/8 (0%)
FIRST INCIDENCE	218	227	702	276	548

STATISTICAL TESTS

LIFE TABLE

P=0.111N	P=0.481N	P=0.137N	P=0.388N	P=0.120N
P=0.081N	P=0.559N	P=0.207N	P=0.446N	P=0.084N
P=0.065N	P=0.579N	P=0.225N	P=0.465N	P=0.072N
P=0.105N	P=0.535N	P=0.187N	P=0.426N	P=0.105N
P=0.033N*	P=0.535	P=0.254N	P=0.584N	P=0.049N*
P=0.046N*	P=0.620N	P=0.244N	P=0.500N	P=0.056N
P=0.080N	(e)	(e)	(e)	(e)

LOGISTIC REGRESSION
 COCH-ARM / FISHERS
 ORDER RESTRICTED

Mammary Gland Carcinoma or Adenoma

Dose	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
OVERALL (a)	6/53 (11%)	7/53 (13%)	3/53 (6%)	5/53 (9%)
POLY-3 RATE (b)	6/38.75	7/42.36	3/41.42	5/41.78
POLY-3 PERCENT (g)	15.5%	16.5%	7.2%	12.0%
TERMINAL (d)	2/16 (13%)	3/23 (13%)	1/24 (4%)	2/23 (9%)
FIRST INCIDENCE	218	227	702	276

Mammary Gland Fibroadenoma

Dose	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
OVERALL (a)	6/53 (11%)	7/53 (13%)	3/53 (6%)	5/53 (9%)
POLY-3 RATE (b)	6/38.75	7/42.36	3/41.42	5/41.78
POLY-3 PERCENT (g)	15.5%	16.5%	7.2%	12.0%
TERMINAL (d)	2/16 (13%)	3/23 (13%)	1/24 (4%)	2/23 (9%)
FIRST INCIDENCE	218	227	702	276

STATISTICAL TESTS

LIFE TABLE	#	Males		Females	
		TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
POLY 3	P=0.092N	P=0.579N	P=0.137N	P=0.388N	P=0.120N
POLY 1.5	P=0.062N	P=0.570	P=0.207N	P=0.446N	P=0.084N
POLY 6	P=0.050N	P=0.546	P=0.225N	P=0.465N	P=0.072N
LOGISTIC REGRESSION	P=0.082N	P=0.597	P=0.187N	P=0.426N	P=0.105N
COCH-ARM / FISHERS	P=0.026N*	P=0.423	P=0.254N	P=0.584N	P=0.049N*
ORDER RESTRICTED	P=0.035N*	P=0.500	P=0.244N	P=0.500N	P=0.056N
	(e)	(e)	(e)	(e)	(e)

TUMOR RATES	#	Males		Females	
		TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
OVERALL (a)	34/53 (64%)	27/53 (51%)	35/53 (66%)	28/53 (53%)	18/53 (34%)
POLY-3 RATE (b)	27/45.66	27/47.68	35/48.71	28/45.80	18/36.95
POLY-3 PERCENT (g)	74.5%	56.6%	71.9%	61.1%	48.7%
TERMINAL (d)	11/16 (69%)	8/23 (35%)	16/24 (67%)	10/23 (44%)	6/8 (75%)
FIRST INCIDENCE	176	362	263	333	409

LIFE TABLE	#	Males		Females	
		TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
POLY 3	P=0.258N	P=0.041N*	P=0.145N	P=0.047N*	P=0.183N
POLY 1.5	P=0.024N*	P=0.047N*	P=0.477N	P=0.115N	P=0.008N**
POLY 6	P=0.006N**	P=0.067N	P=0.565N	P=0.129N	P=0.003N**
LOGISTIC REGRESSION	P=0.089N	P=0.033N*	P=0.400N	P=0.100N	P=0.031N*
COCH-ARM / FISHERS	P=0.002N**	P=0.107N	P=0.561	P=0.126N	P=0.003N**
ORDER RESTRICTED	P=0.001N**	P=0.119N	P=0.500	P=0.162N	P=0.002N**
	(e)	(e)	(e)	(e)	(e)

Mammary Gland
 Fibroma, Fibroadenoma or Adenoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
OVERALL (a)	34/53 (64%)	28/53 (53%)	35/53 (66%)	28/53 (53%)
POLY-3 RATE (b)	34/45.66	28/47.72	35/48.71	28/45.80
POLY-3 PERCENT (g)	74.5%	58.7%	71.9%	61.1%
TERMINAL (d)	11/16 (69%)	8/23 (35%)	16/24 (67%)	10/23 (44%)
FIRST INCIDENCE	176	362	263	333

Mammary Gland
 Fibroma, Fibroadenoma, Carcinoma, or Adenoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
OVERALL (a)	34/53 (64%)	28/53 (53%)	35/53 (66%)	28/53 (53%)
POLY-3 RATE (b)	34/45.66	28/47.72	35/48.71	28/45.80
POLY-3 PERCENT (g)	74.5%	58.7%	71.9%	61.1%
TERMINAL (d)	11/16 (69%)	8/23 (35%)	16/24 (67%)	10/23 (44%)
FIRST INCIDENCE	176	362	263	333

Mammary Gland
 Fibroma, Fibroadenoma, Carcinoma, or Adenoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
OVERALL (a)	37/53 (70%)	33/53 (62%)	36/53 (68%)	31/53 (58%)
POLY-3 RATE (b)	37/48.01	33/50.04	36/48.82	31/48.14
POLY-3 PERCENT (g)	77.1%	65.9%	73.7%	64.4%
TERMINAL (d)	11/16 (69%)	10/23 (44%)	16/24 (67%)	10/23 (44%)
FIRST INCIDENCE	176	227	263	276

STATISTICAL TESTS

TEST	P=0.156N	P=0.093N	P=0.092N	P=0.055N	P=0.123N
LIFE TABLE	P=0.008N**	P=0.151N	P=0.441N	P=0.116N	P=0.005N**
POLY 3	P=0.001N**	P=0.188N	P=0.490N	P=0.128N	P=0.002N**
POLY 1.5	P=0.042N*	P=0.118N	P=0.394N	P=0.104N	P=0.026N*
POLY 6	P<0.001N**	P=0.316N	P=0.475N	P=0.168N	P<0.001N**
LOGISTIC REGRESSION	P<0.001N**	P=0.269N	P=0.500N	P=0.156N	P<0.001N**
COCH-ARM / FISHERS	P=0.007N**	(e)	(e)	(e)	(e)
ORDER RESTRICTED	(e)	(e)	(e)	(e)	(e)

Oral Cavity (Oral Mucosa, Tongue, Pharynx, Tooth, Gingiva)
 Squamous Cell Carcinoma

Dose	Males		Females	
	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
TUMOR RATES	#	#	#	#
OVERALL (a)	1/53 (2%)	0/53 (0%)	0/53 (0%)	2/53 (4%)
POLY-3 RATE (b)	1/36.48	0/41.29	0/39.44	2/33.59
POLY-3 PERCENT (g)	2.7%	0.0%	0.0%	6.0%
TERMINAL (d)	0/16 (0%)	0/24 (0%)	0/23 (0%)	0/8 (0%)
FIRST INCIDENCE	668	563	434	434

STATISTICAL TESTS

LIFE TABLE

POLY 3	P=0.232	P=0.730N	P=0.454N	P=0.443N	P=0.450
POLY 1.5	P=0.261	P=0.737N	P=0.475N	P=0.484N	P=0.471
POLY 6	P=0.270	P=0.746N	P=0.486N	P=0.490N	P=0.484
LOGISTIC REGRESSION	P=0.251	P=0.727N	P=0.464N	P=0.478N	P=0.449
COCH-ARM / FISHERS	P=0.318	P=0.758	P=0.485N	P=0.488N	P=0.516
ORDER RESTRICTED	P=0.283	P=0.752N	P=0.500N	P=0.500N	P=0.500

