

AR226-0437

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3M

TWO YEAR ORAL (DIET) TOXICITY / CARCINOGENICITY
STUDY OF FLUOROCHEMICAL FC-143 IN RATS

(RIKER EXPERIMENT No. 0281CR0012)

VOLUME 1 OF 4

CONDUCTED DURING
APRIL, 1981 - MAY, 1983

RIKER LABORATORIES, Inc. / 3M COMPANY
ST. PAUL, MINNESOTA 55144-1000 U.S.A.

000383

STUDY REPORT AMENDMENT NO. 1

EFFECTIVE DATE: NOVEMBER 2, 1987

Study Title: Two Year Oral (Diet) Toxicity/Oncogenicity Study of
Fluorochemical FC-143 in Rats

RIKER Experiment No.: 0281CR0012

The Table of Contents and the titles for individual clinical chemistry values for the males (Table 14; pages 66-70) and females (Table 15; pages 73-77) should read "Individual Plasma Chemistry Values"

Reason: This was an inadvertent typographical error only and does not change the interpretation of the clinical data.

Approval:

 11/2/87
L.J. Sibinski Date
Study Director

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**TWO YEAR ORAL (DIET) TOXICITY/CARCINOGENICITY
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TABLE OF CONTENTS

	PAGE(s)
REPORT SUMMARY	1
INTRODUCTION	3
MATERIALS AND METHODS	4
RESULTS	10
DISCUSSION	19
CONCLUSIONS	25
PRINCIPAL PERSONNEL LIST	26
SIGNATURE PAGE	27
REFERENCES	28
REPORT TABLES	29-92
TABLE 1 - Analysis of FC-143 in the Diet	29
TABLE 2 - Summary of Mean Body Weights - Males	30
TABLE 3 - Summary of Mean Body Weights - Females	32
TABLE 4 - Summary of Mean Feed Consumption Per Kilogram Body Weight - Males	34
TABLE 5 - Summary of Mean Feed Consumption Per Kilogram Body Weight - Females	36
TABLE 6 - Summary of Mean Absolute Feed Consumption - Males	38
TABLE 7 - Summary of Mean Absolute Feed Consumption - Females	40
TABLE 8 - Estimated Mean FC-143 Consumption In Milligrams Per Kilogram Per Day	42

000385

TABLE OF CONTENTS - Continued

	PAGE(s)
TABLE 9 - Mortality Data	44
TABLE 10 - Summary of Clinical Signs	46
TABLE 11 - Summary of Ophthalmologic Changes	48
TABLE 12 - Mean and Individual Hemogram Values - Males	50
TABLE 13 - Mean and Individual Hemogram Values - Females	57
TABLE 14 - Mean and Individual Serum Chemistry Values - Males	64
TABLE 15 - Mean and Individual Serum Chemistry Values - Females	71
TABLE 16 - Urinalysis Values	78
TABLE 17 - Individual Organ Weight, And Absolute Mean Organ Weights, Mean Organ Relative Percent To Whole Body Weight, And Organ To Brain Weight Ratios At One Year	81
TABLE 18 - Individual Organ Weight, And Absolute Mean Organ Weights, Mean Organ Relative Percent To Whole Body Weight, And Organ To Brain Weight Ratios At Two Years	86
TABLE 19 - Summary of Major Microscopic Findings - Neoplastic Lesions	91
TABLE 20 - Summary of Major Microscopic Findings - Non-Neoplastic Lesions	92
REPORT FIGURES	93-96
FIGURE 1 - Mean Body Weights - Males	93
FIGURE 2 - Mean Body Weights - Females	94
FIGURE 3 - Mean Feed Consumption Per Kilogram Mean Body Weight - Males	95
FIGURE 4 - Mean Feed Consumption Per Kilogram Mean Body Weight - Females	96

TABLE OF CONTENTS - Continued

	PAGE(s)
APPENDIX	97-1223
ITEM A - Air Monitoring of Animal Rooms	98
ITEM B - Diet Analytical Data Sheets	103
ITEM C - Acceptable Ranges for Clinical Pathology Parameters	116
ITEM D - Histopathologic Examination and Pathology Report by Dr. Robert G. Geil, External Consultant Veterinary Pathologist	119
ITEM E - Biostatistical Analysis Procedures	407
ITEM F - Summary of Mean Body Weights and Individual Animal Body Weight and Feed Jar Weight Data	411
ITEM G - Ophthalmoscopic Evaluation and Data by Dr. Stephen I. Bistner, External Consultant Veterinary Ophthalmologist	1203
ITEM H - Copy of the Study Protocol with Amendments	1206
ITEM I - Quality Assurance Unit Statement	1214
ITEM J - Chemical Analyses of FC-143 and Stability Analyses of FC-143 in Diet	1215

**TWO YEAR ORAL (DIET) TOXICITY/ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN RATS**

(RIKER Experiment No. 0281CR0012)

REPORT SUMMARY

The purpose of this study was to assess the potential toxicity and oncogenicity of FC-143 (ammonium perfluoroalkyl carboxylate) mixed in the diet and fed to 50 rats per sex per group for two years. An interim sacrifice and evaluation was performed at one year on 15 additional rats per sex from the control and high-dose groups.

A total of 360 Sprague-Dawley male and female rats were assigned to three experimental groups. The FC-143-treated groups were fed diets containing either 300 or 30 ppm of FC-143 for two years, while a control group received only untreated feed.

In-life observations performed during the course of the study included: daily observations for abnormal signs; periodic physical examinations; body weight and feed consumption; ophthalmoscopic examinations; and clinical pathology including hematology, clinical chemistry and urinalysis.

Macroscopic postmortem examinations were performed on all animals that died or were terminated prior to the end of the scheduled dosing. Selected organ weights were obtained from all of the rats necropsied at 1 year as well as from 15 rats/sex/group, randomly selected from the control and both FC-143-treated groups, at the termination of the study. Selected tissue specimens were harvested from each animal at necropsy, and preserved for future histopathologic examination. Microscopic evaluation was performed on all tissues saved from all of the control and high-dose rats, while a similar evaluation was performed on a modified list of tissues obtained from the low-dose animals.

The major in-life findings associated with FC-143 administration consisted of: a dose-related decrease in mean body weight and a treatment-related

increase in feed consumption per kilogram of mean body weight in males; and a slight treatment-related increase in the incidence of ataxia in the females. There was no increase in mortality in the high-dose treatment group when compared to similar values for the control population.

FC-143 related hematologic changes in both treated groups consisted of a decrease in red blood cell counts, hemoglobin concentration and hematocrit values at various times throughout the study. Generally, these hematology parameters remained within the acceptable ranges for the rat.

The primary FC-143 associated changes were found in the liver. These alterations were characterized by increased liver weights, hepatomegalocytosis with vacuolation of the cytoplasm, and some evidence of hepatocellular degeneration with occasional signs of necrosis. These liver changes were found early in the study and showed very little evidence of progression at the end of two years.

The incidence of almost all neoplasms in this study was relatively low, and the types and incidence of neoplasms were generally not different from those commonly found in geriatric Sprague-Dawley rats. Hepatocellular tumors were very slightly increased in the high-dose male rats. The other neoplasms in this study were associated with endocrine and/or endocrine-sensitive organs. The increased incidence of mammary or testicular tumors in the high- and low-dose groups was not statistically significant and/or was similar to the spontaneous incidence reported for Sprague-Dawley rats.

Under the conditions of this study and based on tumor incidence, types of tumors, time of tumor appearance, and the survival rate at two years, FC-143 is not considered to be carcinogenic in the rat.

**TWO YEAR ORAL (DIET) TOXICITY - CARCINOGENICITY
STUDY OF FLUOROchemical FC-143 IN RATS**

INTRODUCTION

This study was designed to evaluate the chronic toxicologic and carcinogenic potential of FC-143, an industrial grade of ammonium perfluoroalkyl carboxylate, in rats following oral administration in the diet for a period of two years. The study was sponsored by the Commercial Chemical Division of 3M Company and was performed by the Pathology and Toxicology Department of Riker Laboratories, Inc., 3M Company, St. Paul, Minnesota, U.S.A. The study and subsequent reporting was coordinated for the sponsor by the 3M Corporate Toxicology Services staff. The in-life or dosing portion of the study began on April 21, 1981, and was completed on May 5, 1983. A copy of the study protocol with amendments is contained in this report as Appendix Item H.

The study was designed to evaluate two separate fluorochemicals, FM-3924 and FC-143, using a common set of control animals. This report will describe the results of the FC-143 treatment while the results relating to the FM-3924 study will be reported separately.

The study was conducted in accordance with the Department's Standard Operating Procedures (ie., SOPs) and in compliance with the Food and Drug Administration's Good Laboratory Practice (GLP) regulations (21 CFR Part 58). Various phases of the study were inspected by the RIKER Quality Assurance Unit; their statement is presented in Appendix Item I of this report. The original signed protocol with amendments, list of study personnel, raw data, study specimens, and other pertinent study samples/documents will be maintained within the Pathology and Toxicology Department archives currently located at 3M Center in St. Paul, Minnesota.

MATERIALS AND METHODS

Test System: Three-hundred and sixty Sprague-Dawley rats [CrI:COBS^R CD(SD)BR, Charles River, Portage, MI], 39 to 41 days of age when treatment began, were divided by means of a table of random numbers into three groups. The control and high-dose groups each contained 65 males and 65 females, whereas the low-dose group contained 50 male and 50 female rats.

The rats were housed in hanging stainless steel cages with wire mesh floors and fronts. The males were housed individually, but the females were housed two per cage. The control animals were housed in separate rooms from those which received FC-143 in order to prevent a possible cross contamination by potential vaporization and/or sublimation of the test article which has a finite vapor pressure at room temperature. Air samples were taken from each of the animal treatment rooms four months after the initiation of the study in order to assay for the presence of airborne contaminants. The samples were analyzed by the Analytical Section of the 3M Central Research Laboratory and were found to be below detectable limits for the suspected fluorochemicals. In addition to the air monitoring, 30 untreated sentinel rats were placed in each of the two animal rooms. From each animal room, 5 male and 5 female sentinel rats were euthanized during the first week of the study, and at 1 and 3 months after the start of the study. Plasma samples obtained from these rats were analyzed for organic fluorine and were found to contain less than one part per million (see Appendix Item A).

Each animal room was temperature and humidity controlled with the lighting on a 12 hour light/dark cycle. Individual rats were uniquely identified by an animal number on a cage card and on a tag affixed to their ear. Feed (Certified Purina Laboratory Chow, Ralston-Purina Co., St. Louis, MO) and tap water were provided ad libitum.

Test Substance/Diet Preparation: FC-143 (Lot 37) was analyzed by the Commercial Chemicals Divisions (CCD) Analytical Laboratory prior to the start of the study, after approximately one year from the start of the study, and at the termination of the dosing period. No detectable changes were found in the test substance during this time (see CCD Analytical Reports Nos. 308, 348 and 413 in Appendix Item J).

The test substance was a white powder which was added (ie, stratified) directly into an appropriate quantity of untreated diet and mixed in a Hobart^R blender for approximately 20 minutes for each separate batch. Prior to initiating compound administration to any animals, the test substance/diet mixture was assayed. FC-143 was found to be uniformly blended and stable for one to two weeks in the ground feed (see CCD Analytical Report No. 209 in Appendix Item J).

Test article/diet mixtures were prepared fresh weekly during the study and representative samples of each were collected and assayed for test article content and homogeneity during the first month of the study and at 3 month intervals thereafter (see Appendix Item B). The results of these assays indicated that the level of FC-143 was generally within a few percent of that desired (Table 1).

The rats received either FC-143 treated or control (ie, untreated) diets in glass jars 10.2 cm high x 8.9 cm in diameter. A 5.1 cm access hole was cut in the stainless steel lid. On a weekly basis the diet jars were removed and replaced with clean jars containing fresh diet mixtures.

Experimental Design: The study consisted of one control group and two treatment groups. The dosage levels and animal distribution are listed hereinafter.

Treatment Groups	Dosage Levels (ppm)	<u>Group Size & Animal Numbers</u>	
		Males (An. Nos.)	Females (An. Nos.)
1 - Control	0	65 (3516-3580)	65 (4576-4640)
5 - High	300	65 (3581-3645)	65 (4641-4705)
6 - Low	30	50 (3646-3695)	50 (4706-4755)

An interim termination at one year involved 15 male and 15 female rats from both the control and high-dose groups. The remaining 50 animals per sex per group continued on study.

In-Life Observations: All animals were observed daily throughout the two year dosing period. Weekly physical examinations included palpation for the presence of masses as well as observations for pharmacotoxic signs; mortality was recorded daily. During the study, moribund animals were closely monitored, and euthanized when in the judgement of the Study Director death appeared to be imminent in order to harvest non-autolysed tissue for subsequent histopathologic examination.

Body weights and feed consumption were recorded once per week for the first six months, and then once every two weeks for the remainder of the study.

Eye examinations using indirect ophthalmoscopy and/or slit lamp biomicroscopy were performed on the control and high-dose rats by the Staff Veterinarian prior to compound administration and at approximately one year. The eyes of the surviving control and high-dose animals were examined 2-3 weeks prior to the termination of the study by a consulting Veterinary Ophthalmologist (see Appendix Item G).

Clinical pathology determinations included hematology, clinical (serum) chemistry and urinalysis. Tests were conducted on samples obtained from 15 rats per sex from each group at 3, 6, 12, 18 and 24 months; animals were randomly selected at each time interval. Hematologic tests included total red and white blood cell counts, hemoglobin, hematocrit, and a differential white blood cell count. Clinical chemistry parameters included total bilirubin, total protein, albumin, blood urea nitrogen (BUN), glucose, alkaline phosphatase (AP), creatine phosphokinase (CPK), aspartate aminotransferase (AST-formerly known as SGOT), alanine aminotransferase (ALT-formerly SGPT), and calcium. Urine tests included pH, specific gravity, albumin, glucose, bilirubin, occult blood and ketones.

Blood samples were collected from the retrobulbar venous plexus of anesthetized rats which had been fasted overnight. Blood was generally collected from the right eye. Urine samples were obtained by placing each rat in an individual metabolism cage for 20-22 hours. The specific methods

used for hematology, clinical chemistry and urinalysis are outlined in Appendix C. The mean hematology and clinical chemistry values from the treated groups were compared to both the concurrent control group as well as normal ranges for these parameters obtained from historical control animal data generated in this laboratory (Appendix C).

Metabolic Examination: Overnight (ie, about 24 hour) urine and fecal samples were collected at 2, 5, 11 and 23 months from five rats per sex per group for total organic fluoride analysis, and for the presence of FC-143. At the scheduled one and two year necropsies, samples of liver, blood, kidney, spleen, lung and bone marrow (ie, from the femur) were saved from five rats/sex/group. After collection, all specimens were frozen pending subsequent analysis by the RIKER Drug Metabolism Department.

Once these specimens are analyzed, a separate report regarding this experimental work will be prepared by the Drug Metabolism department.

Postmortem Examinations: Gross postmortem examinations were performed on all rats which died during the study and those which were terminated at the one year interim and two year necropsies. At necropsy, an examination was made of the external body surface and body orifices. The carcass was then opened and the contents of the abdomen, thorax and cranium were examined in situ and following removal from the body.

Organ weights (ie, wet tissue) were obtained at the interim termination from both the control and high-dose groups, and from the control and both FC-143 treated groups at the two year necropsy. The weights of the adrenal glands, brain, testes, heart, kidneys, liver, spleen and uterus were recorded for 15 randomly selected rats/sex/group. Body weights were obtained just prior to necropsy from the same rats in order to calculate organ weights relative to whole body weights.

Representative samples of the following tissues and organs from each rat were fixed in 10% neutral, buffered formalin for subsequent histologic processing:

Aorta	Liver (2 Sections)
Adrenals (2)	Lung (2 Sections)
Brain (3 Sections including	Lymph node (mesenteric)

frontal cortex and basal ganglia, parietal cortex and thalamus; cerebellum and pons)	Mammary Gland (females)
Eyes	Pancreas
Gonads	Pituitary
Ovaries (2)	Salivary Gland
Testes/Epididymides (2)	Spinal Cord/Bone Marrow (vertebrae)
Heart	Spleen
Small Intestine (3 Sections)	Stomach
Large Intestine	Thyroid/Parathyroid/Trachea/Esophagus
Kidneys (2 Sections)	Urinary Bladder
	Uterus or Prostate
	Any tissue masses (suspected tumors)
	Any gross lesion

Light microscopic examination was performed on hematoxylin and eosin stained, paraffin-embedded tissue sections from all tissues listed above, when available, and from all rats in the control (Group 1) and high-dose (Group 5) populations regardless of the cause of death. Microscopic examination of tissues from the low-dose (Group 6) rats included the tissues listed above except: aorta, brain, eyes, small and large intestines, lymph node(s), and spinal cord/bone marrow. The histopathologic examination and evaluation of these tissues was performed by Dr. Robert G. Geil, consulting Veterinary Pathologist (see Appendix Item D).

Biostatistical Methods: The means and standard deviations for body weights, feed consumption, absolute organ weight, relative organ weight to whole body weight, organ weight to brain weight ratios and other laboratory data were determined separately for each sex and dose group.

These data were analyzed using Bartlett's test for homogeneity of variance. If this test was not significant at $\alpha = 0.001$, the data were further analyzed by comparing each treated group to the control group using a two-tailed Dunnett's test at the $\alpha = 0.05$ significance level. The results of Dunnett's test have been indicated by asterisks on the mean tables. If Bartlett's test was significant at $\alpha = 0.001$, the data were ranked and a two-tailed Dunnett's test was performed on the ranks. These results have been indicated by the pound sign (#) on the mean tables.