Oral Cavity (Oral Mucosa, Tongue, Pharynx, Tooth, Gingiva)
 Squamous Cell Carcinoma, Papilloma Squamous, or Papilloma

Dose	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
TUMOR RATES	#	#	#	#
OVERALL (a)	1/53 (2%)	1/53 (2%)	0/53 (0%)	0/53 (0%)
POLY-3 RATE (b)	1/36.48	1/40.53	0/41.29	0/39.44
POLY-3 PERCENT (g)	2.7%	2.5%	0.0%	0.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	0/24 (0%)	0/23 (0%)
FIRST INCIDENCE	668	563	434	434

STATISTICAL TESTS

LIFE TABLE

POLY 3	P=0.232	P=0.730N	P=0.454N	P=0.443N	P=0.450
POLY 1.5	P=0.261	P=0.737N	P=0.475N	P=0.484N	P=0.471
POLY 6	P=0.270	P=0.746N	P=0.486N	P=0.490N	P=0.484
LOGISTIC REGRESSION	P=0.251	P=0.727N	P=0.464N	P=0.478N	P=0.449
COCH-ARM / FISHERS	P=0.318	P=0.758	P=0.485N	P=0.488N	P=0.516
ORDER RESTRICTED	P=0.283	P=0.752N	P=0.500N	P=0.500N	P=0.500

Oral Mucosa Squamous Cell Carcinoma

Dose	Females			
	TERT_MIX CONTROL	TERT_MIX TEQ=10	TERT_MIX TEQ=22	TERT_MIX TEQ=46
				TERT_MIX TEQ=100

TUMOR RATES

	#	#	#	#
OVERALL (a)	1/53 (2%)	1/53 (2%)	0/53 (0%)	0/53 (0%)
POLY-3 RATE (b)	1/36.48	1/40.53	0/41.29	0/39.44
POLY-3 PERCENT (g)	2.7%	2.5%	0.0%	0.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	0/24 (0%)	0/23 (0%)
FIRST INCIDENCE	668	563	---	---

STATISTICAL TESTS

	P=0.232	P=0.730N	P=0.454N	P=0.443N	P=0.450
LIFE TABLE					
POLY 3	P=0.261	P=0.737N	P=0.475N	P=0.484N	P=0.471
POLY 1.5	P=0.270	P=0.746N	P=0.486N	P=0.490N	P=0.484
POLY 6	P=0.251	P=0.727N	P=0.464N	P=0.478N	P=0.449
LOGISTIC REGRESSION	P=0.318	P=0.758	P=0.485N	P=0.488N	P=0.516
COCH-ARM / FISHERS	P=0.283	P=0.752N	P=0.500N	P=0.500N	P=0.500
ORDER RESTRICTED	P=0.155	(e)	(e)	(e)	(e)

Ovary Granulosa Cell Tumor: Benign, Malignant, NOS

Dose	Females			
	TERT_MIX CONTROL	TERT_MIX TEQ=10	TERT_MIX TEQ=22	TERT_MIX TEQ=46
				TERT_MIX TEQ=100

TUMOR RATES

	0/52 (0%)	0/52 (0%)	2/53 (4%)	1/53 (2%)	1/51 (2%)
OVERALL (a)					
POLY-3 RATE (b)	0/35.78	0/39.75	2/41.67	1/39.44	1/32.46
POLY-3 PERCENT (g)	0.0%	0.0%	4.8%	2.5%	3.1%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	1/24 (4%)	1/23 (4%)	0/8 (0%)
FIRST INCIDENCE	---	---	621	729 (T)	682

STATISTICAL TESTS

	P=0.229	P=0.297	P=0.272	P=0.572	P=0.443
LIFE TABLE					
POLY 3	P=0.327	P=0.272	P=0.258	P=0.519	P=0.481
POLY 1.5	P=0.354	P=0.258	P=0.288	P=0.514	P=0.490
POLY 6	P=0.289	P=0.288	P=0.260	P=0.572	P=0.465
LOGISTIC REGRESSION	P=0.322	P=0.260	P=0.252	P=0.572	P=0.468
COCH-ARM / FISHERS	P=0.379	P=0.252	P=0.505	P=0.505	P=0.495
ORDER RESTRICTED	P=0.291	(e)	(e)	(e)	(e)

Pancreas Adenoma

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
				TERT.MIX TEQ=100

TUMOR RATES

OVERALL (a)	0/52 (0%)	0/53 (0%)	2/53 (4%)	0/53 (0%)	0/51 (0%)
POLY-3 RATE (b)	0/35.78	0/39.99	2/41.29	0/39.44	0/32.27
POLY-3 PERCENT (g)	0.0%	0.0%	4.8%	0.0%	0.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	2/24 (8%)	0/23 (0%)	0/8 (0%)
FIRST INCIDENCE			729 (T)		
STATISTICAL TESTS					
LIFE TABLE					
POLY 3	P=0.656N	(e)	P=0.330	(e)	(e)
POLY 3	P=0.506N	(e)	P=0.270	(e)	(e)
POLY 1.5	P=0.504N	(e)	P=0.257	(e)	(e)
POLY 6	P=0.509N	(e)	P=0.284	(e)	(e)
LOGISTIC REGRESSION	(e)	(e)	P=0.330	(e)	(e)
COCH-ARM / FISHERS	P=0.504N	(e)	P=0.252	(e)	(e)
ORDER RESTRICTED	P=0.432	(e)	(e)	(e)	(e)

Pancreas Carcinoma

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
				TERT.MIX TEQ=100

TUMOR RATES

OVERALL (a)	0/52 (0%)	1/53 (2%)	0/53 (0%)	2/53 (4%)	0/51 (0%)
POLY-3 RATE (b)	1/39.78	1/39.99	0/41.29	2/39.44	0/32.27
POLY-3 PERCENT (g)	0.0%	2.5%	0.0%	5.1%	0.0%
TERMINAL (d)	0/16 (0%)	1/23 (4%)	0/24 (0%)	2/23 (9%)	0/8 (0%)
FIRST INCIDENCE		729 (T)		729 (T)	
STATISTICAL TESTS					
LIFE TABLE					
POLY 3	P=0.573	P=0.572	(e)	P=0.320	(e)
POLY 3	P=0.623	P=0.522	(e)	P=0.259	(e)
POLY 1.5	P=0.662	P=0.516	(e)	P=0.253	(e)
POLY 6	P=0.560	P=0.529	(e)	P=0.266	(e)
LOGISTIC REGRESSION	(e)	P=0.572	(e)	P=0.320	(e)
COCH-ARM / FISHERS	P=0.648N	P=0.505	(e)	P=0.252	(e)
ORDER RESTRICTED	P=0.333	(e)	(e)	(e)	(e)

Pancreas
 Carcinoma or Adenoma

Dose	Females		
	TERT MIX CONTROL	TERT MIX TEQ=10	TERT MIX TEQ=22
			TERT MIX TEQ=46
			TERT MIX TEQ=100

TUMOR RATES

OVERALL (a)	1/53 (2%)	2/53 (4%)	2/53 (4%)	0/51 (0%)
POLY-3 RATE (b)	1/39.99	2/41.29	2/39.44	0/32.27
POLY-3 PERCENT (g)	2.5%	4.8%	5.1%	0.0%
TERMINAL (d)	1/23 (4%)	2/24 (8%)	2/23 (9%)	0/8 (0%)
FIRST INCIDENCE	729 (T)	729 (T)	729 (T)	---

STATISTICAL TESTS

LIFE TABLE	P=0.572	P=0.330	P=0.320	(e)
POLY 3	P=0.533N	P=0.270	P=0.259	(e)
POLY 1.5	P=0.506N	P=0.257	P=0.253	(e)
POLY 6	P=0.574N	P=0.284	P=0.266	(e)
LOGISTIC REGRESSION	(e)	P=0.330	P=0.320	(e)
COCH-ARM / FISHERS	P=0.483N	P=0.252	P=0.252	(e)
ORDER RESTRICTED	P=0.338	(e)	(e)	(e)

Pituitary Gland: Pars Distalis or Unspecified Site
 Adenoma

Dose	Females		
	TERT MIX CONTROL	TERT MIX TEQ=10	TERT MIX TEQ=22
			TERT MIX TEQ=46
			TERT MIX TEQ=100

TUMOR RATES

OVERALL (a)	29/53 (55%)	22/53 (42%)	20/53 (38%)	10/53 (19%)
POLY-3 RATE (b)	29/41.67	22/43.67	20/41.29	10/33.29
POLY-3 PERCENT (g)	62.2%	50.4%	48.4%	30.0%
TERMINAL (d)	11/16 (69%)	12/24 (50%)	15/23 (65%)	4/8 (50%)
FIRST INCIDENCE	416	592	490	633

STATISTICAL TESTS

LIFE TABLE	P=0.239N	P=0.018N*	P=0.008N**	P=0.048N*
POLY 3	P=0.001N**	P=0.075N	P=0.052N	P=0.001N**
POLY 1.5	P=0.001N**	P=0.108N	P=0.057N	P=0.001N**
POLY 6	P=0.003N**	P=0.052N	P=0.056N	P=0.002N**
LOGISTIC REGRESSION	P=0.001N**	P=0.052N	P=0.029N*	P=0.001N**
COCH-ARM / FISHERS	P=0.001N**	P=0.165N	P=0.086N	P=0.001N**
ORDER RESTRICTED	P=0.001N**	(e)	(e)	(e)

Pituitary Gland: Pars Distalis or Unspecified Site
 Carcinoma or Adenoma

Dose	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
OVERALL (a)	28/53 (53%)	29/53 (55%)	23/53 (43%)	20/53 (38%)
POLY-3 RATE (b)	28/41.67	29/46.41	23/43.77	20/41.29
POLY-3 PERCENT (g)	67.2%	62.5%	52.5%	48.4%
TERMINAL (d)	11/16 (69%)	11/23 (48%)	12/24 (50%)	15/23 (65%)
FIRST INCIDENCE	416	416	592	490

TUMOR RATES

LIFE TABLE	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
POLY 3	P=0.025N*	P=0.239N	P=0.026N*	P=0.008N**
POLY 1.5	P<0.001N**	P=0.401N	P=0.110N	P=0.052N
LOGISTIC REGRESSION	P=0.003N**	P=0.500N	P=0.151N	P=0.057N
COCH-ARM / FISHERS	P<0.001N**	P=0.288N	P=0.078N	P=0.056N
ORDER RESTRICTED	P<0.001N**	P=0.523N	P=0.075N	P=0.029N*
		P=0.500	P=0.218N	P=0.086N
		(e)	(e)	(e)

Skin
 Fibroma

Dose	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
OVERALL (a)	1/53 (2%)	2/53 (4%)	2/53 (4%)	3/53 (6%)
POLY-3 RATE (b)	1/36.39	2/40.22	2/42.04	3/40.39
POLY-3 PERCENT (g)	2.8%	5.0%	4.8%	7.4%
TERMINAL (d)	0/16 (0%)	1/23 (4%)	1/24 (4%)	1/23 (4%)
FIRST INCIDENCE	693	668	456	542

STATISTICAL TESTS

LIFE TABLE	Males		Females	
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
POLY 3	P=0.422N	P=0.588	P=0.595	P=0.371
POLY 1.5	P=0.363N	P=0.535	P=0.550	P=0.343
LOGISTIC REGRESSION	P=0.330N	P=0.522	P=0.529	P=0.328
COCH-ARM / FISHERS	P=0.412N	P=0.550	P=0.574	P=0.361
ORDER RESTRICTED	P=0.287N	P=0.546	P=0.498	P=0.315
	P=0.280N	P=0.500	P=0.500	P=0.309
		(e)	(e)	(e)

Skin
 Fibroma, Fibrosarcoma, Sarcoma, Myxoma, Myxosarcoma,
 or Fibrous Histiocytoma

Dose	Females			
	TERT MIX CONTROL	TERT MIX TEQ=10	TERT MIX TEQ=22	TERT MIX TEQ=46
				TERT MIX TEQ=100

TUMOR RATES

	#	#	#	#
OVERALL (a)	2/53 (4%)	2/53 (4%)	2/53 (4%)	4/53 (8%)
POLY-3 RATE (b)	2/36.63	2/40.22	2/42.04	4/40.58
POLY-3 PERCENT (g)	5.5%	5.0%	4.8%	9.9%
TERMINAL (d)	0/16 (0%)	1/23 (4%)	1/24 (4%)	1/23 (4%)
FIRST INCIDENCE	666	668	456	542

STATISTICAL TESTS

LIFE TABLE

	P=0.362N	P=0.607N	P=0.595N	P=0.427	P=0.327N
POLY 3	P=0.320N	P=0.661N	P=0.644N	P=0.384	P=0.265N
POLY 1.5	P=0.281N	P=0.672N	P=0.666N	P=0.366	P=0.252N
LOGISTIC REGRESSION	P=0.379N	P=0.648N	P=0.621N	P=0.407	P=0.288N
COCH-ARM / FISHERS	P=0.249N	P=0.655N	P=0.693N	P=0.356	P=0.271N
ORDER RESTRICTED	P=0.232N	P=0.691N	P=0.691N	P=0.339	P=0.248N
	P=0.226N	(e)	(e)	(e)	(e)

Dose

	TERT MIX CONTROL	TERT MIX TEQ=10	TERT MIX TEQ=22	Females TERT MIX TEQ=46	TERT MIX TEQ=100
Thyroid Gland: C-Cell Adenoma					

TUMOR RATES

	17/53 (32%)	10/53 (19%)	18/51 (35%)	9/52 (17%)	5/51 (10%)
OVERALL (a)	17/38.32	10/40.85	18/42.15	9/40.48	5/34.12
POLY-3 RATE (b)	44.4%	24.5%	42.7%	22.2%	14.7%
POLY-3 PERCENT (g)	7/16 (44%)	6/23 (26%)	10/24 (42%)	6/23 (26%)	0/8 (0%)
TERMINAL (d)	568	627	617	548	542
FIRST INCIDENCE					

STATISTICAL TESTS

LIFE TABLE

	P=0.070N	P=0.020N*	P=0.241N	P=0.012N*	P=0.067N
POLY 3	P=0.005N**	P=0.045N*	P=0.531N	P=0.027N*	P=0.004N**
POLY 1.5	P=0.004N**	P=0.057N	P=0.557	P=0.036N*	P=0.004N**
POLY 6	P=0.009N**	P=0.037N*	P=0.433N	P=0.021N*	P=0.006N**
LOGISTIC REGRESSION	P=0.009N**	P=0.032N*	P=0.443N	P=0.023N*	P=0.009N**
COCH-ARM / FISHERS	P=0.004N**	P=0.090N	P=0.444	P=0.063N	P=0.005N**
ORDER RESTRICTED	P=0.005N**	(e)	(e)	(e)	(e)