In addition, for each organ/lesion classification the sexes were analyzed separately using a two-tailed Fisher's Exact Test comparing each treated group to the controls. An alpha = 0.05 significance level with Bonferroni's adjustment for multiple comparisons was used within each organ/lesion/sex category. If the expected value of each cell was greater than 20, then Yates' corrected Chi-Square test was used. An asterisk on the summary tables indicates a significant difference between the controls and the treated group.

Internal RIKER memoranda pertaining to these biostatistical procedures are presented within Appendix Item E.

RESULTS

In-Life Findings: Body weight gains were depressed in excess of 10% in the FC-143 high-dose males compared to the control males through 66 weeks of the study. There was an approximate 21% decrease in the high-dose body weights by week 6. This difference was statistically significant from week 2 of the study until week 98 when the high-dose and control male body weights had gradually equalized. Likewise in the low-dose male group, a 5% decrease in body weights was observed at week 6, however, there was little additional decrease thereafter (Table 2, Figure 1 and Appendix F). The occurrence of a mild SDA virus outbreak at different times during the study may have had a slight influence on the body weight data (see p. 12).

Mean body weights were only very slightly decreased in the FC-143-treated females compared to the control female values through the first 18 months of the study. At 18 months, there was a gradual decrease in mean body weights of high-dose females that reached a maximum of -11% at 92 weeks. The low-dose females also showed a decreased body weight, but the effect was not statistically significant and the change was of a much lower magnitude (Table 3, Figure 2 and Appendix F).

Mean feed consumption, presented as grams of diet consumed per day per kilogram of mean body weight, was increased in all of the FC-143-treated males throughout the study when compared to the male control feed consumption. This change was more pronounced in the high dose group where there was roughly a 13% increase noted with sporadic values going as high as 29% during the two year test period. In the females the pattern was less consistent, but there was a trend toward lowered feed consumption in both FC-143-treated groups compared to the female control values (Tables 4 and 5 and Figures 3 and 4). Overall, these variations were related to the variation of body weight among groups.

Actual mean feed consumption (without regard for body weight change) was slightly decreased in the high-dose males relative to control males, for the first year of the study. Feed consumption in low-dose males, while somewhat inconsistent, was slightly increased during this same period.

During the second year, the feed consumption of both FC-143-treated male groups was reasonably stable and consumption was comparable to that of the control group. All of the treated female groups tended to consume less feed than the comparable controls throughout the study. The greatest decreases occurred from 18 months to termination with the high- and low-dose groups being equally affected (Table 6 and 7 and Appendix F).

The test article concentration measured as parts per million in the diet was determined at 3 month intervals with a duplicate analysis performed when aberrant values were detected. The mean deviations from the target concentration of the high- and low-dose FC-143 groups were less than 3% (Table 1).

Actual test article consumption was determined for each 2 week period for each sex and each experimental group, and expressed as mg/kg/day. The mean test article consumption was estimated to be: males, 14.2 and 1.3 mg/kg/day; females 16.1 and 1.6 mg/kg/day for the high- and low-dose groups, respectively. Mean test article consumption values calculated at 2 week intervals for the entire study are presented in Table 8.

Overall survival rates for the FC-143-treated rats were good during the full two years of the test period. There were fewer deaths recorded in the high-dose males and females than in the comparable control populations. At the end of 1 year, 15 rats/sex from the control and high-dose groups were terminated to fulfill the protocol requirement for the interim sacrifice. The final survival rate then based on 50 rats/sex/group at the end of 104 weeks was: males, 70%, 88% and 72%; and females, 50%, 58% and 48% for the control, high- and low-dose groups, respectively. The increased survival rate observed in the high-dose male rats compared to the control male rats, was statistically significant ($p \leq 0.05$). Monthly mortality data are presented in Table 9.

A summary of the most commonly seen clinical signs is contained in Table 10. The only clinical sign that occurred more frequently in the test article-treated groups was a dose-related increase in ataxia reported for the FC-143- treated females. While the ataxia was most commonly associated

with morbid animals and was seen in the control males and females, only the treated females showed an increase in the incidence of this clinical sign; 2, 15 and 9 cases in the control, high- and low-dose groups, respectively. The incidences of all other clinical signs in the FC-143-treated groups were generally less than or equal to the incidence of the same signs in the control group.

Rats administered the test article experienced a suspected outbreak of sialodacryoadenitis (SDA) viral infection between the first and second months of the study. Clinical signs included swollen submandibular salivary glands and occasional ocular manifestations. The submandibular swelling was resolved within 10 days, and the incidence of ocular changes was extremely low. Similarly, the control animals had comparable symptoms during the sixteenth month of the study. Thirteen males and 13 females in the control group demonstrated signs of this condition which lasted for about 16 days from the time of onset. One male and 3 females developed ocular opacities during this period.

The incidence of palpable tissue masses in FC-143-treated groups was comparable to that of the control group. There were more animals with masses in the male controls than in the male treated groups; that is, 19, 10 and 7 animals in the control, high- and low-dose groups, respectively. Likewise, when the number of palpable masses which regressed or resolved before the termination of the experimental period were evaluated, there were still fewer masses found in the FC-143-treated animals than in the control group (Table 10).

The results of the final ophthalmoscopic examinations were negative relative to any FC-143 treatment-related effects. Changes that were observed included a random distribution of cataracts believed to be normal geriatric changes of the lens and some cases of chronic uveitis and superficial keratitis which were also considered to be within normal limits for aging populations of rats (Table 11 and Appendix G). Many of the rats found to have ocular lesions were identified as rats which were used to obtain blood samples via the retrobulbar venous plexus.

Red blood cell counts, hemoglobin and hematocrit values were minimally decreased in the high-dose male rats compared to control values, from 3 through 18 months. Statistically significant ($p = <0.05$) decreases were seen at various times in the following parameters: erythrocytes at 6, 12 and 18 months; hemoglobin, 3 and 18 months; and hematocrit at 3, 12 and 18 months. While some of these parameters were also altered in the low-dose males, the changes were of a lesser magnitude and in some cases, were increased as well as decreased (Table 12). The female high-dose erythrocyte counts and hematocrits were slightly decreased at 3 months, but were slightly increased at 6 months compared to control values. At 12 months there was a statistically significant decrease in erythrocyte count, hemoglobin, and hematocrit (Table 13).

Mean leucocyte counts were increased in both male treatment groups compared to control values, through the first year of the study. These changes were due to increases in absolute counts of lymphocytes at 3 and 6 months, and in neutrophils at 12 months. Statistically significant increases were observed: in lymphocyte counts at 3 months in the high- and low-dose groups, and at 6 and 18 months in the low-dose group; and in neutrophil counts at 12 months in both groups (Table 12). Similar changes were not seen in the FC-143-treated females with the exception of a slight increase in neutrophils and a slight decrease in lymphocytes seen in the low-dose group at 18 months (Table 13).

Clinical chemistry findings at 3 months included slight increases in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (AP), as well as a moderate decrease in creatine phosphokinase (CPK) in both FC-143-treated male groups. From 6 until 18 months, the high- and low-dose male ALT, AST and AP values were increased above the concurrent control values, whereas these values in the high-dose group were still elevated at 24 months. Albumin values remained very slightly elevated in the high-dose males until the end of the study. Similar changes in clinical chemistry were not observed in the FC-143-treated female groups (Tables 14 and 15).

Urinary findings included increases in incidence and severity of albumin and occult blood in all of the male and female control and FC-143-treated groups at 12, 18, and 24 months. These findings were more pronounced in the males than in the females at the termination of the study. Other than an occasional incident of slight ketonuria in both control and FC-143-treated animals, there were no other remarkable urinary findings (Table 16).

Postmortem Findings: The Consulting Pathologist's complete report is located in Appendix D. The gross pathology findings seen at the 1 year interim sacrifice were unremarkable with the possible exception of a single high-dose male having small testes and 3/15 high-dose females with mammary masses compared to an incidence of 1/15 in control female rats.

Possible FC-143-related gross findings seen in male and female high-dose rats which were either found dead, euthanized in extremis, or euthanized at the termination of the study, included liver and testicular observations in the males and only a very slight increase in the incidence of mammary masses in the low-dose females. The liver findings seen in the males consisted of a slight increase in the incidence of liver masses, nodules and raised lesions, mottled livers and yellow or pale liver foci. While small testes were observed grossly in the control males as well as in both treated groups, testicular masses were found in 6/50 high-dose and 1/50 low-dose rats, but not in any of the controls. Mammary masses reported at necropsy in 1 high-dose and 2 low-dose males were found microscopically to be non-mammary lesions. Mammary masses were observed in 27/50, 26/50 and 37/50 of the control, high- and low-dose female rats, respectively. No remarkable FC-143-related liver changes were seen grossly in the female rats. Other gross pathologic findings were typical of findings in aging rats of this strain (Appendix D).

Organ weights presented as either absolute or relative (ratio of organ/body weight or organ/brain weight) values are contained in Tables 17 and 18. At the 1 year interim sacrifice where the only groups examined were the high-dose and controls (n = 15/sex/group), there was no change in male body weight (absolute) but a statistically significant ($p = <0.05$) increase in

relative liver and kidney weights (vs. body weight) for the FC-143-treated males only. At the terminal necropsy, slight increases in relative (organ vs. body weight) liver weights were noted for both the males and females of both dose groups, but the increases were not statistically significant. Slight increases in relative kidney weights were observed in both the male and female rats in the high-dose group; however, only in the females was this finding statistically significant.

Complete details of the histopathologic findings are contained in Appendix D and a summary of the major neoplastic and non-neoplastic microscopic changes found after 2 years of continuous oral administration of FC-143 are listed in Tables 19 and 20.

Histopathologic evaluation of the tissues from the animals necropsied at 1 year indicated the major FC-143 effects were confined to the liver. Diffuse hepatomegalocytosis (12/15 animals), hepatocellular necrosis (6/15 animals), and portal mononuclear cell infiltration (13/15 animals) were seen in the high-dose males while incidences in the control group were 0/15, 0/15 and 7/15, respectively. Testicular tubular atrophy with marked aspermatogenesis was found in 2/15 high-dose males but was absent in the control males. The only remarkable change seen in the high-dose females was minimal to mild hepatocellular vacuolation; the incidence for this finding was 11/15 at the high dose and 5/15 in the control group.

The majority of neoplasms observed after 2 years of dosing with FC-143, involved either the liver or one of several endocrine or endocrine-related organs (Table 19). Hepatocellular carcinomas were found in 6%, 10%, and 2% of the males from the control, high-, and low-dose groups, respectively. For the females, hepatocellular carcinomas were found only in the high-dose group with an incidence of 2%. The organ with the highest incidence of tumors was the pituitary gland where the incidences of adenomas in the males was 35%, 28% and 36%, and in the females at 71%, 71% and 83% for the control, high- and low-dose groups, respectively.

Mammary gland adenocarcinomas were present in both control and treated females at an incidence of 15%, 11% and 31% for the control, high- and

low-dose groups, respectively. In a similar comparison, fibroadenomas were seen in 22%, 48% and 42% of the female rats at the end of the study. Mammary gland adenomas (7%) and carcinomas (2%), were seen only in the female controls, while one high-dose female had a lymphangiosarcoma. An increase in testicular Leydig cell adenomas was statistically significant ($p = <0.05$) in the high-dose males. The incidence for this lesion was 0%, 14% and 4% in the control, high- and low-dose groups, respectively. There were minor variations in the tumor incidence patterns in the adrenals (pheochromocytomas) and thyroids which represent deviations in two commonly occurring spontaneous tumors of this strain of rat. Only the incidence of C-cell adenomas of the thyroid in male rats, appeared to show a slight dose dependent increase; namely, 0%, 9% and 4% for the control, high- and low-dose groups, respectively. However, C-cell carcinomas were seen only in the controls at an incidence of 5%.

Non-neoplastic changes were found at the termination of the study in the adrenals, heart, liver, lung, pancreas, ovaries, salivary glands, spleen, testes, thyroids and uterus (Table 20). As noted in the 1 year interim histopathologic evaluation, the liver was the primary organ associated with FC-143 treatment-related effects, and there was a remarkable consistency in the type of findings observed in the males after the second full year of test article administration. Megalocytosis, cystoid degeneration, and portal mononuclear cell infiltration were the major dose-related changes seen in both male and female test article-treated groups. Megalocytosis was found at an incidence of 0%, 80% and 12% in the males, and 0%, 16% and 2% in the females from the control, high- and low-dose groups, respectively. Hepatic cystoid degeneration, a condition characterized by areas of multilocular microcysts in the liver parenchyma, was more commonly seen in male rats with a control incidence of 8%, whereas the high- and low-dose males had incidences of 56% and 14%, respectively. The incidence of this lesion in females was 2% in both of the FC-143-treated groups. Hepatocellular necrosis was equally distributed between the control and FC-143-treated groups. The incidence of hyperplastic nodules, a localized proliferation of hepatic parenchymal cells, was slightly increased in the high dose groups with an incidence of 6% in the males and 2% in the females as compared to 0% and 2% in the control males and females, respectively.

No hyperplastic nodules were found in the low-dose group. The incidences of other hepatic changes such as basophilic hepatocyte alteration and/or chronic inflammatory changes consisting of portal mononuclear cell infiltration were slightly increased in the high-dose males, but only against a high incidence of similar changes in the control group.

Pulmonary changes that may be associated with the administration of FC-143 in the high-dose males, consisted of an increase in the incidence of alveolar macrophages (62%) and hemorrhage (44%) compared to control incidences of 20%. However, the incidence of chronic interstitial pneumonia and perivascular mononuclear infiltration was greatly reduced in the high-dose males when compared to the male controls. Pulmonary vascular mineralization was observed commonly in both control and test article-treated male and female rats; however, the FC-143-treated females displayed an increase that was inversely related to the dose.

The incidence of chronic sialadenitis, an inflammatory change of the salivary gland and often associated in rats with an antemortem viral infection, was increased in both the high- and low-dose males.

Hemosiderin, an iron rich pigment, was found in greater concentrations in the spleens of both high-dose males and females, but in greatly reduced amounts in the low-dose males and females as compared to controls.

Two changes observed in the gonads of both sexes, appeared to be related to the administration of FC-143. Vascular mineralization of the testes occurred in 18% of the high-dose males and 6% of the low-dose males, but was not seen in the controls. The incidence of testicular tubular atrophy was only slightly increased in the high-dose (22%) and low-dose (20%) males compared to the control males (14%).

In the test article-treated females, there was a dose-related, statistically significant increase in tubular hyperplasia of the ovarian stroma. Tubular hyperplasia is considered to be a diffuse, non-neoplastic increase in stromal tubular elements which is usually bilateral and associated with decreased or absent follicular development. The incidence

of this change was 0%, 32% and 14% in the control, high- and low-dose groups, respectively. Cystic glands of the uterine endometrium were found at a higher incidence in the low-dose females (24%) when compared to the controls (14%) and high-dose females (10%).

Other non-neoplastic lesions (Table 20) are commonly associated with either endemic diseases and/or geriatric changes found in this strain of rat. The following changes were considered equivocal test article-related findings or were usually decreased below the concurrent incidence in control rats. Adrenal changes are commonly seen in aging rats of this strain and the incidences were inconsistently either higher or lower than the control values. The incidence of sinusoidal ectasia (dilatation) was increased very slightly only in the high-dose males (32%) compared to the control males (22%), while the control and FC-143-treated females were almost equally affected (82 and 86%). The incidence of chronic myocarditis was reduced in an apparent dose-related fashion in the females while being increased above the control incidence in the high- and low-dose males. The incidence of thyroid C-cell hyperplasia was slightly increased in the high dose females, while only the low-dose males showed a similar change. The incidence of acinar atrophy of the pancreas was very slightly increased in the treated males, while being slightly depressed below control values in the high-dose female.

DISCUSSION

The purposes of this study was to define the long term toxicity and oncogenicity profile of FC-143, an anionic fluorochemical surfactant belonging to the chemical class of ammonium perfluoroalkyl carboxylates. The study was successfully completed with sufficient numbers of animals surviving in all of the experimental groups. The survival rates for the high-dose male and female rats were actually higher than those of the control rats after 24 months of the test.

The general health of a rat exposed to the experimental conditions of a 2 year feeding study may be examined at the beginning of the test by evaluating body weight gains and feed consumption compared to the study control animal population. Body weight gains of the FC-143-treated males decreased as early as the second week of the study, stabilized after 6 weeks, but remained slightly depressed in the high-dose males by at least 10% through 66 weeks. The treated females did not demonstrate any real decrease in body weight until the 18th month, so there appeared to be a rather obvious sex difference in this parameter. The body weight changes did not appear to be associated with the palatability of the diet admix since feed consumed on a body weight basis was actually increased. Further, since there was a modest dose-related effect seen in the male FC-143-treated rats, it appears that these body weight changes could be associated with a direct test article effect.

The concentration of the test article in the diet was within a 3% range of the proposed levels of 300 and 30 ppm for the full 2 years of the study. The average daily dose of FC-143 for the same time period and for both sexes combined, was estimated to be 15 and 1.5 mg/kg/day. Both in-life and postmortem results confirmed the systemic absorption of the test article and the 300 ppm dosage level appeared to adequately comply with the concept of a maximum tolerated dose for a long term study in this strain of rat.

The only clinical sign seen during the study which was associated with a test article effect was ataxia. The incidence of ataxia was increased in a dose related manner in the females, but not in the treated males. A

background incidence of this finding was seen in the male and female control population.

During the early course of the study, a decrease in red blood cell parameters was observed in the high-dose males. While these hematologic values were often decreased below the control male measurements at a statistically significant level ($p \leq 0.05$), generally the decreased values were still within the acceptable ranges for these parameters in the rat.

The elevation of serum alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase activities only in test article-treated male rats, suggested that FC-143 affected hepatocytes. These changes were seen from 3 to 18 months in both of the male FC-143-treatment groups, but only in the high-dose males at 24 months. These findings were substantiated by organ weight changes and histopathology observed at the 1 and 2 year sacrifices.