Thyroid Gland: C-Cell Carcinoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
				TERT. MIX TEO=100

TUMOR RATES

Overall (a)	Poly-3 Rate (b)	Poly-3 Percent (g)	Terminal (d)	First Incidence
2/53 (4%)	2/36.76	5.4%	1/16 (6%)	575

STATISTICAL TESTS

Life Table	Logistic Regression	Coch-Arm / Fishers	Order Restricted
P=0.521	P=0.596	P=0.621	P=0.216N

Thyroid Gland: C-Cell Carcinoma or Adenoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEO=10	TERT. MIX TEO=22	TERT. MIX TEO=46
				TERT. MIX TEO=100

TUMOR RATES

Overall (a)	Poly-3 Rate (b)	Poly-3 Percent (g)	Terminal (d)	First Incidence
18/53 (34%)	18/38.83	46.4%	7/16 (44%)	568

STATISTICAL TESTS

Life Table	Logistic Regression	Coch-Arm / Fishers	Order Restricted
P=0.115N	P=0.007N**	P=0.007N**	P=0.006N**

Thyroid Gland: Follicular Cell
 Carcinoma or Adenoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES				
OVERALL (a)	0/53 (0%)	0/53 (0%)	2/51 (4%)	0/52 (0%)
POLY-3 RATE (b)	0/36.25	0/39.99	2/40.56	0/39.36
POLY-3 PERCENT (g)	0.0%	0.0%	4.9%	0.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	1/24 (4%)	0/23 (0%)
FIRST INCIDENCE	---	---	659	---
				689

STATISTICAL TESTS				
LIFE TABLE				
POLY 3	P=0.298	(e)	P=0.317	(e)
POLY 3	P=0.399	(e)	P=0.263	(e)
POLY 1.5	P=0.413	(e)	P=0.247	(e)
POLY 6	P=0.376	(e)	P=0.283	(e)
LOGISTIC REGRESSION	P=0.375	(e)	P=0.265	(e)
COCH-ARM / FISHERS	P=0.425	(e)	P=0.238	(e)
ORDER RESTRICTED	P=0.284	(e)	(e)	(e)

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

Uterus
 Carcinoma

TUMOR RATES				
OVERALL (a)	1/53 (2%)	1/53 (2%)	2/53 (4%)	2/53 (4%)
POLY-3 RATE (b)	1/36.52	1/39.99	2/41.29	2/40.11
POLY-3 PERCENT (g)	2.7%	2.5%	4.8%	5.0%
TERMINAL (d)	0/16 (0%)	1/23 (4%)	2/24 (8%)	1/23 (4%)
FIRST INCIDENCE	658	729 (T)	729 (T)	505
				562

STATISTICAL TESTS				
LIFE TABLE				
POLY 3	P=0.465	P=0.702N	P=0.621	P=0.577
POLY 1.5	P=0.549	P=0.741N	P=0.543	P=0.533
POLY 6	P=0.582	P=0.748N	P=0.524	P=0.521
LOGISTIC REGRESSION	P=0.501	P=0.733N	P=0.563	P=0.547
COCH-ARM / FISHERS	P=0.596	P=0.736N	P=0.572	P=0.501
ORDER RESTRICTED	P=0.601N	P=0.752N	P=0.500	P=0.500
	P=0.608	(e)	(e)	(e)

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
Uterus Leiomyoma				

TUMOR RATES	Females			
	#	#	#	#
OVERALL (a)	0/53 (0%)	0/53 (0%)	2/53 (4%)	0/53 (0%)
POLY-3 RATE (b)	0/36.25	0/39.99	2/41.55	0/32.33
POLY-3 PERCENT (g)	0.0%	0.0%	4.8%	0.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	1/24 (4%)	0/8 (0%)
FIRST INCIDENCE			659	

LIFE TABLE	Females			
	P=0.607N	(e)	P=0.317	(e)
POLY 3	P=0.503N	(e)	P=0.268	(e)
POLY 1.5	P=0.502N	(e)	P=0.254	(e)
POLY 6	P=0.504N	(e)	P=0.286	(e)
LOGISTIC REGRESSION	P=0.547N	(e)	P=0.271	(e)
COCH-ARM / FISHERS	P=0.499N	(e)	P=0.248	(e)
ORDER RESTRICTED	P=0.431	(e)	(e)	(e)

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
Uterus Polyp Stromal				

TUMOR RATES	Females			
	#	#	#	#
OVERALL (a)	4/53 (8%)	1/53 (2%)	3/53 (6%)	3/53 (6%)
POLY-3 RATE (b)	4/36.88	1/39.99	3/41.39	2/33.09
POLY-3 PERCENT (g)	10.9%	2.5%	7.3%	6.0%
TERMINAL (d)	1/16 (6%)	1/23 (4%)	2/24 (8%)	0/8 (0%)
FIRST INCIDENCE	627	729 (T)	702	562

LIFE TABLE	Females			
	P=0.492	P=0.114N	P=0.333N	P=0.489N
POLY 3	P=0.512N	P=0.153N	P=0.437N	P=0.387N
POLY 1.5	P=0.480N	P=0.161N	P=0.464N	P=0.364N
POLY 6	P=0.552N	P=0.145N	P=0.447N	P=0.424N
LOGISTIC REGRESSION	P=0.551N	P=0.142N	P=0.398N	P=0.388N
COCH-ARM / FISHERS	P=0.431N	P=0.181N	P=0.500N	P=0.339N
ORDER RESTRICTED	P=0.373N	(e)	(e)	(e)

Uterus
Schwannoma Malignant

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

	#	#	#	#	#
OVERALL (a)	1/53 (2%)	0/53 (0%)	1/53 (2%)	2/53 (4%)	1/53 (2%)
POLY-3 RATE (b)	1/36.84	0/39.99	1/41.70	2/40.01	1/33.16
POLY-3 PERCENT (g)	2.7%	0.0%	2.4%	5.0%	3.0%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	0/24 (0%)	0/23 (0%)	0/8 (0%)
FIRST INCIDENCE	540	---	609	619	409

STATISTICAL TESTS

LIFE TABLE

POLY 3	P=0.385	P=0.472N	P=0.725N	P=0.535	P=0.753
POLY 1.5	P=0.372	P=0.484N	P=0.733N	P=0.529	P=0.738
POLY 6	P=0.407	P=0.489N	P=0.745N	P=0.518	P=0.749
LOGISTIC REGRESSION	P=0.323	P=0.477N	P=0.718N	P=0.543	P=0.719
COCH-ARM / FISHERS	P=0.490	P=0.533N	P=0.751	P=0.493	P=0.733N
ORDER RESTRICTED	P=0.455	P=0.500N	P=0.752N	P=0.500	P=0.752N
		(e)	(e)	(e)	(e)

All Organs
Histiocytic Sarcoma

Dose	Females			
	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46
				TERT. MIX TEQ=100

TUMOR RATES

	#	#	#	#	#
OVERALL (a)	0/53 (0%)	0/53 (0%)	0/53 (0%)	0/53 (0%)	4/53 (8%)
POLY-3 RATE (b)	0/36.25	0/39.99	0/41.29	0/39.44	4/34.26
POLY-3 PERCENT (g)	0.0%	0.0%	0.0%	0.0%	11.7%
TERMINAL (d)	0/16 (0%)	0/23 (0%)	0/24 (0%)	0/23 (0%)	1/8 (13%)
FIRST INCIDENCE	---	---	---	---	312

STATISTICAL TESTS

LIFE TABLE

POLY 3	P<0.001 **	(e)	(e)	(e)	P=0.036 *
POLY 1.5	P<0.001 **	(e)	(e)	(e)	P=0.051
POLY 6	P<0.001 **	(e)	(e)	(e)	P=0.056
LOGISTIC REGRESSION	P<0.001 **	(e)	(e)	(e)	P=0.044 *
COCH-ARM / FISHERS	P<0.001 **	(e)	(e)	(e)	P=0.072
ORDER RESTRICTED	P<0.001 **	(e)	(e)	(e)	P=0.059

All Organs
 Malignant Lymphoma: Histiocytic, Lymphocytic, Mixed, NOS, or Undifferentiated Cell Type

TUMOR RATES	Males		Females	
	#	%	#	%
OVERALL (a)	2/53 (4%)	1/53 (2%)	1/53 (2%)	1/53 (2%)
POLY-3 RATE (b)	2/36.91	1/39.99	1/39.84	1/32.54
POLY-3 PERCENT (g)	5.4%	2.5%	2.5%	3.1%
TERMINAL (d)	1/16 (6%)	1/23 (4%)	0/23 (0%)	0/8 (0%)
FIRST INCIDENCE	508	729 (T)	616	674
STATISTICAL TESTS				
LIFE TABLE	P=0.648	P=0.406N	P=0.183N	P=0.596N
POLY 3	P=0.558N	P=0.472N	P=0.213N	P=0.544N
POLY 1.5	P=0.546N	P=0.481N	P=0.223N	P=0.483N
LOGISTIC REGRESSION	P=0.567N	P=0.461N	P=0.201N	P=0.461N
COCH-ARM / FISHERS	P=0.546N	P=0.484N	P=0.240N	P=0.574N
ORDER RESTRICTED	P=0.525N	P=0.500N	P=0.248N	P=0.519N
	P=0.316N	(e)	(e)	P=0.500N
		(e)	(e)	(e)

All Organs
 Benign Tumors

TUMOR RATES	Males		Females	
	#	%	#	%
OVERALL (a)	45/53 (85%)	43/53 (81%)	46/53 (87%)	43/53 (81%)
POLY-3 RATE (b)	45/48.33	43/49.69	46/50.24	43/47.21
POLY-3 PERCENT (g)	93.1%	86.5%	91.6%	91.1%
TERMINAL (d)	14/16 (88%)	18/23 (78%)	22/24 (92%)	21/23 (91%)
FIRST INCIDENCE	176	362	263	333
STATISTICAL TESTS				
LIFE TABLE	P=0.104	P=0.082N	P=0.080N	P=0.066N
POLY 3	P=0.242N	P=0.211N	P=0.539N	P=0.506N
POLY 1.5	P=0.077N	P=0.267N	P=0.645N	P=0.445N
LOGISTIC REGRESSION	P=0.546N	P=0.182N	P=0.473N	P=0.580N
COCH-ARM / FISHERS	P=0.037N*	P=0.268N	P=0.610	P=0.230N
ORDER RESTRICTED	P=0.010N*	P=0.398N	P=0.500	P=0.398N
	P=0.167N	(e)	(e)	P=0.033N*
		(e)	(e)	(e)

All Organs
 Malignant Tumors

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
				TERT.MIX TEQ=100

TUMOR RATES

	#	#	#	#	#
OVERALL (a)	18/53 (34%)	14/53 (26%)	19/53 (36%)	21/53 (40%)	23/53 (43%)
POLY-3 RATE (b)	18/43.25	14/45.06	19/44.70	21/45.77	23/41.67
POLY-3 PERCENT (g)	41.6%	31.1%	42.5%	45.9%	55.2%
TERMINAL (d)	5/16 (31%)	7/23 (30%)	8/24 (33%)	9/23 (39%)	2/8 (25%)
FIRST INCIDENCE	218	227	203	276	312

STATISTICAL TESTS

LIFE TABLE	P=0.003 **	P=0.126N	P=0.307N	P=0.508N	P=0.078
POLY 3	P=0.029 *	P=0.204N	P=0.553	P=0.423	P=0.140
POLY 1.5	P=0.038 *	P=0.216N	P=0.524	P=0.394	P=0.162
LOGISTIC REGRESSION	P=0.023 *	P=0.205N	P=0.585	P=0.455	P=0.117
COCH-ARM / FISHERS	P=0.092	P=0.354N	P=0.489	P=0.295	P=0.233
ORDER RESTRICTED	P=0.068	P=0.263N	P=0.500	P=0.344	P=0.213

All Organs
 Malignant and Benign Tumors

Dose	Females			
	TERT.MIX CONTROL	TERT.MIX TEQ=10	TERT.MIX TEQ=22	TERT.MIX TEQ=46
				TERT.MIX TEQ=100

TUMOR RATES

	#	#	#	#	#
OVERALL (a)	51/53 (96%)	46/53 (87%)	50/53 (94%)	50/53 (94%)	45/53 (85%)
POLY-3 RATE (b)	51/53.00	46/51.78	50/52.00	50/51.35	45/47.10
POLY-3 PERCENT (g)	96.2%	88.8%	96.2%	97.4%	95.6%
TERMINAL (d)	14/16 (88%)	18/23 (78%)	22/24 (92%)	22/23 (96%)	8/8 (100%)
FIRST INCIDENCE	176	227	203	276	312

STATISTICAL TESTS

LIFE TABLE	P=0.022 *	P=0.045N*	P=0.054N	P=0.094N	P=0.196
POLY 3	P=0.319	P=0.136N	P=0.686N	P=0.591	P=0.649N
POLY 1.5	P=0.574N	P=0.109N	P=0.684N	P=0.679	P=0.348N
LOGISTIC REGRESSION	P=0.153	P=0.172N	P=0.686N	P=0.531	P=0.557
COCH-ARM / FISHERS	P=0.139N	P=0.105N	P=0.480N	P=0.478N	P=0.064N
ORDER RESTRICTED	P=0.081N	P=0.080N	P=0.500N	P=0.500N	P=0.046N*

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

- (d) Observed incidence at terminal kill.
- (f) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death.
- Logistic regression is an alternative method for analyzing the incidence of non-fatal tumors. The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates and for all tests a negative trend is indicated by N
- (e) Value of Statistic cannot be computed.
- (g) Poly-3 adjusted lifetime tumor incidence.
- (I) Interim sacrifice
- (T) Terminal sacrifice
- # Tumor rates based on number of animals necropsied.
- * To the right of any statistical result, indicates significance at ($P \leq 0.05$).
- ** To the right of any statistical result, indicates significance at ($P \leq 0.01$).