Changes in the character of the urine specimens were similar in both control and treated rats examined during the course of the study. These findings were considered to be associated with the slowly developing degenerative changes of naturally occurring chronic renal disease commonly found in rats of this strain.

The liver was the primary target organ affected as seen by an increase in relative organ weights, gross findings at necropsy, and histopathologic alterations. These changes seen at the 1 year necropsy showed remarkably little progression 1 year later. The FC-143-treated males were more obviously affected than the females. The sex differences seen in this study were consistent with earlier pharmacokinetic studies using carbon-14 labeled ammonium perfluorooctanoate, in which the females during 24 hours had excreted essentially 100% of an intravenous dose in the urine while the males excreted only 20%. Radioactive tissue residues were not detectable after 17 days in the females, while at 36 days, male rats had 2.8% of the carbon-14 in the liver, 1.1% in plasma, and lower but still detectable amounts in other organs.¹ Similar results were reported by Hanhijarvi, et al.⁶

Hepatomegalocytosis and hepatocellular vacuolation are characteristic of increased metabolic activity in the rat. Following chronic hepatic stimulation, evidence of cystoid degeneration and, occasionally, hepatocellular necrosis may also be observed. Since the liver in the rat rarely repairs parenchymal cell loss with fibrosis or scar tissue, the most common finding is hepatocellular hyperplasia. In this study, the incidence of hyperplastic nodules was increased very slightly in the high-dose group, but the incidence was not significantly different from controls. It is also important to note that no proliferative hepatic lesions (i.e. neither hyperplasia nor neoplasia) were seen in any of the high-dose rats receiving FC-143 for 1 year. The observed hepatomegalocytosis was similar to that reported by Pastoor et al in which perfluorooctanoic acid was administered orally to male rats at a higher dosage (50 mg/kg/day).² It was proposed that the hepatocytic enlargement was due to proliferation of smooth, endoplasmic reticulum, mitochondria, and peroxisomes.

The only hepatic neoplasms found in this study were hepatocellular carcinomas. The incidence of this tumor was 6%, 10% and 2% in the control, high- and low-dose male rats, respectively. Only one high-dose female was found to have this liver tumor. The incidence of hepatocellular carcinomas in high-dose males was not significantly greater than that of the control males and was comparable with the reported spontaneous incidence of this tumor.³ Based on these findings, FC-143 was not considered to be a hepatic carcinogen in the rat.

The other neoplasms observed in this study originated from endocrine and/or endocrine sensitive organs; namely, the adrenal gland, mammary gland, pituitary gland, testes, and thyroid gland. The incidence for each of these tumors are presented in Table 19.

The incidence of mammary gland adenocarcinomas was 15%, 11% and 31% for the control, high- and low-dose female groups, respectively. While mammary gland carcinomas and adenomas were found only in the controls, there was an increased incidence of fibroadenomas in the high-dose (48%, statistically significant: $p \leq 0.05$), and the low-dose (42%) compared to controls (22%). It should also be noted that 2/13 of the high-dose females necropsied at 1

year were found to have fibroadenomas, while 0/15 of the controls were similarly affected. Although the incidence of fibroadenomas in high-dose females was significantly greater than that for the control females, the incidence was similar to that reported for untreated aging rats.⁴ In addition, when the incidences for benign mammary gland tumors (adenoma and fibroadenoma) are combined, the tumor incidence in the high-dose group is no longer statistically significant.

Leydig cell adenomas (i.e. benign tumors of the testicular interstitial tissue), were found at an incidence of 0%, 14% and 4% in the control, high- and low-dose groups, respectively. The high-dose incidence for this lesion was statistically significant ($p \leq 0.05$) because the incidence in the control group was unusually low (0%). In addition, the spontaneous incidence reported for this neoplasm in this strain of rat was 7.4% for rats 24 to 29 months of age and was 14.6% at 30 to 38 months of age³. Based on another set of Sprague-Dawley two year study data compiled by Hazleton Laboratories, the spontaneous incidence of interstitial cell tumors was 28.7%.⁵

The remaining non-neoplastic findings reported from the histopathologic evaluation of all of the animals originally scheduled for the 2 year phase of the study were mostly geriatric lesions common to this strain of rat. The organs in which these lesions were found included: adrenal, heart, kidney, lung, testes, ovary, thyroid, urinary bladder and uterus. Specific deviations from control values seen in FC-143-treated groups were addressed in the results section of this report; however, the following changes may be considered incidental or equivocal test article-related effects.

The incidence of nodular hyperplasia of the adrenal cortex was increased (not statistically significant) in the high-dose males (18%) compared to the same finding in the controls (4%), while the high-dose females showed a much lower incidence (2%). Increases in the incidences of adrenal gland sinusoidal ectasia (dilatation) were reported in the high- (32%) and low- (26%) dose males compared to male controls (22%) while the incidences in

all test article-treated females were equal to control values. It should be noted that adrenal lesions are commonly seen in old rats.

Thyroid C-cell hyperplasia was seen in the control males and FC-143-treated groups with an incidence of 10% and 7% for the low-dose males and the high-dose females, respectively. The incidences were not dose-related or statistically significant and were lower than the reported spontaneous incidence of this lesion.³

Chronic myocarditis (inflammation) was seen at a slightly higher incidence in the low-dose (36%) and the high-dose (34%) males compared to the control (28%) group. The female incidence for this lesion was 32%, 20% and 10% in the control, high- and low-dose groups, respectively. Inflammation of the heart is common in old rats. The lack of a true dose-related effect in either sex suggests that this finding is probably not a treatment related phenomenon.

Chronic renal histopathologic changes, commonly observed in aging rats, were not meaningfully altered by FC-143 treatment. None of these changes were apparently severe enough to produce pathologic lesions over a 2 year period. Therefore, none of these findings are considered to be directly related to treatment.

Lung changes which were seen more commonly in FC-143-treated rats than in controls included an increase in alveolar macrophages, pulmonary hemorrhage (agonal) and vascular mineralization. The first two lesions were seen predominantly in the high-dose males where the incidences were statistically significant ($p \leq 0.05$). Control males on the other hand, had higher incidences of interstitial pneumonia and pulmonary perivascular mononuclear cell infiltration. Pulmonary changes are common in aging rats.³ Other than the possibility that an increase in the alveolar macrophages may be associated with FC-143 administration, all of the pulmonary changes were not considered related to test article treatment.

Chronic sialadenitis or inflammation of the salivary glands was significantly ($p \leq 0.05$) increased in the test article-treated males, but

not in the test article-treated females. These changes were attributed to outbreaks of sialodacryoadenitis viral infections which occurred in both the control and FC-143 animal rooms, but at different time periods and apparently with different levels of intensity.

The incidence of splenic hemosiderosis, depositions of iron-containing pigment in the sinusoids of the spleen, was increased above control levels by approximately 12% in only the high-dose males. However, the incidence in high-dose males was not significantly greater than the control incidence. The incidence of this lesion in FC-143 treated females was significantly lower than the incidence of splenic hemosiderosis in control females.

A statistically significant, dose-related increase in the incidences of ovarian (stromal) tubular hyperplasia was found in low and high-dose groups. The interpretation of these changes in the absence of any observable progressive pathologic lesion after 2 years of treatment, must be considered as equivocally related to FC-143 treatment.

CONCLUSIONS

The results obtained under the conditions of this study when FC-143 was administered in the diet of male and female rats at concentrations of 300 and 30 ppm for 2 years may be summarized as follows:

1. FC-143-related changes were found more commonly in males than in females of each of the two treatment groups. This finding supports earlier pharmacokinetic studies that demonstrated a increased FC-143 retention by treated males compared to treated female rats.
2. The major dose-related findings were observed in the liver and consisted of megalocytosis and cystoid degeneration with only a minimal proliferative response and related elevations of serum enzyme activities.
3. Other non-neoplastic findings reported in this study were not considered primary test article-related effects, but rather were related to spontaneous changes occurring in aging rats.
4. Based on the incidence, types of tumors, time of tumor appearance, malignancy patterns of tumors and survival rate after 2 years, FC-143 is not considered to be carcinogenic in the rat.

**PRINCIPAL PERSONNEL INVOLVED WITH THE CONDUCT AND REPORTING OF
RIKER EXPERIMENT NO. 0281CRO012 - TWO YEAR ORAL (DIET)
TOXICITY/CARCINOGENICITY STUDY OF FLUOROCEMICAL FC-143 IN RATS**

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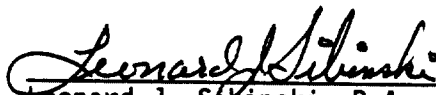
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TWO YEAR ORAL (DIET) TOXICITY/CARCINOGENICITY STUDY OF
FLUOROCEMICAL FC-143 IN RATS

RIKER Experiment No. 0281CR0012

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Table 1

Two Year Oral (Diet) Toxicity - Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Analytical Analysis of FC-143^a
(% Above/Below Desired Concentration)

Approximate Study Month	CCD Analytical Report Numbers	Dosage Levels (ppm)	
		300	30
0 (Initial)	213	+ 0.6%	- 1.0%
1	229	+ 0.3%	+ 1.0%
4	250	+ 5.0%	- 2.3%
7	289	+ 1.2%	+ 0.0%
10	319	^b -34.0%	- 6.7%
11	328	- 6.1%	----
13	340	- 2.3%	+ 7.7%
16	366	+ 2.6%	+ 4.4%
19	384	+ 2.0%	+ 2.2%
22	395	+ 3.0%	+ 3.3%
24	404	+ 9.4%	+10.0%
Mean Deviation for the Study		^c + 1.6%	+ 1.9%

^a Commercial Chemicals Division (CCD)

^b Incorrect values given at this level due to instrument malfunction:
this dosage level was reanalyzed after new detector was installed.

^c Excluding from mean deviation the percentages over + 20% acceptable limit.

Table 2

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Body Weights (g) $\pm$ % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
0	165.3	162.1	- 1.9	167.0	+ 1.0
2	270.9	234.3	-13.5	271.0	+ 0.0
4	334.0	276.7	-17.2	328.5	- 1.6
6	390.7	308.6	-21.0	369.4	- 5.4
8	429.2	353.2	-17.7	410.3	- 4.4
10	456.2	380.1	-16.7	441.5	- 3.2
12	475.5	398.0	-16.3	458.1	- 3.7
14	493.2	412.8	-16.3	475.4	- 3.6
16	502.9	425.4	-15.4	487.9	- 3.0
18	515.3	436.0	-15.4	498.5	- 3.3
20	526.8	447.4	-15.1	512.1	- 2.8
22	542.3	456.1	-15.9	519.4	- 4.2
24	550.4	464.2	-15.7	526.3	- 4.4
26	561.0	475.0	-15.3	538.9	- 3.9
28	567.5	484.9	-14.6	546.2	- 3.8
30	576.3	497.2	-13.7	558.6	- 3.1
32	580.6	505.7	-12.9	566.4	- 2.4
34	582.9	511.8	-12.2	571.3	- 2.0
36	591.0	514.2	-13.0	575.4	- 2.6
38	599.4	524.8	-12.4	584.0	- 2.6
40	608.4	535.2	-12.0	592.5	- 2.6
42	612.9	540.9	-11.7	600.5	- 2.0
44	619.8	550.8	-11.1	610.4	- 1.5
46	623.5	552.0	-11.5	612.1	- 1.8
48	626.1	558.5	-10.8	618.9	- 1.1
50	639.2	566.7	-11.3	627.1	- 1.9
52	638.6	570.1	-10.7	633.6	- 0.8

Table 2 (concluded)

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Body Weights (g) $\pm$ % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	654.3	577.6	-11.7	641.9	- 1.9
56	661.6	583.1	-11.9	646.4	- 2.3
58	668.0	587.9	-12.0	652.7	- 2.3
60	673.2	590.8	-12.2	656.8	- 2.4
62	674.4	593.2	-12.0	655.7	- 2.8
64	664.5	596.8	-10.2	658.3	- 0.9
66	650.8	598.2	- 8.1	662.5	+ 1.8
68	656.6	604.9	- 7.9	666.5	+ 1.5
70	661.9	608.2	- 8.1	666.2	+ 0.6
72	658.3	608.5	- 7.6	664.4	+ 0.9
74	660.8	601.1	- 7.6	659.2	- 0.2
76	667.7	605.4	- 9.3	663.8	- 0.6
78	668.8	604.6	- 9.6	661.7	- 1.1
80	670.6	611.8	- 8.8	669.2	- 0.2
82	663.1	610.0	- 8.0	666.9	+ 0.6
84	668.1	617.5	- 7.6	662.3	- 0.9
86	675.6	617.4	- 8.6	664.5	- 1.6
88	678.9	614.7	- 9.5	654.7	- 3.6
90	690.0	624.6	- 9.5	662.4	- 4.0
92	686.0	621.8	- 9.4	652.9	- 4.8
94	678.3	627.6	- 7.5	660.0	- 2.7
96	677.5	621.0	- 8.3	653.4	- 3.6
98	675.7	627.2	- 7.2	659.7	- 2.4
100	671.1	625.5	- 6.8	660.0	- 1.7
102	665.9	629.4	- 5.5	664.0	- 0.3
104	642.0	613.3	- 4.5	650.8	+ 1.4

Table 3

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Body Weights (g) $\pm$ % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
0	138.2	138.1	$\pm$ 0.0	137.2	- 0.7
2	159.2	167.3	$\pm$ 5.1	166.0	+ 4.3
4	209.5	213.8	+ 2.1	214.9	+ 2.6
6	238.7	237.4	- 0.5	235.7	- 1.3
8	256.9	254.6	- 0.9	253.8	- 1.2
10	269.2	263.3	- 2.2	261.3	- 2.9
12	279.5	274.2	- 1.9	275.5	- 1.4
14	289.7	286.4	- 1.1	282.8	- 2.4
16	291.8	285.4	- 2.2	285.9	- 2.0
18	306.8	299.4	- 2.4	298.0	- 2.9
20	311.6	307.6	- 1.3	304.1	- 2.4
22	319.1	314.6	- 1.4	309.9	- 2.9
24	324.5	322.5	- 0.6	318.6	- 1.8
26	327.3	326.0	- 0.4	323.6	- 1.1
28	333.7	331.6	- 0.6	330.4	- 1.0
30	338.3	338.6	+ 0.1	339.0	+ 0.2
32	345.5	344.1	- 0.4	344.9	- 0.2
34	350.7	352.8	+ 0.6	353.5	+ 0.8
36	355.5	357.1	+ 0.5	358.0	+ 0.7
38	359.3	362.3	+ 0.8	363.1	+ 1.1
40	363.2	366.0	+ 0.8	367.5	+ 1.2
42	371.2	373.2	+ 0.5	375.9	+ 1.3
44	380.1	380.4	+ 0.1	382.0	+ 0.5
46	385.7	385.9	$\pm$ 0.0	389.7	+ 1.0
48	392.3	391.6	- 0.2	395.8	+ 0.9
50	398.6	399.3	+ 0.2	399.7	+ 0.3
52	406.1	406.1	$\pm$ 0.0	406.2	$\pm$ 0.0

Table 3 (concluded)

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Body Weights (g) $\pm$ % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	414.1	411.5	- 0.6	412.6	- 0.4
56	419.1	421.2	+ 0.5	420.7	+ 0.4
58	420.9	426.4	+ 1.3	427.3	+ 1.5
60	423.6	427.0	+ 0.8	430.0	+ 1.5
62	426.6	431.9	+ 1.2	435.7	+ 2.1
64	426.1	434.0	+ 1.9	439.9	+ 3.2
66	424.9	435.5	+ 2.5	446.5	+ 5.1
68	427.5	433.0	+ 1.3	445.3	+ 4.2
70	431.4	429.1	- 0.5	443.5	+ 2.8
72	435.2	432.8	- 0.6	448.6	+ 3.1
74	446.5	444.6	- 0.4	463.3	+ 3.8
76	455.2	447.4	- 1.7	468.8	+ 3.0
78	464.8	452.7	- 2.6	471.3	+ 1.4
80	474.9	457.0	- 3.8	475.8	+ 0.2
82	484.0	461.8	- 4.6	485.7	+ 0.4
84	484.8	457.6	- 5.6	476.3	- 1.8
86	492.7	458.2	- 7.0	479.7	- 2.6
88	499.1	456.6	- 8.5	483.4	- 3.1
90	500.6	451.8	- 9.7	485.2	- 3.1
92	512.5	455.9	-11.0	486.3	- 5.1
94	505.7	451.0	-10.8	492.0	- 2.7
96	506.9	464.5	- 8.4	504.3	- 0.5
98	500.0	468.0	- 6.4	505.5	+ 1.1
100	501.2	464.2	- 7.4	505.6	+ 0.9
102	503.6	462.8	- 8.1	503.3	- 0.1
104	502.0	450.3	-10.3	501.8	+ 0.0

Table 4

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption Per Kilogram Body Weight
(g of diet consumed per day) + % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
1	102.0	98.6	- 3.3	103.8	+ 1.8
2	85.2	96.8	+13.6	85.0	- 0.2
4	76.4	84.0	+10.0	77.0	+ 0.8
6	69.4	67.7	- 2.5	61.2	-11.8
8	61.5	70.6	+14.8	64.1	+ 4.2
10	53.7	63.0	+17.3	57.4	+ 6.9
12	50.7	58.1	+14.6	51.3	+ 1.2
14	51.7	59.5	+15.1	53.5	+ 3.5
16	48.0	55.2	+15.0	49.3	+ 2.7
18	46.8	52.6	+12.4	47.7	+ 1.9
20	46.9	54.5	+16.2	48.9	+ 4.3
22	44.9	51.9	+15.6	47.3	+ 5.4
24	45.0	52.0	+15.6	46.3	+ 2.9
26	43.7	49.2	+12.6	44.9	+ 2.8
28	42.8	48.3	+12.9	44.5	+ 4.0
30	43.2	48.7	+12.7	43.7	+ 1.2
32	42.9	47.2	+10.0	44.0	+ 2.6
34	41.8	46.5	+11.2	42.8	+ 2.4
36	38.4	42.5	+10.7	39.7	+ 3.4
38	40.7	46.0	+13.0	42.2	+ 3.7
40	39.5	43.9	+11.1	41.8	+ 5.8
42	39.3	44.0	+12.0	41.3	+ 5.1
44	38.9	43.6	+12.1	40.5	+ 4.1
46	39.0	42.6	+ 9.2	39.7	+ 1.8
48	39.0	43.3	+11.0	38.9	- 0.3
50	38.5	43.2	+12.2	39.4	+ 2.3
52	36.5	41.1	+12.6	36.1	- 1.1