NTP Experiment-Test: 96007-04
Study Type: CHRONIC
Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
WITH AVERAGE SEVERITY GRADES [b]
TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

FINAL#1/RATS

Report: PETRPT18
Date: 04/24/03
Time: 09:00:40

Facility: Battelle Columbus Laboratory

Chemical CAS #: TEPDIOXINMIX

Lock Date: 09/12/01

Cage Range: All

Reasons For Removal: 25018 Dosing Accident
25020 Natural Death

25019 Moribund Sacrifice
25021 Terminal Sacrifice

Removal Date Range: All

Treatment Groups: Include All

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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DISPOSITION SUMMARY

Animals Initially In Study	98	98	98	98	98
Early Deaths					
Moribund Sacrifice	26	25	22	25	33
Natural Death	11	5	6	4	10
Dosing Accident			1	1	2
Survivors					
Terminal Sacrifice	16	23	24	23	8
Animals Examined Microscopically	53	53	53	53	53

ALIMENTARY SYSTEM

Esophagus	(53)	(53)	(53)	(53)	(53)
Muscularis, Inflammation		2 [1.0]	1 [2.0]	1 [1.0]	(53)
Intestine Large, Colon	(53)	(52)	(53)	(53)	(51)
Parasite Metazoan			1		
Intestine Large, Rectum	(52)	(53)	(53)	(53)	(52)
Parasite Metazoan	2	4	5	1	
Artery, Inflammation, Chronic Active				2 [2.5]	3 [3.0]
Serosa, Inflammation				(53)	1 [3.0]
Intestine Large, Cecum	(51)	(53)	(53)	(53)	(51)
Artery, Inflammation, Chronic Active				(53)	1 [2.0]
Intestine Small, Duodenum	(52)	(53)	(53)	(53)	(52)
Serosa, Inflammation, Chronic Active				(53)	1 [3.0]
Liver					(51)
Angiectasis	(53)	(53)	(53)	(53)	(53)
Basophilic Focus	3 [1.7]	2 [1.5]	10	5	3 [1.0]
Basophilic Focus, Multiple	9	14	3	7	8
Cholangiofibrosis	15	12	3	4	17 [2.3]
Clear Cell Focus			1		8
Clear Cell Focus, Multiple					
Degeneration, Cystic	1			1	
Eosinophilic Focus	1 [1.0]	2	5	1	2 [1.0]
Fatty Change, Diffuse	4	7	6	5	19
Fatty Change, Focal	3 [2.3]	5 [1.0]	14 [1.0]	34 [1.1]	36 [1.3]
Hematopoietic Cell Proliferation	3 [1.3]	4 [1.5]	7 [1.6]	2 [1.5]	1 [1.0]
Hepatodiphragmatic Nodule	16 [1.1]	18 [1.1]	19 [1.1]	8 [1.0]	9 [1.1]
Inflammation			1		
Karyomegaly	36 [1.1]	50 [1.1]	45 [1.2]	50 [1.3]	50 [1.3]
Mixed Cell Focus	4	5	5	1	

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PETRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
ALIMENTARY SYSTEM - CONT					
Mixed Cell Focus, Multiple	17	28	30	37	17
Necrosis	3 [1.7]	1 [2.0]	9 [2.2]	3 [1.7]	15 [2.2]
Pigmentation	4 [1.5]	35 [1.3]	41 [1.2]	48 [1.9]	51 [2.2]
Regeneration		1	3	10	38
Toxic Hepatopathy		5 [1.0]	14 [1.0]	38 [1.6]	47 [3.1]
Bile Duct, Cyst	1 [3.0]	3 [2.7]	3 [2.3]	4 [2.3]	9 [2.0]
Bile Duct, Dilatation	1 [1.0]		1 [1.0]	5 [1.4]	1 [3.0]
Bile Duct, Fibrosis	3 [1.7]	3 [1.3]	5 [1.4]	25 [1.4]	1 [2.0]
Bile Duct, Hyperplasia	2 [1.5]	2 [2.0]	1 [3.0]	1 [2.0]	42 [1.9]
Centrilobular, Degeneration	3 [1.7]		1 [3.0]	1 [2.0]	6 [2.2]
Centrilobular, Fibrosis					1 [1.0]
Hepatocyte, Hypertrophy	1 [1.0]	27 [1.1]	34 [1.2]	46 [1.5]	50 [3.0]
Hepatocyte, Multinucleated		12 [1.0]	10 [1.2]	39 [1.5]	51 [2.1]
Oval Cell, Hyperplasia		1 [1.0]	1 [1.0]	26 [1.4]	42 [2.2]
Portal, Fibrosis					11 [1.9]
Serosa, Fibrosis					1 [2.0]
Serosa, Inflammation, Chronic	1 [2.0]	(1)	(2)	(6)	(8)
Mesentery					2 [3.0]
Inflammation, Chronic Active					6 [3.7]
Necrosis					2 [3.0]
Artery, Inflammation, Chronic Active		1 [4.0]	1 [3.0]	3 [3.7]	6 [3.7]
Fat, Necrosis	(10)	(18)	(19)	(29)	(31)
Oral Mucosa	8 [1.5]	17 [1.5]	18 [1.4]	26 [1.6]	30 [1.6]
Gingival, Hyperplasia, Squamous	(52)	(53)	(53)	(53)	(51)
Pancreas					
Degeneration	1 [2.0]		6 [1.3]	7 [1.7]	16 [1.8]
Inflammation, Chronic Active	3 [1.7]	1 [3.0]	7 [1.7]	1 [2.0]	20 [2.0]
Inflammation, Granulomatous					
Acinus, Atrophy	3 [1.3]	2 [1.0]	7 [1.7]	7 [1.7]	20 [2.0]
Acinus, Hyperplasia	2 [1.5]		1 [2.0]	3 [1.3]	30 [1.1]
Acinus, Vacuolization	1 [1.0]		3 [1.7]	3 [1.7]	14 [2.9]
Artery, Inflammation, Chronic Active		6 [2.2]		8 [2.6]	
Duct, Cyst			1 [2.0]		
Duct, Dilatation					
Duct, Inflammation, Chronic Active	(53)	(53)	(53)	(53)	5 [3.0]
Salivary Glands					2 [3.5]
Atrophy	1 [3.0]				
Inflammation	2 [2.0]				
Mineralization					
Stomach, Forestomach	(53)	(53)	(53)	(53)	(52)
Cyst					1 [3.0]
Diverticulum	1 [3.0]		1 [3.0]		
Edema					

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMICAL SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRP18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTR.	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
ALIMENTARY SYSTEM - CONT					
Erosion			1 [1.0]	2 [2.0]	6 [2.5]
Hyperkeratosis	2 [2.4]	1 [2.0]	2 [2.5]	9 [1.7]	3 [1.7]
Hyperplasia, Squamous	2 [2.5]		4 [2.3]	1 [3.0]	2 [2.0]
Inflammation	1 [2.0]		2 [2.5]	2 [1.0]	1 [3.0]
Mineralization	3 [3.0]		4 [1.5]	1 [2.0]	2 [2.0]
Ulcer			2 [2.5]	2 [2.5]	1 [3.0]
Artery, Inflammation, Chronic Active	(53)	(53)	(53)	(53)	(52)
Stomach, Glandular	1 [2.0]	4 [1.5]	3 [1.3]	3 [1.7]	1 [2.0]
Erosion	2 [2.0]				2 [3.0]
Mineralization					(1)
Artery, Inflammation, Chronic Active	(1)				1 [3.0]
Tongue					(1)
Infiltration Cellular	(24)	(23)	(27)	(37)	1 [3.0]
Tooth	23 [1.1]	21 [1.3]	22 [1.2]	34 [1.3]	30 [1.7]
Peridental Tissue, Inflammation					

CARDIOVASCULAR SYSTEM

Blood Vessel	(53)	(53)	(53)	(52)	(53)
Aorta, Mineralization				1 [2.0]	3 [2.3]
Heart	(53)	(53)	(53)	(52)	(53)
Cardiomyopathy	11 [1.0]	26 [1.0]	31 [1.1]	30 [1.1]	32 [1.1]
Inflammation, Suppurative	1 [3.0]			1 [2.0]	1 [4.0]
Mineralization					1 [3.0]
Necrosis					1 [3.0]
Thrombosis	1 [3.0]			1 [2.0]	1 [2.0]
Artery, Degeneration				1 [2.0]	1 [2.0]
Artery, Inflammation, Chronic Active				1 [2.0]	1 [2.0]

ENDOCRINE SYSTEM

Adrenal Cortex	(52)	(53)	(53)	(53)	(51)
Angiectasis	15 [1.7]	20 [1.6]	18 [1.5]	17 [1.6]	8 [1.6]
Atrophy		3 [2.3]			18 [2.7]
Degeneration, Cystic	9 [2.4]	15 [2.3]	19 [2.3]	25 [2.3]	16 [2.1]
Hematopoietic Cell Proliferation			1 [1.0]		1 [1.0]
Hyperplasia	12 [2.5]	26 [2.4]	23 [2.8]	25 [2.6]	21 [2.5]
hypertrophy	44 [2.1]	45 [2.2]	47 [2.4]	46 [2.5]	45 [2.3]
Inflammation				1 [2.0]	
Mineralization					1 [3.0]
Necrosis	2 [3.0]	1 [3.0]	2 [2.5]		2 [2.5]

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
ENDOCRINE SYSTEM - CONT					
Thrombosis					
Vacuolization Cytoplasmic	6 [1.2]	1 [3.0]	11 [1.5]	7 [1.7]	15 [1.5]
Capsule, Inflammation	(52)	(53)	(53)	1 [2.0]	1 [3.0]
Adrenal Medulla	10 [2.2]	21 [2.0]	12 [1.8]	15 [1.7]	(51)
Hyperplasia	(52)	(53)	(53)	(53)	(51)
Islets, Pancreatic				2 [2.0]	(53)
Hyperplasia	(53)	(53)	(53)	(53)	(53)
Pituitary Gland	6 [1.7]	1 [1.0]	1 [1.0]	2 [2.5]	3 [2.3]
Angiectasis	1 [2.0]		1 [2.0]	2 [1.5]	
Cyst					
Cytoplasmic Alteration	1 [2.0]	3 [1.3]			
Hemorrhage					
Vacuolization Cytoplasmic		1 [1.0]	2 [1.0]	3 [1.3]	1 [1.0]
Pars Distalis, Hyperplasia	18 [2.5]	19 [2.3]	24 [2.5]	20 [2.5]	19 [2.1]
Pars Intermedia, Cyst			1 [3.0]		
Thyroid Gland	(53)	(53)	(51)	(52)	(51)
C-Cell, Hyperplasia	24 [2.3]	24 [2.3]	20 [2.1]	18 [2.3]	14 [2.0]
Follicular Cell, Hyperplasia	1 [1.0]				
Follicular Cell, Hypertrophy	4 [1.5]	13 [1.1]	12 [1.5]	18 [1.7]	23 [1.9]
GENERAL BODY SYSTEM					
None					

GENITAL SYSTEM	(51)	(53)	(53)	(51)	(50)
Clitoral Gland					
Hyperplasia, Squamous	42 [1.7]	40 [1.7]	37 [1.3]	1 [2.0]	29 [1.1]
Inflammation	39 [2.3]	41 [2.5]	44 [2.1]	39 [2.3]	44 [2.3]
Duct, Cyst	(52)	(52)	(53)	(53)	(51)
Ovary					
Atrophy	44 [4.0]	44 [4.0]	43 [4.0]	49 [3.9]	40 [4.0]
Cyst	8 [2.6]	16 [2.4]	20 [2.3]	14 [2.3]	7 [2.3]
Fibrosis		1 [3.0]			
Hemorrhage					
Inflammation, Chronic Active		2 [3.0]		2 [3.5]	1 [2.0]
Artery, Inflammation, Chronic Active		(2)		(2)	5 [3.6]
Oviduct		2 [2.0]			1 [4.0]
Cyst					(5)
Inflammation, Chronic Active	(52)	(53)	(53)	2 [4.0]	1 [2.0]
Uterus				(53)	4 [4.0]

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

NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
GENITAL SYSTEM - CONT					
Adenomyosis		1 [2.0]		1 [2.0]	1 [2.0]
Hemorrhage	1 [3.0]			2 [2.0]	1 [2.0]
Inflammation, Chronic Active	1 [2.0]	1 [3.0]	1 [3.0]	1 [4.0]	1 [2.0]
Inflammation, Suppurative	6 [1.8]	5 [2.2]	9 [1.8]	13 [1.8]	3 [3.0]
Metaplasia, Squamous	21 [2.0]	32 [2.2]	32 [2.3]	35 [2.4]	6 [3.2]
Thrombosis				1 [3.0]	30 [2.4]
Ulcer		1 [2.0]		1 [3.0]	
Cervix, Hyperplasia, Stromal	1 [4.0]				
Endometrium, Fibrosis	37 [1.9]	35 [2.2]	34 [2.1]	33 [2.2]	1 [2.0]
Epithelium, Necrosis	1 [4.0]				23 [2.1]

HEMATOPOIETIC SYSTEM					
Bone Marrow	(53)	(53)	(53)	(53)	(53)
Hyperplasia	36 [3.1]	36 [2.8]	34 [2.7]	41 [3.0]	48 [3.0]
Lymph Node	(4)	(1)	(2)	(9)	(11)
Lumbar, Ectasia			1 [2.0]	1 [2.0]	
Lumbar, Hemorrhage			1 [2.0]	1 [2.0]	1 [2.0]
Lumbar, Hyperplasia, Lymphoid			1 [2.0]	3 [2.3]	1 [2.0]
Lumbar, Hyperplasia, Plasma Cell	1 [2.0]	1 [2.0]		4 [2.0]	2 [2.0]
Mediastinal, Ectasia				1 [2.0]	
Mediastinal, Fibrosis				1 [2.0]	
Mediastinal, Hemorrhage				1 [2.0]	
Mediastinal, Hyperplasia, Histiocytic				1 [2.0]	2 [2.0]
Mediastinal, Hyperplasia, Lymphoid				1 [2.0]	1 [2.0]
Mediastinal, Hyperplasia, Plasma Cell				3 [2.3]	2 [2.5]
Pancreatic, Ectasia	1 [3.0]				3 [2.3]
Pancreatic, Hyperplasia, Histiocytic				1 [3.0]	1 [2.0]
Popliteal, Hyperplasia, Plasma Cell				2 [3.0]	
Renal, Hyperplasia, Histiocytic	1 [3.0]	(53)	(53)	(53)	(53)
Lymph Node, Mandibular	(53)	1 [2.0]	1 [2.0]	2 [3.0]	(53)
Ectasia				1 [1.0]	
Hemorrhage				22 [2.3]	27 [2.3]
Hyperplasia, Plasma Cell	31 [2.1]	42 [2.1]	30 [2.1]	1 [3.0]	
Necrosis, Focal				1 [3.0]	
Lymph Node, Mesenteric	(52)	(53)	(53)	(53)	(50)
Ectasia	1 [2.0]				
Hemorrhage	1 [3.0]				
Hyperplasia, Histiocytic				1 [2.0]	1 [2.0]
Hyperplasia, Lymphoid					1 [2.0]
Pigmentation					

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NTP Experiment-Test: 96007-04
 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES (b)
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE

	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
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HEMATOPOIETIC SYSTEM - CONT					
Spleen	(52)	(53)	(53)	(53)	(51)
Hematopoietic Cell Proliferation	43 [1.8]	48 [1.5]	42 [1.5]	44 [1.6]	42 [1.6]
Hemorrhage					1 [2.0]
Inflammation, Suppurative					1 [2.0]
Necrosis	1 [3.0]				1 [3.0]
Pigmentation	45 [1.4]	50 [1.3]	52 [1.4]	47 [1.4]	46 [1.1]
Lymphoid Follicle, Atrophy	2 [2.0]	2 [3.0]	3 [2.0]	2 [2.5]	3 [2.3]
Red Pulp, Atrophy	1 [2.0]	1 [2.0]	3 [2.0]		
Thymus	(52)	(48)	(50)	(53)	(50)
Atrophy	32 [2.3]	43 [2.9]	45 [3.3]	50 [3.7]	48 [3.9]
Cyst	2 [2.5]				
Ectopic Thyroid				1 [4.0]	
Hemorrhage				1 [3.0]	

INTEGUMENTARY SYSTEM					
Mammary Gland	(53)	(53)	(53)	(53)	(52)
Cyst		3 [2.7]	1 [2.0]	1 [3.0]	
Hyperplasia	22 [1.2]	7 [1.6]	14 [1.1]	12 [1.0]	9 [1.0]
Inflammation, Granulomatous	3 [1.3]	4 [1.8]	1 [3.0]	3 [3.0]	1 [2.0]
Inflammation, Suppurative				1 [2.0]	
Skin	(53)	(53)	(53)	(53)	(53)
Cyst Epithelial Inclusion		2	1	3	3
Hyperkeratosis			1 [2.0]		
Inflammation, Suppurative				1 [2.0]	
Ulcer				1 [3.0]	
Hair Follicle, Atrophy		1 [4.0]			1 [2.0]

MUSCULOSKELETAL SYSTEM					
Bone	(53)	(53)	(53)	(53)	(53)
Mineralization			1 [1.0]		

NERVOUS SYSTEM					
Brain	(53)	(53)	(53)	(53)	(53)
Edema				1 [1.0]	3 [2.0]
Gliosis	1 [3.0]				1 [3.0]
Hemorrhage		1 [2.0]			
Hydrocephalus	1 [1.0]	4 [1.3]	2 [2.0]	2 [2.0]	

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 Study Type: CHRONIC
 Route: GAVAGE

INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
 WITH AVERAGE SEVERITY GRADES [b]
 TOXIC EQUIVALENCY FACTOR EVALUATION (DIOXIN MIXTURE)

Report: PEIRPT18
 Date: 04/24/03
 Time: 09:00:40

	SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
NERVOUS SYSTEM - CONT						
Inflammation, Granulomatous	1 [2.0]			1 [2.0]	1 [1.0]	3 [1.7]
Mineralization				1 [1.0]		1 [3.0]
Necrosis						
Artery, Degeneration						

	SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
RESPIRATORY SYSTEM						
Lung						
Congestion	(53)	(53)	(53)	1 [3.0]	(53)	(53)
Cyst				2 [2.0]	2 [2.5]	1 [3.0]
Edema				1 [2.0]	1 [1.0]	1 [2.0]
Hemorrhage				2 [2.0]	2 [2.5]	1 [1.0]
Infiltration Cellular, Histocyte	43 [1.9]	50 [1.9]	48 [1.6]	3 [2.0]	48 [1.6]	50 [1.4]
Inflammation	4 [1.5]	2 [2.0]	3 [2.0]	2 [2.0]	1 [3.0]	2 [3.0]
Metaplasia, Squamous	2 [2.0]		2 [2.0]		8 [2.0]	11 [1.9]
Mineralization					1 [1.0]	
Alveolar Epithelium, Hyperplasia	21 [1.3]	25 [1.0]	10 [1.3]	3 [1.6]	4 [1.8]	2 [1.5]
Alveolar Epithelium, Metaplasia		20 [1.8]	2 [1.0]		2 [1.0]	40 [1.9]
Perivascular, Inflammation, Chronic Active	(53)	(53)	(53)	3 [1.6]	4 [1.8]	1 [3.0]
Nose						
Inflammation	1 [1.0]	2 [1.0]	2 [2.0]	2 [2.0]	(53)	1 [2.0]
Goblet Cell, Hyperplasia					1 [1.0]	
Goblet Cell, Septum, Hyperplasia					1 [2.0]	
Nasalacromial Duct, Inflammation					1 [2.0]	
Respiratory Epithelium, Hyperplasia		1 [1.0]			1 [3.0]	
Turbinate, Cyst					4 [1.8]	
Turbinate, Respiratory Epithelium, Hyperplasia					1 [2.0]	
						1 [2.0]

	SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX CONTROL	TERT. MIX TEQ=10	TERT. MIX TEQ=22	TERT. MIX TEQ=46	TERT. MIX TEQ=100
SPECIAL SENSES SYSTEM						
Eye						
Anterior Chamber, Ciliary Body, Iris, Inflammation, Suppurative	(53)	(53)	(53)	(53)	(53)	(53)
Cornea, Inflammation, Suppurative						1 [2.0]
Lens, Degeneration	1 [3.0]	1 [4.0]	2 [2.0]		1 [2.0]	3 [2.0]
Retina, Atrophy	(53)	(53)	(52)		(53)	(53)
Harderian Gland	8 [1.1]	11 [1.0]	4 [1.3]		5 [1.0]	8 [1.4]
Inflammation						

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INCIDENCE RATES OF NONNEOPLASTIC LESIONS BY ANATOMIC SITE (a)
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Report: PEFRPT18
 Date: 04/24/03
 Time: 09:00:40

SPRAGUE-DAWLEY RATS FEMALE	TERT. MIX				
	CONTROL	TEQ=10	TEQ=22	TEQ=46	TEQ=100
URINARY SYSTEM					
Kidney	(52)	(53)	(53)	(53)	(51)
Calculus Micro Observation Only	9 [1.6]	5 [1.8]	8 [1.6]	4 [2.0]	1 [2.0]
Casts Protein		1 [2.0]	1 [1.0]	1 [1.0]	
Cyst				1 [3.0]	
Developmental Malformation				1 [4.0]	1 [2.0]
Fibrosis				1 [4.0]	
Inflammation, Chronic	1 [2.0]	1 [4.0]	1 [3.0]	3 [1.7]	6 [2.8]
Inflammation, Chronic Active	3 [1.3]	2 [1.0]	3 [1.0]	42 [1.1]	35 [1.2]
Inflammation, Suppurative	41 [1.0]	48 [1.0]	47 [1.1]	47 [1.3]	49 [2.1]
Mineralization	26 [1.1]	41 [1.2]	40 [1.3]	1 [3.0]	1 [2.0]
Nephropathy	2 [2.0]		1 [3.0]	2 [2.5]	1 [2.0]
Pelvis, Dilatation	2 [2.0]	1 [1.0]	1 [3.0]	2 [1.5]	
Pelvis, Inflammation					
Renal Tubule, Hyperplasia	1 [2.0]		1 [2.0]		8 [2.5]
Renal Tubule, Necrosis	5 [2.0]	5 [1.8]	8 [1.9]	10 [2.0]	(1)
Transitional Epithelium, Hyperplasia	(1)		(1)	(1)	
Ureter	1 [3.0]				
Cyst					
Inflammation			1 [2.0]	1 [2.0]	
Metaplasia, Squamous			1 [3.0]	1 [3.0]	
Transitional Epithelium, Hyperplasia	(52)	(52)	(53)	(53)	(50)
Urinary Bladder				1 [2.0]	
Edema					
Hemorrhage				8 [1.4]	1 [2.0]
Inflammation	12 [1.0]	3 [1.0]	4 [1.5]	1 [3.0]	5 [2.0]
Metaplasia, Squamous				3 [2.7]	
Transitional Epithelium, Hyperplasia					4 [1.8]

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