Table 4 (concluded)

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption Per Kilogram Body Weight
(g of diet consumed per day), $\pm$ % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	37.0	42.2	+14.1	36.3	- 1.9
56	36.6	41.2	+12.6	37.9	+ 3.6
58	36.1	40.7	+12.7	37.5	+ 3.9
60	35.4	40.6	+14.7	37.3	+ 5.4
62	35.9	37.1	+ 3.3	37.1	+ 3.3
64	31.0	40.2	+29.7	34.5	+11.3
66	36.3	40.8	+12.4	36.4	+ 0.3
68	32.9	36.5	+10.9	33.5	+ 1.8
70	32.6	37.7	+15.6	33.0	+ 1.2
72	33.0	37.5	+13.6	34.9	+ 5.8
74	34.4	37.9	+10.2	36.7	+ 6.7
76	37.1	39.2	+ 5.7	36.9	- 0.5
78	36.6	39.7	+ 8.5	34.9	- 4.9
80	34.6	39.4	+13.9	36.8	+ 6.4
82	36.3	36.7	+ 1.1	37.6	+ 3.6
84	35.6	38.5	+ 8.2	34.3	- 3.7
86	35.1	38.6	+10.0	35.4	+ 0.9
88	34.8	33.0	- 5.2	33.0	- 5.2
90	34.9	36.3	+ 4.9	34.7	- 0.6
92	35.1	37.3	+ 6.3	35.1	+ 0.0
94	38.5	40.5	+ 5.2	36.8	- 4.4
96	37.1	40.1	+ 8.1	37.5	+ 1.1
98	37.3	38.9	+ 4.3	37.4	+ 0.3
100	36.7	38.1	+ 3.8	37.3	+ 1.6
102	35.0	38.3	+ 9.4	37.2	+ 6.3
104	33.8	37.8	+11.8	37.5	+11.0

Table 5

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption Per Kilogram Body Weight
(g of diet consumed per day). + % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
1	98.8	96.6	- 2.2	96.1	- 2.7
2	107.0	101.6	- 5.1	103.0	- 3.7
4	97.2	81.8	-15.8	83.6	-14.0
6	81.0	81.1	+ 0.1	82.8	+ 2.2
8	74.1	74.9	+ 1.1	73.4	- 0.9
10	72.6	72.5	- 0.1	73.5	+ 1.2
12	70.2	70.4	+ 0.3	69.7	- 0.7
14	64.2	62.0	- 3.4	64.9	+ 1.1
16	57.2	56.3	- 1.6	58.8	+ 2.8
18	64.3	62.9	+ 2.2	64.6	+ 0.5
20	63.4	61.5	- 3.0	65.5	+ 3.3
22	58.6	61.2	+ 4.4	63.2	+ 7.9
24	59.5	58.0	- 2.5	61.2	+ 2.9
26	57.0	56.2	- 1.4	57.0	+ 0.0
28	61.7	58.1	- 5.8	58.3	- 5.5
30	59.7	57.4	- 3.9	59.0	- 1.2
32	58.4	56.1	- 3.9	55.7	- 4.6
34	52.9	51.4	- 2.8	51.5	- 2.7
36	56.7	54.2	- 4.4	57.0	+ 0.5
38	56.8	52.7	- 7.2	54.3	- 4.4
40	58.4	51.6	-11.6	50.3	-13.9
42	54.2	53.6	- 1.1	52.9	- 2.4
44	54.7	51.8	- 5.3	53.9	- 1.5
46	48.5	50.8	+ 4.7	52.1	+ 7.4
48	49.2	50.3	+ 2.2	51.8	+ 5.3
50	51.4	45.1	-12.3	50.0	- 2.7
52	48.3	48.3	+ 0.0	48.0	- 0.6

Table 5 (concluded)

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption Per Kilogram Body Weight
(g of diet consumed per day) $\pm$ % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	48.1	47.1	- 2.1	47.3	- 1.7
56	51.5	48.4	- 6.0	47.1	- 8.5
58	46.3	47.6	+ 2.8	46.3	+ 0.0
60	49.6	49.2	- 0.8	47.7	- 3.8
62	47.1	46.5	- 1.3	44.8	- 4.9
64	48.4	46.1	- 4.8	44.1	- 8.9
66	41.0	39.5	- 3.7	39.6	- 3.4
68	44.9	41.3	- 8.0	39.8	-11.4
70	46.1	43.1	- 6.5	41.0	-11.1
72	45.3	44.1	- 2.7	44.4	- 2.0
74	48.4	45.9	- 5.2	44.5	- 8.1
76	48.3	45.8	- 5.2	44.4	- 8.1
78	44.1	44.0	- 0.2	43.7	- 0.9
80	45.7	44.4	- 2.8	38.5	-15.8
82	44.0	42.0	- 4.6	39.1	-11.1
84	43.5	39.8	- 8.5	38.2	-12.2
86	44.3	39.1	-11.7	37.7	-14.9
88	45.3	42.3	- 6.6	37.2	-21.8
90	46.1	45.6	- 1.1	38.5	-16.5
92	45.9	43.9	- 4.4	39.9	-13.1
94	46.9	47.5	+ 1.3	42.7	- 9.0
96	42.4	44.4	+ 4.7	37.7	-11.1
98	46.8	44.2	- 5.6	41.4	-11.5
100	41.5	44.0	+ 6.0	42.5	+ 2.4
102	42.5	46.2	+ 8.7	46.3	+ 8.9
104	41.6	50.9	+22.4	43.2	+ 3.9

Table 6

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption - Absolute
(g/rat/day) + % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
1	22.2	18.7	-15.8	22.9	+ 3.2
2	23.1	22.7	- 1.7	23.0	- 0.4
4	25.5	23.2	- 9.0	25.3	- 0.8
6	27.1	20.9	-22.9	22.6	-16.6
8	26.4	24.9	- 5.7	26.3	- 0.4
10	24.5	24.0	- 2.0	25.4	+ 3.7
12	24.1	23.1	- 4.2	23.5	- 2.5
14	25.5	24.6	- 3.5	25.4	- 0.4
16	24.1	23.5	- 2.5	24.1	+ 0.0
18	24.1	22.9	- 5.0	23.8	- 1.2
20	24.7	24.4	- 1.2	25.1	+ 1.6
22	24.3	23.7	- 2.5	24.6	+ 1.2
24	24.8	24.1	- 2.8	24.4	- 1.6
26	24.5	23.4	- 4.5	24.2	- 1.2
28	24.3	23.4	- 3.7	24.3	+ 0.0
30	24.9	24.2	- 2.8	24.4	- 2.0
32	24.9	23.9	- 4.0	24.9	+ 0.0
34	24.3	23.8	- 2.1	24.5	+ 0.8
36	22.7	21.9	- 3.5	22.8	+ 0.4
38	24.4	24.1	- 1.2	24.7	+ 1.2
40	24.0	23.5	- 2.1	24.8	+ 3.3
42	24.1	23.8	- 1.2	24.8	+ 2.9
44	24.1	24.0	- 0.4	24.7	+ 2.5
46	24.3	23.5	- 3.3	24.3	+ 0.0
48	24.4	24.2	- 0.8	24.1	- 1.2
50	24.6	24.5	- 0.4	24.7	+ 0.4
52	23.3	23.4	+ 0.4	22.9	- 1.7

Table 6

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption - Absolute
(g/rat/day) $\pm$ % Difference from Control

MALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	24.2	24.4	+ 0.8	23.3	- 3.7
56	24.2	24.0	- 0.8	24.5	+ 1.2
58	24.1	23.9	- 0.8	24.5	+ 1.7
60	23.8	24.0	+ 0.8	24.5	+ 2.9
62	24.2	22.0	- 9.1	24.3	+ 0.4
64	20.6	24.0	+16.5	22.7	+10.2
66	23.6	24.4	+ 3.4	24.1	+ 2.1
68	21.6	22.1	+ 2.3	22.3	+ 3.2
70	21.6	22.9	+ 6.0	22.0	+ 1.9
72	21.7	22.8	+ 5.1	23.2	+ 6.9
74	22.7	22.8	+ 0.4	24.2	+ 6.6
76	24.8	23.7	- 4.4	24.5	- 1.2
78	24.5	24.0	- 2.0	23.1	- 5.7
80	23.2	24.1	+ 3.9	24.6	+ 6.0
82	24.1	22.4	- 7.1	25.1	+ 4.2
84	23.8	23.8	+ 0.0	22.7	- 4.6
86	23.7	23.8	+ 0.4	23.5	- 0.8
88	23.6	20.3	-14.0	21.6	- 8.5
90	24.1	22.7	- 5.8	23.0	- 4.6
92	24.1	23.2	- 3.7	22.9	- 5.0
94	26.1	25.4	- 2.7	24.3	- 6.9
96	25.1	24.9	- 0.8	24.5	- 2.4
98	25.2	24.4	- 3.2	24.7	- 2.0
100	24.6	23.8	- 3.3	24.6	+ 0.0
102	23.3	24.1	+ 3.4	24.7	+ 6.0
104	21.7	23.2	+ 6.9	24.4	+12.4

Table 7

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption - Absolute
(g/rat/day) ± % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
1	13.5	13.5	+ 0.0	13.3	- 1.5
2	17.0	17.0	+ 0.0	17.1	+ 0.6
4	20.4	17.5	-14.2	18.0	-11.8
6	19.3	19.2	- 0.5	19.5	+ 1.0
8	19.0	19.1	+ 0.5	18.6	- 2.1
10	19.5	19.1	- 2.1	19.2	- 1.5
12	19.6	19.3	- 1.5	19.2	- 2.0
14	18.6	17.8	- 4.3	18.4	- 1.1
16	16.7	16.1	- 3.6	16.8	+ 0.6
18	19.7	18.8	- 4.6	19.3	- 2.0
20	19.8	18.9	- 4.6	19.9	+ 0.5
22	18.7	19.2	+ 2.7	19.6	+ 4.8
24	19.3	18.7	- 3.1	19.5	+ 1.0
26	18.7	18.3	- 2.1	18.4	- 1.6
28	20.6	19.3	- 6.3	19.3	- 6.3
30	20.2	19.4	- 4.0	20.0	- 1.0
32	20.2	19.3	- 4.5	19.2	- 5.0
34	18.5	18.1	- 2.2	18.2	- 1.6
36	20.2	19.4	- 4.0	20.4	+ 1.0
38	20.4	19.1	- 6.4	19.7	- 3.4
40	21.2	18.9	-10.9	18.5	-12.7
42	20.1	20.0	- 0.5	19.9	- 1.0
44	20.8	19.7	- 5.3	20.6	- 1.0
46	18.7	19.6	+ 4.8	20.3	+ 8.6
48	19.3	19.7	+ 2.1	20.5	+ 6.2
50	20.5	18.0	-12.2	20.0	- 2.4
52	19.6	19.6	+ 0.0	19.5	- 0.5

Table 7

Two Year Oral (Diet) Toxicity-Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Mean Food Consumption - Absolute
(g/rat/day) ± % Difference from Control

FEMALES

Study Week	Control Mean Wt.	300 ppm Mean Wt.	% Diff.	30 ppm Mean Wt.	% Diff.
54	19.9	19.4	- 2.5	19.5	- 2.0
56	21.6	20.4	- 5.6	19.8	- 8.3
58	19.5	20.3	+ 4.1	19.8	+ 1.5
60	21.0	21.0	<u>±</u> 0.0	20.5	- 2.4
62	20.1	20.1	<u>±</u> 0.0	19.5	- 3.0
64	20.6	20.0	- 2.9	19.4	- 5.8
66	17.4	17.2	- 1.2	17.7	+ 1.7
68	19.2	17.9	- 6.8	17.7	- 7.8
70	19.9	18.5	- 7.0	18.2	- 8.5
72	19.7	19.1	- 3.1	19.9	+ 1.0
74	21.6	20.4	- 5.6	20.6	- 4.6
76	22.0	20.5	- 6.8	20.8	- 5.5
78	20.5	19.9	- 2.9	20.6	+ 0.5
80	21.7	20.3	- 6.5	18.3	-15.7
82	21.3	19.4	- 8.9	19.0	-10.8
84	21.1	18.2	-13.7	18.2	-13.7
86	21.8	17.9	-17.9	18.1	-17.0
88	22.6	19.3	-14.6	18.0	-20.4
90	23.1	20.6	-10.8	18.7	-19.1
92	23.5	20.0	-14.9	19.4	-17.5
94	23.7	21.4	- 9.7	21.0	-11.4
96	21.5	20.6	- 4.2	19.0	-11.6
98	23.4	20.7	-11.5	20.9	-10.7
100	20.8	20.4	- 1.9	21.5	+ 3.4
102	21.4	21.4	<u>±</u> 0.0	23.3	+ 8.9
104	20.9	22.9	+ 9.6	21.7	+ 3.8

TABLE 8
Estimated Mean FC-143 (mg/kg Body Weight)
Consumption Per Day

Study Week	<u>300 ppm</u>		<u>30 ppm</u>	
	Male	Female	Male	Female
1	29.6	29.0	3.1	2.9
2	29.0	30.5	2.6	3.1
4	25.2	24.5	2.3	2.5
6	20.3	24.3	1.8	2.5
8	21.2	22.5	1.9	2.2
10	18.9	21.8	1.7	2.2
12	17.5	21.1	1.5	2.1
14	17.9	18.6	1.6	2.0
16	16.6	16.9	1.5	1.8
18	15.8	18.9	1.4	1.9
20	16.4	18.4	1.5	2.0
22	15.6	18.3	1.4	1.9
24	15.6	17.4	1.4	1.8
26	14.8	16.9	1.4	1.7
28	14.5	17.4	1.3	1.8
30	14.6	17.2	1.3	1.8
32	14.2	16.8	1.3	1.7
34	13.9	15.4	1.3	1.6
36	12.8	16.3	1.2	1.7
38	13.8	15.8	1.3	1.6
40	13.2	15.5	1.3	1.5
42	13.2	16.1	1.2	1.6
44	13.1	15.5	1.2	1.6
46	12.8	15.2	1.2	1.6
48	13.0	15.1	1.2	1.5
50	13.0	13.5	1.2	1.5
52	12.3	14.5	1.1	1.4

TABLE 8 (Continued)
Estimated Mean FC-143 (mg/kg Body Weight)
Consumption Per Day

Study Week	<u>300 ppm</u>		<u>30 ppm</u>	
	Male	Female	Male	Female
54	12.7	14.1	1.1	1.4
56	12.4	14.5	1.1	1.4
58	12.2	14.3	1.1	1.4
60	12.2	14.8	1.1	1.4
62	11.1	14.0	1.1	1.3
64	12.1	13.8	1.0	1.3
66	12.2	11.9	1.1	1.2
68	11.0	12.4	1.0	1.2
70	11.3	12.9	1.0	1.2
72	11.2	13.2	1.1	1.3
74	11.4	13.8	1.1	1.3
76	11.7	13.8	1.1	1.3
78	11.9	13.2	1.1	1.3
80	11.8	13.3	1.1	1.2
82	11.0	12.6	1.1	1.2
84	11.6	11.9	1.0	1.2
86	11.6	11.7	1.1	1.1
88	9.9	12.7	1.0	1.1
90	10.9	13.7	1.0	1.2
92	11.2	13.2	1.1	1.2
94	12.1	14.2	1.1	1.3
96	12.0	13.3	1.1	1.1
98	11.7	13.3	1.1	1.2
100	11.4	13.2	1.1	1.3
102	11.5	13.9	1.1	1.4
104	11.4	15.3	1.1	1.3

TABLE 9

140 YEAR ORAL (DIET) TOXICITY-UNCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MORTALITY DATA

DOSE GROUP	INITIAL NO.	WEEK OF STUDY														
		1- 4	5- 8	9- 12	13- 16	17- 20	21- 24	25- 28	29- 32	33- 36	37- 40	41- 44	45- 48	49- 52	53- 56	
		MALES														
CONTROL 0 ppm	50	0	0	0	0	0	0	0	0	1	0	0	0	0	1	
HIGH DOSE 300 ppm	50	0	0	0	0	1	0	1	0	0	0	0	0	0	0	
LOW DOSE 30 ppm	50	0	0	0	0	0	0	0	0	0	1	0	0	0	0	
FEMALES																
CONTROL 0 ppm	50	0	0	0	0	0	0	1	0	0	1	0	0	1	1	
HIGH DOSE 300 ppm	50	0	0	0	0	0	0	0	0	0	0	0	0	1	1	
LOW DOSE 30 ppm	50	0	0	0	0	0	0	0	0	0	0	1	1	1	0	

TABLE 9

140 DAY ORAL (DIET) TOXICITY-UNGENOTOXICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MORTALITY DATA

DOSE GROUP	INITIAL NO.	WEEK OF STUDY																1-104 WEEK TOTALS	
		57-60	61-64	65-68	69-72	73-76	77-80	81-84	85-88	89-92	93-96	97-100	101-104	105-108	109-112	NO.	%		
MALES																			
CONTROL 0 ppm	50	0	1	0	0	1	0	1	4	1	2	1	2	1	1	16	32		
HIGH DOSE 300 ppm	50	0	0	0	2	0	0	0	0	1	0	1	0	0	0	6	12		
LOW DOSE 30 ppm	50	0	0	2	2	0	0	0	1	1	4	1	2	0	0	14	28		
FEMALES																			
CONTROL 0 ppm	50	0	3	0	0	1	3	2	2	1	3	5	1	0	0	25	50		
HIGH DOSE 300 ppm	50	1	1	0	0	1	2	1	3	1	4	2	3	0	0	21	42		
LOW DOSE 30 ppm	50	0	0	0	1	1	0	5	1	1	6	7	1	0	0	26	52		

CHI-SQUARE TESTS FOR DOSE GROUP DIFFERENCES FROM CONTROL

DOSE GROUP	MALES		FEMALES	
	CHI-SQUARE	PROB.	CHI-SQUARE	PROB.
300 ppm	4.72	0.024	0.36	0.555
30 ppm	0.05	0.811	0.00	1.000

* Significant difference from control at the 5% level

Table 10

Two Year Oral (Diet) Toxicity - Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Clinical Observations

	Control		300 ppm		30 ppm	
	M	F	M	F	M	F
Initial number of rats	65	65	65	65	50	50
Survivors at end of study	34	25	44	29	36	24
Mass(es) ^b in various areas (Mass(es) resolved prior to term)	19 (11)	38 (7)	43.8 (13.9)	10 (8)	40 (7)	38.5 (11.5)
Alopecia in various areas	6	14	15.4	9	16	19.2
Swollen throat ^c	13	10	15.4	2	9	8.5
Pale (blanched) eyes and/or appears thin (emaciated)	9	9	13.9	5	8	10.0
Excessive lacrimation	8	12	15.4	9	7	12.3
Ataxia	4	2	4.6	2	15	13.1
Convulsions (clonic)	3	0	2.3	2	0	1.5
Occasional urinary incontinence and/or hematuria	5	4	6.9	1	2	2.3
Raised ulcerated lesion on hind foot pad(s)	7	0	5.4	1	1	1.5
Occasional bloody nares	3	1	3.0	0	6	4.6
					3	4
					5	0
					0	1
					7	41
					(4)	(5)
					7	41
					(4)	(5)
					6	16
					4	8
					9	10
					8	5
					5	9
					4	0
					3	4
					5	0
					0	1

^a (Incidence in males + incidence in females) / total number of animals in the group x 100^b To be detailed in the pathology report^c Indication of Sialodacryoadenitis (SDA) viral infection

Table 10

Two Year Oral (Diet) Toxicity - Oncogenicity Study
of Fluorocarbon FC-143 in Rats

Summary of Clinical Observations

	Control		300 ppm		30 ppm	
	M	F	M	F	M	F
Occasional bloody feces and/or diarrhea	2	0	2	1	1	0
Occasional episode of dyspnea	1	0	1	0	0	0
Listeing of the head	1	0	0	5	1	2
Circular ulcerated area on skin	4	3	1	0	1	0
Swollen (distended) abdomen	0	2	2	0	0	2
Swelling in inguinal area	1	1	0	0	0	0
Swollen leg and/or foot	3	0	2	1	1	0
Swollen ears	0	0	0	1	0	1
Swollen penis	0	-	0	-	1	-
Paresis of hind leg(s)/feet	1	0	1	0	2	0

Table 11

**Two Year Oral (Diet) Toxicity - Oncogenicity Study
of Fluorocarbon FC-143 in Rats**

Summary of Clinical Ophthalmologic Findings

Observations	Eye(s)	Control - 0 ppm		300 ppm		30 ppm	
		M	F	M	F	M	F
Phthisis Bulbi (Atrophy)	Right	0	1	3	3	1	3
	Left	0	1	0	0	0	0
Posterior Subcapsular Cataract(s)	Right	2	0	1	0	0	0
	Left	2	1	1	0	0	0
	Bilateral	1	0	0	0	0	0
Corneal (ocular) Opacity (Diffused; ulcerated; focal with iris staphyloma; with pannus; partially collapsed).	Right	0	2	0	0	2	0
	Left	0	2	0	0	2	0
	Bilateral	0	1	0	0	0	0
Chronic superficial Keratitis	Right	0	1	2	0	0	0
	Bilateral	1	0	2	0	0	0

Note: Blood samples were taken via the retro-orbital venus plexus from almost all of the above animals with ophthalmologic abnormalities.

Table 11

**Two Year Oral (Diet) Toxicity - Oncogenicity Study
of Fluorocarbon FC-143 in Rats**

Summary of Clinical Ophthalmologic Findings

<u>(N) Group</u>	<u>Eye(s)</u>	<u>Description of Abnormality</u>
<u>Males</u>		
(1) Control	Right	Chronic uveitis (secondary to blood sampling)
(1) Control	Right	Diffused lens opacity and chronic iritis with microphthalmos
(1) Control	Bilateral	Posterior lens opacity
(1) Control	Bilateral	Very pale choroidal circulation
(1) High dose	Right	Dacryadenitis
(1) High dose	Bilateral	Chronic uveitis with anterior synechia in right eye
(1) High dose	Bilateral	Diffused lens opacity
(1) High dose	Left	Focal, posterior, capsul lens opacity
<u>Females</u>		
(1) Control	Left	Chronic uveitis with secondary exophthalmia
(1) Control	Right	Dacryadenitis
(1) Low dose	Left	Diffused lens opacity with pannus and microphthalmia

TABLE 12

TWO YEAR ORAL (DIET) TOXICITY-UNCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN ERYTHROCYTE VALUES WITH STANDARD DEVIATIONS

	N	ERYTHROCYTES (CELLS X 10**6)		HEMOGLOBIN (G/DL)		HEMATOCRIT (% PACKED CELLS)		MCV (MICRONS**3)		MCH (PICOGRAMS)		MCHC (%)	
		MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE													
MONTH 3													
0 PPM	15	8.29	0.322	16.4	0.39	45.9	0.96	55	1.9	19.8	0.80	35.6	0.47
300 PPM	15	7.91	0.743	15.5*	0.50	43.3*	1.10	56	4.3	19.7	1.55	35.8	0.45
30 PPM	15	7.97	0.475	16.1	0.67	44.5*	1.92	57	2.5	20.5	0.83	36.2*	0.55
MONTH 6													
0 PPM	15	8.42	0.384	15.1	0.94	44.5	2.70	58	4.3	17.9	1.41	33.9	0.77
300 PPM	15	7.91*	0.350	14.5	1.01	43.1	1.64	56	3.0	18.4	1.34	33.7	1.93
30 PPM	15	7.58*	0.306	14.8	0.83	43.9	2.39	50*	1.9	19.6*	0.79	33.8	1.02
MONTH 12													
0 PPM	14	8.44	0.554	15.9	1.17	46.7	3.69	55	2.2	18.8	0.84	34.0	0.97
300 PPM	15	8.01*	0.473	15.2	0.70	42.7*	1.98	53*	1.7	19.0	0.54	35.7*	0.76
30 PPM	15	8.38	0.354	15.5	0.52	44.5	1.68	53*	1.2	18.5	0.72	34.8*	0.99
MONTH 18													
0 PPM	15	7.48	2.071	15.1	3.12	40.8	9.14	58	6.2	21.0	3.09	37.2	1.53
300 PPM	15	7.55*	0.635	14.8*	1.15	40.6*	9.00	54	2.2	19.6	0.92	36.4	0.69
30 PPM	15	8.62	1.106	15.8	1.52	46.1*	4.41	54	4.6	18.4*	0.93	34.3*	1.40
MONTH 24													
0 PPM	15	7.84	1.083	14.5	1.59	42.3	5.34	54	3.4	18.6	1.27	34.4	0.89
300 PPM	15	7.92	0.670	14.6	1.42	43.3	5.72	55	5.6	18.4	1.10	33.8	1.70
30 PPM	14	7.95	0.869	14.7	1.23	42.5	4.22	54	2.0	18.5	0.91	34.6	0.78

* : P <= .05. TWO TAILED DUNNETT T ON RAW DATA.
: P <= .05. TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 12
TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN LEUKOCYTE VALUES WITH STANDARD DEVIATIONS

		LEUKOCYTES (CELLS X 10**3)		NEUTROPHILS (CELLS X 10**3)		LYMPHOCYTES (CELLS X 10**3)		MONOCYTES (CELLS X 10**3)		EOSINOPHILS (CELLS X 10**3)	
N		MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE											
MONTH 3											
0 PPM	15	12.73	2.074	1.65	0.656	10.72	1.803	0.18	0.196	0.17	0.136
300 PPM	15	14.93	2.801	1.58	0.936	13.08*	2.206	0.10	0.102	0.16	0.178
30 PPM	15	15.22*	3.052	2.14	0.870	12.83*	2.861	0.17	0.173	0.11	0.157
MONTH 6											
0 PPM	15	10.74	2.423	1.43	0.727	8.85	2.416	0.29	0.180	0.17	0.121
300 PPM	15	12.72	2.160	1.99	0.989	10.06	2.316	0.38	0.154	0.20	0.227
30 PPM	15	14.46*	3.223	1.92	1.146	11.81*	2.978	0.33	0.235	0.31	0.362
MONTH 12											
0 PPM	14	7.94	1.572	1.10	0.612	6.35	1.256	0.48	0.216	0.10	0.107
300 PPM	15	8.14	1.789	2.26*	0.656	5.36	1.246	0.39	0.247	0.14	0.105
30 PPM	15	10.38*	1.747	2.21*	1.396	7.56	2.151	0.44	0.233	0.18	0.117
MONTH 18											
0 PPM	15	11.41	7.325	5.06	6.402	5.61	1.504	0.59	0.405	0.16	0.128
300 PPM	15	9.91	1.479	2.78	1.657	6.30	1.070	0.63	0.294	0.20	0.156
30 PPM	15	11.16	5.157	2.55*	3.353	8.20*	2.568	0.30*	0.190	0.11	0.163
MONTH 24											
0 PPM	15	10.79	7.529	3.72	5.666	6.66	2.140	0.34	0.398	0.08	0.083
300 PPM	15	9.09	2.351	2.41	1.488	6.34	1.619	0.26	0.176	0.08	0.109
30 PPM	14	10.44	3.464	3.24	2.032	6.72	2.171	0.39	0.292	0.09	0.106

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
: P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 12

TWO YEAR UNAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	MEMO	HEMAT	MCV	MCH	MCHC	WBC	PNNAB	LYMAB	MONAB	EOSAB
0 PPM	AIR3519	8.24	15.0	46	55.8252	18.2039	32.6087	7.70	1.3090	6.0830	0.2310	0.0770
0 PPM	AIR3524	8.51	14.4	42	49.3537	16.9213	34.2857	8.98	1.2572	7.6330	0.0000	0.0898
0 PPM	AIR3529	8.23	14.6	44	53.4629	17.7400	33.1818	11.70	1.0530	10.4130	0.2340	0.0000
0 PPM	AIR3533	8.30	15.7	45	54.2169	18.9157	34.8889	9.96	1.5936	7.9680	0.0996	0.2988
0 PPM	AIR3537	8.13	15.9	47	57.8106	19.5572	33.8298	9.14	1.6452	7.0378	0.1828	0.2742
0 PPM	AIR3541	8.42	15.9	46	54.6318	18.8436	34.5652	9.83	0.9830	8.3555	0.1966	0.2949
0 PPM	AIR3547	7.40	14.8	44	59.4595	20.0000	33.6364	14.00	1.2600	12.0400	0.4200	0.2400
0 PPM	AIR3550	8.38	15.4	45	53.6993	18.3771	34.2222	7.71	1.6962	5.6263	0.3455	0.0000
0 PPM	AIR3553	8.30	15.6	46	55.4217	18.7952	33.9130	10.90	3.5970	6.6490	0.4160	0.2180
0 PPM	AIR3557	8.95	13.0	37	41.3408	14.9251	35.1351	13.40	1.7420	11.1220	0.2680	0.2680
0 PPM	AIR3559	9.03	16.2	47	52.0487	17.9402	34.4681	8.20	0.5740	7.0520	0.2460	0.3280
0 PPM	AIR3562	8.58	14.8	45	52.4476	17.2494	32.8889	10.70	1.1770	8.8810	0.5350	0.1070
0 PPM	AIR3567	8.69	16.2	47	54.0852	18.6421	34.4681	11.30	0.3390	10.7350	0.0000	0.2260
0 PPM	AIR3573	8.70	15.0	45	51.7241	17.2414	33.3333	11.30	1.5820	9.0400	0.5650	0.1130
0 PPM	AIR3575	8.44	13.5	41	48.5782	15.9953	32.9268	16.30	1.6300	14.1810	0.4490	0.0000
300 PPM	AIR3583	8.16	14.8	43	52.6461	18.1373	34.4186	13.40	1.0720	10.7200	0.1340	0.1340
300 PPM	AIR3584	7.93	14.5	42	52.9634	18.2850	34.5238	11.70	1.1700	10.0620	0.4680	0.0000
300 PPM	AIR3596	7.63	11.7	43	56.3565	15.3342	27.2093	12.70	1.6510	10.5410	0.5080	0.0000
300 PPM	AIR3598	7.71	15.1	43	55.7717	19.5450	35.1163	9.74	3.6038	5.8440	0.2922	0.0074
300 PPM	AIR3600	8.27	15.6	44	53.2044	18.8634	35.6545	15.30	1.9890	13.1580	0.1530	0.0000
300 PPM	AIR3604	7.79	13.8	41	52.6316	17.7150	33.6585	12.80	1.1520	10.7520	0.3840	0.5120
300 PPM	AIR3608	8.08	14.8	43	53.2178	18.3168	34.4186	10.60	3.2860	6.7840	0.4240	0.1060
300 PPM	AIR3609	8.00	15.7	46	57.5000	19.6250	34.1304	12.60	2.0160	10.2060	0.1260	0.2520
300 PPM	AIR3613	8.03	15.0	44	54.7945	18.6800	34.0909	13.80	4.0020	8.4180	0.5520	0.8280
300 PPM	AIR3617	7.01	15.1	45	64.1948	21.5407	33.5556	10.50	1.9950	8.0850	0.2100	0.2100
300 PPM	AIR3628	8.32	14.4	44	52.8846	17.3077	32.7273	12.70	0.8890	11.1760	0.3810	0.2540
300 PPM	AIR3629	8.07	14.2	43	51.2838	17.5960	33.0253	18.70	2.6180	15.3340	0.5610	0.1870
300 PPM	AIR3631	8.03	14.8	43	53.5492	18.4309	34.4186	11.50	0.9200	10.0050	0.4600	0.1150
300 PPM	AIR3633	7.42	13.3	39	52.5606	17.9245	34.1026	12.60	2.0160	9.7020	0.5040	0.3780
300 PPM	AIR3642	8.20	15.2	44	53.6585	18.5366	34.5455	12.10	1.4520	10.1640	0.4840	0.0000
30 PPM	AIR3646	7.48	14.7	44	58.8235	19.6524	33.4091	14.80	1.6280	12.2840	0.7400	0.1480
30 PPM	AIR3650	7.79	14.8	45	57.7864	18.9947	32.8889	15.30	0.4590	12.5460	0.6120	0.1530
30 PPM	AIR3656	7.71	15.7	45	58.3658	20.3632	34.8889	16.90	4.2250	11.9990	0.1690	0.5070
30 PPM	AIR3658	7.60	15.3	42	55.2632	20.1316	36.4286	9.05	3.1675	5.3395	0.1810	0.3620
30 PPM	AIR3660	7.58	14.2	42	55.4090	18.7335	33.8095	14.10	2.9610	10.7160	0.4230	0.0000
30 PPM	AIR3664	7.51	14.8	41	57.2570	19.7071	34.4186	13.40	2.5460	10.3180	0.1340	0.4020
30 PPM	AIR3665	6.95	15.2	45	58.8235	19.8693	33.7778	14.00	2.2400	11.2000	0.5600	0.1120
30 PPM	AIR3679	7.65	15.8	46	57.8616	19.8742	34.3478	14.00	2.2400	11.2000	0.5600	0.1120
30 PPM	AIR3680	7.31	14.0	41	56.0876	19.1518	34.1461	20.50	1.6400	17.0150	0.4100	1.4350
30 PPM	AIR3682	7.99	14.5	45	56.3204	18.1477	32.2222	14.00	1.8200	11.6200	0.2600	0.2800
30 PPM	AIR3687	7.95	16.7	50	62.4931	21.0083	33.4000	19.00	3.2300	15.5800	0.1900	0.0000
30 PPM	AIR3689	7.05	14.1	42	59.5745	20.0000	31.5714	9.11	0.0911	8.7456	0.0000	0.3644
30 PPM	AIR3691	7.72	15.2	45	58.2402	19.6841	31.7778	17.50	1.0500	12.0520	0.1310	0.1310
30 PPM	AIR3694	7.44	13.6	42	56.4516	18.2746	32.3810	15.00	1.2000	15.7500	0.5250	0.1750
										13.2000	0.0000	0.6000

TABLE 12

TWO YEAR OVAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL HEMOGAM VALUES

MONTH=12												
DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3516	8.33	15.6	48	57.6230	18.7275	32.5000	7.9	1.817	5.293	0.632	0.158
0 PPM	A1R3517	8.07	15.7	45	55.7621	19.4548	34.8889	5.2	0.624	4.420	0.156	0.000
0 PPM	A1R3520	8.49	15.7	45	53.0035	18.4923	34.8889	6.8	0.816	5.440	0.476	0.068
0 PPM	A1R3522	8.47	16.4	47	55.4900	19.3625	34.8936	9.2	0.736	7.728	0.460	0.276
0 PPM	A1R3527	8.84	15.7	46	52.0362	17.7602	34.1304	7.4	0.814	6.068	0.518	0.000
0 PPM	A1R3535	8.47	15.6	45	53.1287	18.4179	34.6667	9.1	2.002	6.097	0.819	0.182
0 PPM	A1R3543	8.97	16.4	48	53.5117	18.2832	34.1667	6.9	0.828	5.796	0.276	0.000
0 PPM	A1R3546	9.47	18.1	55	58.0781	19.1130	32.9091	8.2	0.328	7.298	0.574	0.082
0 PPM	A1R3550	9.12	16.4	51	55.9211	17.4825	32.1569	5.7	0.399	5.073	0.228	0.000
0 PPM	A1R3551	8.48	15.8	47	55.4245	18.6321	33.6170	9.2	1.564	7.268	0.184	0.184
0 PPM	A1R3554	.	.	.	.	.	.	.	.	.	.	.
0 PPM	A1R3568	7.88	15.8	46	58.3756	20.0508	34.3478	8.0	1.520	6.160	0.240	0.080
0 PPM	A1R3570	8.29	16.4	47	56.6948	19.7824	34.8936	7.0	1.260	5.600	0.070	0.070
0 PPM	A1R3575	7.27	12.5	38	52.2696	17.1939	32.8947	9.9	0.495	8.811	0.594	0.000
0 PPM	A1R3580	8.04	15.9	46	57.2139	19.7761	34.5652	10.7	2.140	7.918	0.428	0.321
300 PPM	A1R3584	7.78	15.0	42	53.9846	19.2802	35.7143	7.6	2.660	4.332	0.380	0.228
300 PPM	A1R3588	8.06	15.6	44	54.5906	19.3548	35.4545	5.6	1.232	4.088	0.224	0.056
300 PPM	A1R3589	8.15	14.9	41	50.3067	18.2822	36.3415	6.8	1.836	4.148	0.612	0.204
300 PPM	A1R3592	6.60	13.4	38	57.5758	20.3030	35.2632	6.9	1.932	4.347	0.414	0.207
300 PPM	A1R3598	7.68	14.8	41	53.3854	19.2708	36.0476	8.1	2.511	5.184	0.324	0.081
300 PPM	A1R3604	8.04	14.7	44	54.7264	18.2836	33.4091	8.5	2.380	5.610	0.510	0.000
300 PPM	A1R3613	8.07	15.5	43	53.2838	19.2069	36.0465	9.7	2.522	6.402	0.485	0.291
300 PPM	A1R3617	8.83	16.6	47	53.2276	18.7945	35.3191	4.7	1.175	3.431	0.000	0.094
300 PPM	A1R3620	7.89	14.9	42	53.2319	18.4847	35.4762	8.2	2.214	5.412	0.492	0.082
300 PPM	A1R3622	8.16	15.6	43	52.6961	19.1176	36.2791	9.3	3.069	5.115	1.023	0.093
300 PPM	A1R3627	8.01	15.7	44	51.6605	19.0652	36.9048	9.1	2.639	6.097	0.182	0.182
300 PPM	A1R3638	8.12	15.3	43	54.9313	19.6005	35.6818	9.3	3.162	5.487	0.279	0.372
300 PPM	A1R3642	8.30	15.7	44	53.0120	18.9157	35.5814	6.7	1.206	5.293	0.134	0.134
300 PPM	A1R3643	8.38	15.3	43	51.3126	18.2574	35.5814	10.3	2.369	7.622	0.206	0.103
30 PPM	C1R3649	8.57	16.2	46	53.6756	18.9032	35.5217	11.3	2.938	7.797	0.565	0.000
30 PPM	C1R3650	8.69	15.7	47	54.0452	18.0647	33.4043	11.5	2.185	8.510	0.575	0.230
30 PPM	C1R3652	8.29	14.8	43	51.8697	17.5824	34.4186	7.7	2.233	4.466	0.693	0.304
30 PPM	C1R3663	8.87	15.6	47	52.9876	17.5874	33.1915	9.0	2.160	6.390	0.360	0.090
30 PPM	C1R3668	8.19	15.7	45	54.9451	19.1647	34.8889	8.6	3.354	4.730	0.344	0.080
30 PPM	C1R3670	8.05	15.3	43	53.4161	19.0062	35.5814	8.6	4.692	4.730	0.344	0.172
30 PPM	C1R3672	8.00	14.9	42	52.5000	18.6250	35.4762	10.2	4.364	5.100	0.102	0.306
30 PPM	C1R3676	9.02	16.1	47	51.7052	17.7118	34.2553	12.4	1.364	10.416	0.372	0.248
30 PPM	C1R3679	8.59	16.2	45	52.3865	18.4541	36.0000	13.9	4.170	8.896	0.834	0.000
30 PPM	C1R3680	7.97	14.6	42	52.6976	19.3187	34.7619	12.2	1.586	9.882	0.488	0.244
30 PPM	C1R3681	7.89	15.3	42	53.2314	19.3916	36.4286	10.2	4.590	5.202	0.204	0.204
30 PPM	C1R3683	8.10	16.1	45	55.5556	19.8765	36.4286	11.9	0.238	11.067	0.357	0.238
30 PPM	C1R3685	8.76	15.3	46	52.5114	17.4658	33.2609	10.5	0.840	9.450	0.210	0.000
30 PPM	C1R3691	8.33	15.6	45	54.0216	18.7275	34.6667	9.3	1.488	7.347	0.372	0.093
30 PPM	C1R3694	8.41	15.1	43	51.1296	17.9548	35.1163	10.4	2.184	7.176	0.936	0.104
30 PPM								9.9	0.891	8.316	0.297	0.396

TABLE 12

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUORACARBON FC-143 IN MALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	HEMO	HEPAT	MCV	MCH	MCHC	WBC	PMNAB	LYNAB	MONAB	EOSAB
0 PPM	AIR3519	8.42	15.3	44	52.2565	18.1710	34.7727	10.0	4.400	4.600	1.000	0.000
0 PPM	AIR3521	2.48	7.2	18	72.5806	29.0323	40.0000	35.4	26.196	7.080	1.770	0.354
0 PPM	AIR3528	8.92	16.5	44	49.3274	18.4978	37.5000	4.7	4.176	4.176	0.261	0.087
0 PPM	AIR3531	8.43	16.9	46	54.5670	20.0474	36.7391	9.1	1.729	6.734	0.546	0.091
0 PPM	AIR3538	8.23	15.9	45	54.6780	19.3196	35.3333	6.1	1.769	3.904	0.244	0.183
0 PPM	AIR3539	8.14	16.4	43	52.8256	20.1474	38.1395	7.3	3.139	3.577	0.438	0.146
0 PPM	AIR3542	8.79	16.8	47	53.4699	19.1126	35.7447	7.8	2.418	4.836	0.468	0.079
0 PPM	AIR3552	8.17	16.8	44	53.8556	20.2630	38.1818	9.9	2.574	6.336	0.594	0.396
0 PPM	AIR3553	8.32	16.9	45	54.0665	20.3125	37.5556	6.7	2.211	3.953	0.402	0.134
0 PPM	AIR3555	7.99	15.8	43	53.8173	19.7747	36.7442	8.7	1.218	6.960	0.435	0.087
0 PPM	AIR3561	9.06	17.6	48	52.9801	19.4260	36.6667	9.7	3.977	4.850	0.445	0.368
0 PPM	AIR3565	4.75	12.3	31	65.2632	25.8947	39.6774	10.5	4.725	4.725	0.945	0.105
0 PPM	AIR3567	8.25	16.4	46	55.7576	24.8748	35.6522	12.1	3.872	8.107	0.121	0.000
0 PPM	AIR3574	3.59	8.9	23	64.0664	19.7411	38.6957	19.4	12.028	6.790	0.388	0.194
0 PPM	AIR3577	8.64	16.7	45	52.0433	19.3287	37.1111	9.7	1.455	7.464	0.679	0.097
300 PPM	BIR3583	6.04	11.8	33	54.6358	19.5364	35.7576	9.6	1.440	7.584	0.480	0.096
300 PPM	BIR3593	6.88	13.8	39	56.6860	20.0541	35.3446	6.7	2.680	4.020	0.000	0.000
300 PPM	BIR3596	7.84	15.6	43	54.8469	19.8940	36.2791	9.0	2.070	6.300	0.000	0.180
300 PPM	BIR3600	7.28	13.9	38	52.1978	19.0434	36.5784	9.6	1.440	7.488	0.384	0.288
300 PPM	BIR3601	7.05	14.6	40	56.7376	20.7092	36.5000	9.8	2.352	6.664	0.490	0.294
300 PPM	BIR3605	7.82	16.0	44	56.2660	20.4604	36.3636	9.3	1.209	7.533	0.465	0.093
300 PPM	BIR3608	7.71	14.2	39	50.5837	18.4176	36.4103	11.4	5.700	4.788	0.684	0.228
300 PPM	BIR3610	7.11	15.5	41	57.6651	21.4003	37.8049	9.5	1.805	6.935	0.760	0.000
300 PPM	BIR3612	7.59	14.7	40	52.7004	19.3676	36.7500	13.6	7.208	4.896	0.952	0.544
300 PPM	BIR3615	8.03	15.6	42	52.3034	19.4271	37.1429	9.2	2.116	5.980	0.828	0.276
300 PPM	BIR3624	8.16	14.9	42	51.4706	18.2594	35.4762	10.5	3.360	5.985	1.155	0.000
300 PPM	BIR3632	8.55	16.3	45	52.6316	19.4152	36.8889	11.2	3.584	6.496	0.784	0.336
300 PPM	BIR3641	7.48	14.6	39	52.1390	19.1176	36.6667	9.3	2.046	5.859	1.023	0.372
300 PPM	BIR3644	8.31	15.5	44	52.9483	18.6522	35.2273	10.0	2.700	6.700	0.500	0.100
300 PPM	BIR3645	7.36	14.6	40	54.3478	19.4370	36.5000	9.9	1.980	7.227	0.495	0.198
30 PPM	CIR3647	6.20	11.7	35	56.4516	18.8710	33.4286	21.9	11.826	9.198	0.657	0.219
30 PPM	CIR3651	8.70	16.3	47	54.0230	18.7356	34.6804	10.5	1.260	8.715	0.420	0.105
30 PPM	CIR3654	8.19	15.6	45	54.9451	19.0476	34.6667	9.5	0.570	8.740	0.095	0.035
30 PPM	CIR3658	8.98	15.9	47	52.3385	17.7060	33.8294	6.5	1.560	4.680	0.130	0.130
30 PPM	CIR3662	11.48	19.1	53	46.1672	16.6376	36.0377	21.5	7.955	12.900	0.645	0.000
30 PPM	CIR3663	9.21	16.1	47	51.0315	17.4810	34.2553	9.3	1.953	6.975	0.372	0.000
30 PPM	CIR3664	9.26	16.5	48	51.8359	17.8146	34.3750	8.7	0.609	7.830	0.261	0.000
30 PPM	CIR3667	7.95	16.5	48	67.9245	20.7547	30.5556	7.6	0.608	6.916	0.076	0.000
30 PPM	CIR3668	8.79	16.2	47	53.4694	18.4300	34.4681	6.7	0.402	5.963	0.335	0.000
30 PPM	CIR3676	8.90	16.2	46	51.6854	18.2022	35.2174	14.1	5.474	9.660	0.322	0.644
30 PPM	CIR3679	8.90	16.5	46	51.6854	18.5393	35.8896	12.5	0.375	11.750	0.250	0.125
30 PPM	CIR3681	7.65	14.8	41	53.5948	19.4464	36.0976	14.5	1.740	12.180	0.435	0.145
30 PPM	CIR3685	8.74	15.9	46	52.6316	18.1422	34.5652	8.6	3.010	5.332	0.258	0.000
30 PPM	CIR3689	8.37	15.2	46	54.4542	18.1401	33.0435	7.1	0.426	6.319	0.284	0.071
30 PPM	CIR3695	8.02	14.7	44	54.4624	18.3242	33.4091	6.4	0.448	5.824	0.000	0.128

TABLE 12

TWO YEAR UHAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYNAB	MONAB	EOSAB
0 PPM	AIR351A	7.44	13.1	37	49.7312	17.6075	35.4054	13.2	3.036	9.108	0.924	0.132
0 PPM	AIR352A	8.08	14.4	43	53.2178	17.8218	33.4884	6.8	1.632	4.760	0.340	0.068
0 PPM	AIR352B	8.70	15.5	45	51.7241	17.8161	34.4444	7.2	0.432	6.624	0.000	0.144
0 PPM	AIR3531	8.33	16.0	47	56.4226	19.2077	34.0426	8.4	1.092	6.972	0.336	0.000
0 PPM	AIR3534	7.96	15.3	46	57.7889	19.2211	33.2684	36.3	22.506	12.342	1.452	0.000
0 PPM	AIR353A	8.54	15.1	45	52.6932	17.6815	33.5556	7.2	1.584	5.256	0.288	0.072
0 PPM	AIR3542	8.86	16.0	46	51.9187	18.0547	34.7826	7.1	0.710	6.248	0.071	0.071
0 PPM	AIR354A	8.09	15.6	46	56.8603	19.2431	33.9130	8.5	1.445	6.885	0.170	0.000
0 PPM	AIR355A	6.08	11.8	34	55.9211	19.4079	34.7059	4.4	0.264	4.136	0.000	0.000
0 PPM	AIR3557	9.47	16.7	50	52.7983	17.6346	33.4000	8.0	1.840	6.000	0.080	0.080
0 PPM	AIR3562	7.74	13.2	37	47.8036	17.0543	35.6757	12.6	5.922	6.300	0.378	0.000
0 PPM	AIR356A	7.68	14.4	42	54.6875	18.7500	34.2457	12.4	4.712	6.820	0.620	0.248
0 PPM	AIR3569	5.38	12.0	33	61.3383	22.3048	36.3636	9.7	0.776	8.924	0.000	0.000
0 PPM	AIR3573	8.52	16.1	47	55.1643	18.8967	34.2553	7.4	1.554	5.328	0.296	0.000
0 PPM	AIR3578	6.70	12.7	37	55.2239	18.4552	34.3243	12.7	8.255	4.191	0.127	0.127
300 PPM	AIR3581	7.94	15.5	46	54.6318	18.4086	33.6957	6.2	0.868	4.960	0.372	0.000
300 PPM	AIR3585	7.94	14.8	43	54.1562	18.6398	34.4186	10.5	2.100	8.085	0.210	0.105
300 PPM	AIR3591	7.98	16.0	44	60.1504	20.0501	33.3333	8.4	3.528	4.620	0.252	0.000
300 PPM	AIR3594	8.17	14.4	43	52.6316	17.6255	33.4884	5.7	0.741	4.845	0.114	0.000
300 PPM	AIR3597	8.03	15.3	44	54.7945	19.0535	34.7727	8.7	2.697	5.655	0.261	0.087
300 PPM	AIR3601	6.21	12.0	35	56.3607	19.3237	34.2497	9.6	4.608	4.416	0.384	0.192
300 PPM	AIR3605	8.02	15.8	53	66.0848	19.7007	29.8113	6.3	1.197	5.040	0.000	0.063
300 PPM	AIR360A	8.21	13.6	39	47.5030	16.5652	34.8718	9.8	1.862	7.742	0.196	0.000
300 PPM	AIR361A	8.04	15.2	43	53.4426	18.9055	35.3488	11.0	1.540	8.910	0.330	0.220
300 PPM	AIR3623	8.58	15.3	45	52.4476	17.8322	34.0000	9.5	1.722	6.232	0.246	0.000
300 PPM	AIR3630	8.59	16.3	52	65.0000	19.5000	30.0000	7.5	1.805	7.410	0.190	0.095
300 PPM	AIR3633	6.51	11.6	33	55.8789	18.4756	33.9583	7.5	1.050	6.300	0.075	0.075
300 PPM	AIR3636	8.15	13.4	38	50.6912	17.8187	35.1515	14.2	4.544	9.514	0.142	0.000
300 PPM	AIR3641	7.92	13.8	40	46.6254	16.4417	35.2632	12.6	5.544	5.922	0.756	0.378
30 PPM	AIR3646	8.35	15.0	45	50.5051	17.4242	34.5000	8.2	2.378	5.494	0.328	0.000
30 PPM	AIR3650	7.90	14.2	41	53.8922	17.4641	33.3333	9.3	5.208	3.813	0.279	0.000
30 PPM	AIR3654	8.96	16.0	47	51.4987	17.4747	34.6341	13.1	3.537	8.908	0.655	0.000
30 PPM	AIR3663	8.34	15.2	44	52.4554	17.4571	34.0426	5.0	1.400	3.450	0.100	0.050
30 PPM	AIR3667	7.34	15.2	43	52.7578	18.2254	34.5455	8.7	2.349	5.829	0.435	0.087
30 PPM	AIR3670	7.21	13.7	39	58.5831	20.7044	35.3488	7.4	1.776	5.254	0.222	0.148
30 PPM	AIR3672	8.87	15.4	46	54.0915	19.0014	35.1282	12.8	4.096	7.808	0.768	0.128
30 PPM	AIR3676	5.93	11.2	31	51.8602	17.3619	33.4783	14.7	7.644	6.468	0.588	0.000
30 PPM	AIR3679	9.14	15.7	46	52.2766	18.4870	36.1290	18.0	6.120	10.800	1.080	0.000
30 PPM	AIR3682	8.37	15.1	44	50.3282	17.1772	34.1304	12.5	2.375	9.750	0.125	0.250
30 PPM	AIR3684	7.73	14.7	42	52.5687	18.0406	34.3182	10.2	4.590	5.202	0.306	0.102
30 PPM	AIR3689	8.14	15.2	45	54.3338	19.0168	35.0000	9.5	1.900	7.410	0.190	0.000
30 PPM	AIR3691	6.97	13.4	38	55.2826	18.6732	33.7778	7.4	1.850	4.958	0.370	0.222
30 PPM	AIR3694	8.02	15.3	44	54.5194	19.2253	35.2632	10.4	1.976	7.904	0.208	0.312
					54.8628	19.0773	34.7727	7.2	0.576	6.552	0.072	0.000

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN ERYTHROCYTE VALUES WITH STANDARD DEVIATIONS

FEMALE													

MONTH 3													

0 PPM													
	15	6.91	0.319	15.8	0.48	43.7	1.11	63	2.2	22.9	0.75	36.2	0.44
	15	6.67	0.266	15.4	0.56	42.0*	1.85	63	2.3	23.0	0.63	36.6	0.58
	15	7.26*	0.505	16.0	0.70	43.9	1.75	61*	3.5	22.1*	1.37	36.3	0.49
MONTH 6													

0 PPM													
	15	7.32	0.413	15.0	0.55	42.3	1.84	58	2.2	20.6	0.95	35.4	1.01
	15	7.37	0.327	15.4	0.64	42.5	1.60	58	2.2	21.0	0.93	36.3	0.83
	15	6.92*	0.475	13.7*	0.95	38.7*	3.20	56	4.9	19.9	1.93	35.5	1.65
MONTH 12													

0 PPM													
	15	7.60	0.300	15.6	0.40	44.3	1.39	58	2.1	20.6	0.71	35.3	0.48
	15	6.92*	1.193	14.6*	1.74	40.5*	4.73	60	8.1	21.5	3.19	36.0	1.20
	15	7.29	1.212	15.1	1.70	42.5	4.76	59	6.8	21.0	2.47	35.5	0.64
MONTH 18													

0 PPM													
	15	7.37	0.668	15.4	1.43	42.9	4.13	58	1.7	21.0	0.68	36.0	0.85
	15	7.24	0.809	14.9	1.33	41.9	3.86	58	2.6	20.7	0.96	35.6	0.52
	15	7.01	0.763	14.8	1.32	41.5	3.85	59	3.0	21.2	1.09	35.8	0.65
MONTH 24													

0 PPM													
	15	7.06	1.129	14.8	1.80	42.3	5.40	60	3.5	21.2	1.45	35.1	0.87
	15	7.14	0.744	14.4	1.26	40.4	2.66	58*	2.1	20.3*	0.74	35.8	0.99
	15	7.06	1.097	14.6	2.03	41.7	5.97	59	2.5	20.7	0.91	35.0	0.81

* : P <= .05; TWO TAILED DUNNETT T ON RAW DATA.
: P <= .05; TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
 MEAN LEUKOCYTE VALUES WITH STANDARD DEVIATIONS

LEUKOCYTES (CELLS X 10³) NEUTROPHILS (CELLS X 10³) LYMPHOCYTES (CELLS X 10³) MONOCYTES (CELLS X 10³) EOSINOPHILS (CELLS X 10³)
 N MEAN S.DEV. MEAN S.DEV. MEAN S.DEV. MEAN S.DEV. MEAN S.DEV.

FEMALE
-----MONTH 3

0 PPM
 300 PPM
 30 PPM

15 18.98 2.698 2.57 1.406 15.73 23970 0.37 0.217 0.31 0.262
 15 18.51 3.778 3.24 1.728 14.78 23834 0.28 0.312 0.22 0.258
 15 18.06 3.470 3.33 1.347 14.23 32105 0.22 0.250 0.30 0.258

MONTH 6

0 PPM
 300 PPM
 30 PPM

15 7.52 2.559 1.44 1.586 5.87 23160 0.18 0.096 0.08 0.067
 15 8.60 1.953 1.55 0.705 6.73 13784 0.20 0.122 0.11 0.102
 15 7.18 1.723 1.76 1.023 5.06 13607 0.20 0.142 0.15 0.119

MONTH 12

0 PPM
 300 PPM
 30 PPM

15 5.73 2.120 1.27 1.562 4.13 13049 0.21 0.108 0.12 0.125
 15 5.72 1.818 1.45 1.281 3.95 13061 0.22 0.165 0.09 0.094
 15 5.83 1.135 1.34 0.679 4.13 03792 0.25 0.098 0.10 0.091

MONTH 18

0 PPM
 300 PPM
 30 PPM

15 5.75 2.230 1.01 1.631 4.48 03973 0.28 0.249 0.82 0.057
 15 6.30 2.368 2.21 1.950 3.62 13305 0.36 0.226 0.10* 0.108
 15 6.83 2.608 2.89* 2.240 3.51* 13061 0.36 0.148 0.07 0.074

MONTH 24

0 PPM
 300 PPM
 30 PPM

15 6.73 4.064 2.87 2.959 3.67 13329 0.11 0.151 0.07 0.074
 15 6.39 1.691 2.15 0.962 4.04 13190 0.10 0.062 0.06 0.057
 15 8.57 3.434 3.44 2.915 4.81 13641 0.24 0.241 0.08 0.094

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL HEMOGHAM VALUES

DOSE	ANIMAL	ERYTH	HEMU	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4576	6.98	15.6	43	61.6046	22.3496	36.2791	17.5	1.925	14.525	0.700	0.350
0 PPM	N1R4578	7.72	16.1	44	56.9948	20.4549	36.5989	20.1	3.417	16.080	0.402	0.201
0 PPM	N1R4582	6.79	15.7	43	63.3284	23.1222	36.5116	17.0	2.040	14.280	0.510	0.170
0 PPM	N1R4583	6.74	15.6	43	63.7982	23.1454	36.2791	19.4	2.134	17.072	0.000	0.194
0 PPM	N1R4584	6.31	14.9	42	66.5610	23.6133	35.4762	20.5	4.715	14.555	0.410	0.820
0 PPM	N1R4592	7.03	16.2	45	64.0114	23.0441	36.0000	17.3	5.882	11.072	0.173	0.173
0 PPM	N1R4610	6.94	15.6	44	63.4006	22.4784	35.4545	15.4	2.156	12.782	0.154	0.308
0 PPM	N1R4612	6.88	15.7	44	63.9535	22.8198	35.6818	21.0	2.310	18.480	0.210	0.000
0 PPM	N1R4613	6.73	15.0	42	62.4071	22.2883	35.7143	16.1	2.898	12.397	0.322	0.483
0 PPM	N1R4619	7.35	16.5	45	61.2245	22.4490	36.6667	21.0	0.630	19.320	0.420	0.630
0 PPM	N1R4621	6.60	15.5	42	63.6364	23.4848	36.9048	24.3	1.944	21.384	0.243	0.729
0 PPM	N1R4626	6.98	16.0	44	63.0372	22.9226	36.3636	21.1	4.009	16.458	0.211	0.422
0 PPM	N1R4627	6.84	16.4	45	65.7895	23.9766	36.4444	19.6	1.176	18.032	0.392	0.000
0 PPM	N1R4633	6.84	16.0	44	64.3275	23.3918	36.3636	20.4	2.040	17.544	0.816	0.000
0 PPM	N1R4640	6.99	16.4	45	64.3777	23.4621	36.4444	14.0	1.260	12.040	0.560	0.140
300 PPM	N1R4645	6.51	15.3	42	64.5161	23.5023	36.4286	12.4	1.860	10.168	0.124	0.248
300 PPM	N1R4654	6.77	16.2	45	66.4697	23.9291	36.0000	16.7	2.171	14.028	0.167	0.334
300 PPM	N1R4660	6.34	14.6	40	63.0915	23.0284	36.5000	19.2	1.728	17.088	0.384	0.000
300 PPM	N1R4664	6.36	14.8	40	62.8931	23.2704	37.0000	18.3	6.771	11.163	0.366	0.000
300 PPM	N1R4668	7.02	15.8	43	61.2536	22.5071	36.7442	18.6	2.046	15.624	0.372	0.558
300 PPM	N1R4669	6.99	15.5	42	60.0858	22.1745	36.9048	15.3	1.224	13.923	0.153	0.000
300 PPM	N1R4672	6.35	14.8	40	62.9921	23.3071	37.0000	17.8	3.204	13.706	0.172	0.178
300 PPM	N1R4673	6.42	14.8	40	62.3053	23.0530	37.0000	28.4	6.532	21.016	0.284	0.852
300 PPM	N1R4674	6.88	16.1	44	63.9535	23.4012	36.5409	16.3	2.282	13.855	0.163	0.000
300 PPM	N1R4679	6.72	14.7	39	58.0357	21.8750	37.6923	18.0	2.340	15.480	0.000	0.180
300 PPM	N1R4680	6.46	15.4	42	61.0465	22.0930	36.6667	23.7	4.977	17.301	1.185	0.237
300 PPM	N1R4693	6.88	15.2	42	62.9471	22.7468	36.1364	18.3	3.660	14.091	0.000	0.549
300 PPM	N1R4698	6.99	15.9	44	63.5838	23.2654	36.5409	21.6	3.456	18.144	0.000	0.000
300 PPM	N1R4700	6.92	16.1	44	66.9782	23.5202	35.1163	16.9	2.028	14.703	0.169	0.000
300 PPM	N1R4701	6.42	15.1	43	66.9782	23.5202	37.1111	15.3	4.347	11.431	0.161	0.161
30 PPM	N1R4708	7.79	16.7	45	57.7664	21.4377	36.0465	20.4	2.448	12.546	0.153	0.459
30 PPM	N1R4710	6.95	15.5	43	61.8705	22.3022	36.5116	15.5	2.170	12.710	0.155	0.465
30 PPM	N1R4721	6.83	15.7	43	62.9575	22.9868	36.5818	22.0	4.400	16.940	0.000	0.660
30 PPM	N1R4730	6.71	15.7	44	65.5738	23.3979	36.4444	16.6	1.992	14.110	0.166	0.332
30 PPM	N1R4731	7.44	16.4	45	60.4839	22.0430	36.1364	18.1	3.077	14.842	0.181	0.000
30 PPM	N1R4734	6.41	16.0	43	67.0827	24.9610	37.2093	13.2	3.077	11.616	0.000	0.264
30 PPM	N1R4735	7.65	15.8	43	56.2092	20.6536	36.7442	26.8	3.752	21.976	0.804	0.268
30 PPM	N1R4736	7.88	17.1	47	59.6447	21.7005	36.8889	19.4	3.880	15.326	0.000	0.194
30 PPM	N1R4737	7.12	16.6	45	63.2022	23.3166	36.8889	20.6	3.708	16.068	0.618	0.206
30 PPM	N1R4738	7.40	15.8	44	59.4599	21.3514	35.9091	16.0	4.960	10.720	0.160	0.160
30 PPM	N1R4744	7.14	15.8	44	61.6246	22.1249	35.9091	18.0	5.220	11.700	0.360	0.720
30 PPM	N1R4749	7.05	14.9	41	58.1560	21.1348	36.3415	17.3	3.287	14.013	0.000	0.000
30 PPM	N1R4752	8.30	17.0	47	56.6265	20.4819	36.1702	17.9	5.728	10.919	0.537	0.716
30 PPM	N1R4753	7.39	14.6	41	55.4804	19.7564	35.6098	13.8	1.932	11.868	0.000	0.000

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL HEMOGRAM VALUES

MONTH#6												
DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONAB	EOSAB
0 PPM	N1R4582	7.32	15.0	43	58.7432	20.4918	34.8837	8.59	0.6872	7.5592	0.2577	0.0859
0 PPM	N1R4584	7.85	15.8	46	58.5987	20.1274	34.3478	6.45	0.5160	5.8695	0.0000	0.0645
0 PPM	N1R4586	6.81	13.8	39	57.2687	20.2643	35.3846	6.24	1.9344	4.0560	0.0624	0.1872
0 PPM	N1R4590	7.19	15.3	43	59.8053	21.2796	35.5814	7.95	1.1925	6.5190	0.2385	0.0000
0 PPM	N1R4598	7.31	15.1	42	57.4555	20.6566	35.9524	7.43	0.9659	6.3155	0.0000	0.1486
0 PPM	N1R4603	6.60	14.7	40	60.6061	22.2727	36.7500	7.69	0.4614	7.0748	0.0769	0.0769
0 PPM	N1R4607	7.88	15.8	44	55.8376	20.0508	35.9091	6.43	0.5787	5.7227	0.1286	0.0000
0 PPM	N1R4616	8.03	14.6	44	54.7945	18.1818	33.1818	6.95	0.4170	6.3940	0.1390	0.0000
0 PPM	N1R4619	7.70	15.3	44	57.1429	19.8701	34.7727	5.98	0.5382	5.3222	0.0598	0.0598
0 PPM	N1R4621	6.80	14.3	42	61.7647	21.0294	34.0476	6.61	1.2559	5.2219	0.0661	0.0661
0 PPM	N1R4622	7.23	14.4	41	56.7082	19.9170	35.1220	4.59	0.4131	4.0392	0.0918	0.0459
0 PPM	N1R4629	7.32	15.1	42	57.3770	20.6284	35.9524	14.90	4.7680	9.8340	0.1490	0.1490
0 PPM	N1R4631	7.36	14.8	40	54.3478	20.1087	37.0000	11.00	1.2100	9.2400	0.3300	0.2200
0 PPM	N1R4632	7.28	15.1	42	57.6423	20.7418	35.9524	4.76	1.0948	3.5224	0.0952	0.0476
0 PPM	N1R4639	7.05	15.4	43	60.9929	21.8440	35.8140	7.28	5.6056	1.3832	0.2184	0.0728
300 PPM	O1R4650	6.91	15.1	42	60.7815	21.8524	35.9524	7.98	2.1546	5.7456	0.0000	0.0798
300 PPM	O1R4653	7.47	16.6	43	57.5636	22.2222	38.6047	6.80	2.3120	4.1480	0.1360	0.2040
300 PPM	O1R4657	7.32	15.1	41	56.0109	20.6284	36.8293	12.70	2.9210	9.2710	0.3810	0.1270
300 PPM	O1R4660	7.49	15.3	43	57.4099	20.4272	35.5814	11.30	1.4690	9.6050	0.2260	0.0000
300 PPM	O1R4663	7.72	15.0	42	54.4041	19.4301	35.7143	7.86	1.8078	5.8950	0.1572	0.0000
300 PPM	O1R4670	7.38	16.0	43	58.2656	21.6802	37.2093	8.77	1.4032	7.1914	0.1754	0.0000
300 PPM	O1R4673	6.71	14.6	40	59.6125	21.7586	36.5000	9.73	1.5568	7.4921	0.3892	0.2919
300 PPM	O1R4681	6.87	14.8	41	59.6798	21.5424	36.0976	9.50	0.8550	8.2650	0.2850	0.0950
300 PPM	O1R4682	7.44	15.8	44	59.1394	21.2366	35.9091	9.18	0.5508	8.3538	0.1836	0.0918
300 PPM	O1R4692	7.75	15.0	42	54.1935	19.3548	35.7143	7.29	2.3328	4.7385	0.2187	0.0000
300 PPM	O1R4693	7.65	15.0	42	54.9020	19.6078	35.7143	9.41	2.1643	6.7752	0.1882	0.2823
300 PPM	O1R4694	7.64	16.5	45	58.9005	21.5469	36.6667	9.99	1.0989	8.3916	0.3996	0.0999
300 PPM	O1R4698	7.07	14.9	41	57.9415	21.0750	36.3415	6.55	1.0480	5.2400	0.0000	0.2620
300 PPM	O1R4699	7.56	15.5	43	56.8783	20.5026	36.0465	6.39	0.8946	5.3037	0.1278	0.0639
300 PPM	O1R4700	7.53	16.2	46	61.0890	21.5134	35.2174	5.55	0.7215	4.5510	0.1665	0.1110
30 PPM	P1R4710	6.66	13.8	39	58.5586	20.7207	35.3846	10.80	1.6200	8.9640	0.2160	0.0000
30 PPM	P1R4711	6.85	12.2	35	51.0949	17.8102	34.8571	5.65	1.8080	3.5030	0.1695	0.1695
30 PPM	P1R4717	6.98	13.2	37	53.0086	18.9112	35.6757	8.13	3.4146	4.2276	0.2439	0.2439
30 PPM	P1R4719	7.03	14.8	43	61.1664	21.0526	34.4186	6.99	2.0271	4.6134	0.2097	0.1398
30 PPM	P1R4729	7.00	12.4	35	50.0000	17.7143	35.4286	5.16	1.3932	3.1476	0.4644	0.1548
30 PPM	P1R4731	6.78	12.8	36	53.0973	18.8791	35.5556	7.23	1.3014	5.3502	0.5061	0.0723
30 PPM	P1R4732	6.35	15.0	41	64.5669	23.6220	36.5854	9.28	1.0208	7.7024	0.0928	0.4640
30 PPM	P1R4733	7.30	14.7	42	57.5342	20.1370	35.0000	5.49	0.6568	4.7214	0.0549	0.0549
30 PPM	P1R4737	5.95	14.1	35	58.8235	23.6475	40.2857	6.83	1.2977	4.9859	0.2732	0.2732
30 PPM	P1R4740	7.02	12.6	35	49.8575	17.9487	36.0000	4.06	0.5278	3.3292	0.0812	0.1218
30 PPM	P1R4743	6.80	13.0	36	52.9412	19.1176	36.1111	8.81	4.3169	4.0526	0.4405	0.0000
30 PPM	P1R4745	7.18	14.8	43	59.8886	20.6128	34.4146	6.64	2.0584	4.3160	0.1992	0.0664
30 PPM	P1R4746	7.12	14.1	40	56.1798	19.8034	35.2500	7.07	0.7777	5.8681	0.2121	0.2121
30 PPM	P1R4749	8.13	14.3	41	50.4305	17.5842	34.8780	8.14	1.7094	6.2678	0.0814	0.0814
30 PPM	P1R4750	6.71	13.6	42	62.5931	20.2683	32.3810	7.48	2.3936	4.7872	0.1496	0.1496

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCNC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4578	7.55	15.7	44	58.2781	20.7947	35.6818	3.5	0.840	2.450	0.140	0.070
0 PPM	N1R4582	7.57	15.7	44	58.1242	20.7398	35.6818	6.9	0.621	5.865	0.207	0.207
0 PPM	N1R4585	7.84	15.9	45	57.3980	20.2806	35.3333	4.1	0.451	3.280	0.287	0.082
0 PPM	N1R4588	7.23	15.2	43	54.4764	21.0235	35.3488	3.9	0.390	3.276	0.156	0.078
0 PPM	N1R4589	7.94	15.1	43	54.1562	19.0176	35.1163	6.8	3.264	3.468	0.068	0.000
0 PPM	N1R4590	7.44	15.8	44	54.1398	21.2366	35.9091	5.4	0.648	4.482	0.162	0.108
0 PPM	N1R4601	7.17	15.2	43	59.9721	21.1494	35.3488	4.6	0.598	3.542	0.276	0.184
0 PPM	N1R4608	8.26	16.3	46	55.6901	19.7337	35.4340	7.1	0.710	5.822	0.355	0.213
0 PPM	N1R4610	7.32	15.1	42	57.3770	20.6284	35.9524	3.8	0.152	3.534	0.038	0.076
0 PPM	N1R4620	7.80	15.3	43	55.1282	19.6154	35.5814	5.2	0.156	4.888	0.156	0.000
0 PPM	N1R4629	7.84	16.0	47	54.4490	20.4082	34.0420	12.1	6.171	5.324	0.121	0.484
0 PPM	N1R4630	7.44	15.6	44	59.1398	20.9677	35.4545	6.5	1.365	4.810	0.325	0.000
0 PPM	N1R4631	7.68	15.8	45	58.5938	20.5729	35.1111	5.9	1.239	4.189	0.413	0.059
0 PPM	N1R4632	7.55	16.3	46	60.9272	21.5894	35.4340	4.9	1.666	2.891	0.294	0.049
0 PPM	N1R4640	7.30	15.6	45	61.6438	21.3699	34.6667	5.2	0.728	4.056	0.208	0.208
300 PPM	N1R4642	7.22	14.2	40	55.4017	14.6676	35.5000	7.0	0.560	6.230	0.140	0.070
300 PPM	N1R4652	7.31	14.8	40	54.7196	20.2462	37.0000	5.1	1.530	3.264	0.153	0.153
300 PPM	N1R4655	6.96	15.3	41	58.9080	21.9828	37.3171	5.3	1.378	3.657	0.159	0.106
300 PPM	N1R4656	7.81	15.4	44	56.3380	19.7183	35.0000	8.1	2.187	5.508	0.162	0.243
300 PPM	N1R4664	7.11	15.0	42	59.0717	21.0970	35.7143	8.1	2.349	4.941	0.486	0.324
300 PPM	N1R4666	6.90	13.9	39	56.5217	20.1449	35.6410	9.2	5.428	3.036	0.644	0.092
300 PPM	N1R4669	7.16	15.3	43	60.0559	21.3687	35.5814	4.4	0.660	3.608	0.088	0.044
300 PPM	N1R4671	6.95	15.0	40	57.5540	21.5827	37.5000	4.9	1.421	3.087	0.294	0.098
300 PPM	N1R4674	7.92	16.0	44	55.5556	20.2020	36.3636	4.8	0.960	3.552	0.240	0.048
300 PPM	N1R4676	6.76	14.8	40	54.1716	21.8935	37.0000	2.4	0.024	2.352	0.024	0.000
300 PPM	N1R4689	6.54	12.4	38	58.1040	18.9602	32.6316	7.1	1.562	5.325	0.213	0.000
300 PPM	N1R4692	2.83	9.2	25	88.3392	32.5088	36.8000	4.4	0.440	3.784	0.132	0.044
300 PPM	N1R4699	7.45	15.3	43	57.7181	20.5369	35.5814	4.3	0.688	3.569	0.043	0.000
300 PPM	N1R4704	7.18	16.0	44	61.2813	22.2841	36.3636	4.9	0.833	3.626	0.294	0.147
300 PPM	N1R4709	7.67	15.7	44	57.3664	20.4694	35.6818	5.8	1.740	3.770	0.290	0.000
300 PPM	N1R4711	8.03	15.5	44	54.7946	19.3026	35.2273	4.9	1.666	2.744	0.343	0.147
300 PPM	N1R4714	7.69	15.3	43	55.9168	19.8960	35.5814	6.0	1.380	4.380	0.120	0.120
300 PPM	N1R4715	7.74	15.6	45	58.1395	20.1550	34.6667	6.9	2.277	4.416	0.207	0.000
300 PPM	N1R4716	7.18	15.2	44	61.2813	21.1694	34.5455	5.2	0.416	4.524	0.104	0.156
300 PPM	N1R4717	8.56	16.7	48	56.0748	19.5093	34.7917	6.7	2.613	3.618	0.335	0.134
300 PPM	N1R4721	7.74	16.1	46	59.4315	20.8010	35.0000	3.3	0.132	2.937	0.198	0.033
300 PPM	N1R4725	3.15	9.3	27	82.5397	20.5238	35.7692	4.3	0.258	3.913	0.129	0.000
300 PPM	N1R4727	7.45	15.0	42	56.3756	20.1342	35.7143	6.0	1.680	3.540	0.320	0.062
300 PPM	N1R4729	7.89	15.8	45	57.0342	20.0253	35.1111	6.2	1.302	4.464	0.372	0.062
300 PPM	N1R4734	7.13	16.0	44	61.7111	22.4404	36.3636	6.7	1.541	4.623	0.335	0.201
300 PPM	N1R4742	6.97	14.0	39	55.9541	20.0861	35.8974	7.2	1.440	5.400	0.288	0.072
300 PPM	N1R4743	7.46	15.2	43	57.6408	20.3753	35.3488	6.8	1.700	4.760	0.272	0.068
300 PPM	N1R4749	7.27	15.0	41	56.3961	20.6327	36.5854	4.5	1.170	3.060	0.180	0.090
300 PPM	N1R4750	7.52	15.5	43	57.1809	20.6117	36.0465	6.5	1.170	5.005	0.260	0.065
300 PPM	N1R4755	7.57	15.6	43	56.8032	20.6077	36.2791	6.2	1.364	4.588	0.186	0.062

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
						MONTH=18						
0 PPM	N1R4581	6.16	12.3	34	55.1948	19.9675	36.1766	13.2	6.600	5.544	1.056	0.000
0 PPM	N1R4583	7.52	15.6	44	58.5106	20.7447	35.4545	5.2	0.208	4.836	0.156	0.000
0 PPM	N1R4586	7.08	14.5	41	57.9096	20.4802	35.3659	4.7	0.517	3.854	0.188	0.141
0 PPM	N1R4592	8.04	16.8	46	57.2139	20.8955	36.5217	6.5	1.690	4.680	0.130	0.000
0 PPM	N1R4595	7.52	15.3	44	58.5106	20.3457	34.7727	4.3	1.075	2.967	0.129	0.129
0 PPM	N1R4598	7.44	16.4	45	60.4839	22.0430	36.4444	5.0	0.200	4.650	0.150	0.000
0 PPM	N1R4599	7.80	16.1	44	56.4104	20.6410	36.5909	4.8	0.384	4.128	0.144	0.144
0 PPM	N1R4602	7.72	16.6	45	58.2902	21.5026	36.4889	6.5	0.195	6.305	0.065	0.000
0 PPM	N1R4604	7.97	16.4	47	58.9711	20.5772	34.8936	4.9	0.441	4.410	0.049	0.000
0 PPM	N1R4606	5.85	12.4	34	58.1197	21.1966	36.4706	5.1	1.632	3.060	0.408	0.000
0 PPM	N1R4609	7.07	15.5	41	57.9915	21.4236	37.8049	4.9	0.931	3.675	0.294	0.000
0 PPM	N1R4611	6.95	14.7	41	58.9928	21.1511	35.8537	5.3	0.371	4.664	0.265	0.000
0 PPM	N1R4612	8.27	16.5	47	56.8319	19.9516	35.1064	7.0	0.840	5.950	0.210	0.000
0 PPM	N1R4627	7.36	16.2	46	62.5000	22.0109	35.2174	5.0	0.050	4.900	0.050	0.000
0 PPM	N1R4638	7.76	16.4	45	57.9897	21.1340	36.4444	3.8	0.076	3.610	0.114	0.000
300 PPM	N1R4645	7.49	15.4	44	58.7450	20.5607	35.0000	4.5	2.475	1.445	0.405	0.135
300 PPM	N1R4647	7.57	15.2	43	56.8032	20.0793	35.3488	4.5	1.215	2.880	0.315	0.090
300 PPM	N1R4648	5.54	12.0	34	61.3718	21.6606	35.2941	12.6	8.568	3.024	0.882	0.126
300 PPM	N1R4651	7.60	15.3	43	56.5789	20.1316	35.5814	5.3	1.378	3.498	0.371	0.053
300 PPM	N1R4663	7.84	15.7	44	56.1224	20.0255	35.6818	3.7	1.184	2.109	0.370	0.037
300 PPM	N1R4667	5.84	12.2	34	58.2192	20.8904	35.8824	10.1	3.131	6.161	0.808	0.000
300 PPM	N1R4675	8.83	16.8	48	54.3601	19.0260	35.0000	7.8	2.652	4.680	0.390	0.078
300 PPM	N1R4679	7.31	14.4	41	56.0876	19.6990	35.1220	6.3	2.016	4.095	0.189	0.000
300 PPM	N1R4684	6.57	14.3	40	60.8824	21.7656	35.7500	6.3	3.213	2.709	0.063	0.000
300 PPM	N1R4688	7.45	15.7	45	60.4027	21.0738	34.8889	7.1	1.917	4.615	0.426	0.142
300 PPM	N1R4690	7.21	15.3	42	58.2524	21.2205	36.4286	4.2	2.142	1.806	0.168	0.084
300 PPM	N1R4693	7.97	15.4	43	53.9523	19.3225	35.8140	6.1	0.610	4.941	0.183	0.366
300 PPM	N1R4694	7.30	16.4	46	63.0137	22.4658	35.6522	5.4	0.864	4.158	0.324	0.054
300 PPM	N1R4696	6.95	14.4	40	57.5540	20.7194	36.0000	5.3	1.219	3.445	0.318	0.000
30 PPM	N1R4707	6.67	13.5	38	56.9715	20.2399	36.6667	5.3	0.636	4.664	0.000	0.000
30 PPM	N1R4709	6.05	14.4	40	66.1157	23.8017	36.0000	3.7	3.080	4.158	0.462	0.000
30 PPM	N1R4714	7.46	15.3	43	57.6408	20.5094	35.5814	4.9	0.490	4.116	0.245	0.049
30 PPM	N1R4718	6.65	14.7	39	58.6466	22.1053	37.6923	4.9	0.490	3.332	0.343	0.049
30 PPM	N1R4720	6.46	14.1	39	60.3715	21.8266	36.1538	10.3	5.459	4.120	0.618	0.103
30 PPM	N1R4722	5.47	11.8	33	60.3291	21.5722	35.7576	9.2	5.428	3.312	0.460	0.000
30 PPM	N1R4725	7.54	16.8	44	63.6605	22.2412	35.0000	3.9	1.014	2.535	0.195	0.156
30 PPM	N1R4729	7.31	15.2	42	57.4555	20.7434	36.1905	5.1	2.601	2.193	0.306	0.000
30 PPM	N1R4732	6.42	13.7	38	59.1909	21.3396	36.0526	10.8	4.212	6.156	0.216	0.216
30 PPM	N1R4733	8.04	15.7	44	54.4554	19.4307	35.6418	4.1	1.312	2.542	0.205	0.041
30 PPM	N1R4737	6.91	15.2	43	62.2287	21.9971	35.3488	5.8	1.624	3.654	0.348	0.174
30 PPM	N1R4748	7.32	14.7	42	57.3770	20.0420	35.0000	6.6	3.366	2.970	0.198	0.066
30 PPM	N1R4749	7.84	16.2	45	57.1066	20.5584	36.0000	8.2	2.870	4.592	0.574	0.164
30 PPM	N1R4752	8.17	16.9	47	57.5275	20.6454	35.9574	5.9	1.416	4.012	0.413	0.059
30 PPM	N1R4754	6.81	14.5	41	60.2050	21.2422	35.3659	11.4	8.550	2.280	0.570	0.000

TABLE 13

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL HEMOGRAM VALUES

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONAB	EOSAB
0 PPM	N1R45A3	7.48	15.3	42	56.1497	20.4545	36.4286	18.7	12.529	5.984	0.187	0.000
0 PPM	N1R45B6	7.22	14.3	42	58.1717	19.8061	34.0476	4.1	1.148	2.952	0.000	0.000
0 PPM	N1R4591	7.91	15.7	45	56.8900	19.4483	34.8889	4.9	0.735	4.018	0.000	0.147
0 PPM	N1R4595	7.97	15.9	46	57.7164	19.9498	34.5652	4.6	2.714	1.702	0.092	0.134
0 PPM	N1R4598	7.43	16.4	47	63.2571	22.0727	34.8936	6.2	2.232	3.844	0.062	0.062
0 PPM	N1R4603	7.07	14.9	44	62.2348	21.0750	33.8636	4.2	1.092	3.066	0.000	0.042
0 PPM	N1R4606	7.78	15.9	46	59.1280	20.4370	34.5652	4.7	1.081	3.525	0.094	0.000
0 PPM	N1R4611	4.21	10.3	29	68.8836	24.4656	35.5172	9.2	3.496	5.428	0.184	0.092
0 PPM	N1R4614	7.34	16.0	44	59.9455	21.7984	36.3636	5.1	1.989	3.060	0.051	0.000
0 PPM	N1R4616	7.24	15.2	43	59.3923	20.9945	35.3488	4.5	2.115	2.340	0.000	0.045
0 PPM	N1R4626	7.31	14.5	42	57.4555	19.8358	34.5238	5.4	2.592	2.646	0.108	0.054
0 PPM	N1R4628	6.21	13.4	34	61.1916	21.5781	35.2632	8.6	3.870	4.386	0.086	0.258
0 PPM	N1R4634	4.86	11.7	32	65.8436	24.0741	36.5625	12.2	5.246	6.222	0.610	0.122
0 PPM	N1R4636	7.90	16.1	47	59.4437	20.3797	34.2553	5.0	1.650	3.250	0.100	0.000
0 PPM	N1R4638	7.99	16.8	47	58.9235	21.0263	35.7447	3.5	0.630	2.695	0.140	0.035
300 PPM	O1R4644	7.07	14.0	41	57.9915	19.8020	34.1463	4.8	1.056	3.600	0.096	0.048
300 PPM	O1R4646	6.84	14.2	41	59.9415	20.7602	34.6341	7.9	2.607	5.293	0.000	0.000
300 PPM	O1R4649	7.12	14.6	42	58.9888	20.2056	34.7619	8.3	3.652	4.399	0.083	0.166
300 PPM	O1R4657	6.55	14.0	37	56.4885	21.3740	37.8378	6.0	1.920	3.840	0.180	0.060
300 PPM	O1R4659	5.06	11.0	30	59.2885	21.7391	36.6667	8.6	3.956	4.386	0.172	0.086
300 PPM	O1R4661	7.42	15.0	42	56.6038	20.2156	35.7143	6.5	1.365	5.070	0.065	0.000
300 PPM	O1R4663	8.35	16.6	45	53.8922	19.8802	36.8889	3.8	1.216	2.508	0.000	0.076
300 PPM	O1R4672	6.80	13.9	40	58.8235	20.4412	34.7500	6.5	2.600	2.990	0.130	0.130
300 PPM	O1R4679	7.14	14.6	40	56.0224	20.4482	36.5000	5.9	3.363	2.419	0.118	0.000
300 PPM	O1R4683	7.67	15.1	42	54.7588	19.6871	35.9524	8.0	2.080	5.760	0.160	0.000
300 PPM	O1R4688	7.24	15.2	42	58.0110	20.9945	36.1905	5.4	1.134	4.212	0.054	0.000
300 PPM	O1R4693	7.66	15.1	42	54.8303	19.7128	35.9524	4.6	1.794	4.222	0.046	0.138
300 PPM	O1R4695	6.82	13.0	36	52.7854	19.0616	36.1111	9.3	2.790	6.231	0.186	0.093
300 PPM	O1R4697	7.80	15.1	43	55.1282	19.3590	35.1163	5.8	1.508	4.118	0.116	0.058
300 PPM	O1R4701	7.62	15.2	43	56.4304	19.7475	35.3488	4.4	1.232	3.124	0.044	0.000
30 PPM	P1R4708	7.26	15.1	44	60.6061	20.7989	34.3182	7.8	3.588	3.900	0.078	0.137
30 PPM	P1R4711	6.89	13.7	38	55.1524	19.8839	36.0526	13.7	7.672	5.343	0.548	0.134
30 PPM	P1R4714	7.11	15.0	42	59.0717	21.0970	35.7143	5.8	1.914	3.828	0.058	0.000
30 PPM	P1R4716	7.34	15.0	45	61.3079	20.4360	33.4333	4.4	1.936	2.288	0.132	0.044
30 PPM	P1R4720	6.91	14.9	43	62.2287	21.5630	34.6512	8.6	3.698	4.472	0.258	0.172
30 PPM	P1R4723	6.36	12.8	37	58.1761	20.1258	34.5946	9.9	2.574	7.128	0.198	0.000
30 PPM	P1R4726	7.64	16.3	46	60.2094	21.3351	35.4348	6.4	0.640	5.696	0.064	0.000
30 PPM	P1R4729	7.53	15.2	44	58.4329	21.1859	34.5455	7.4	2.146	4.884	0.074	0.296
30 PPM	P1R4733	8.81	17.0	49	55.6186	19.2963	34.6939	5.2	2.340	2.704	0.156	0.000
30 PPM	P1R4736	7.97	16.4	47	58.9711	20.2963	34.8936	6.2	1.736	4.340	0.062	0.062
30 PPM	P1R4739	4.01	8.9	25	62.3441	22.1945	35.6000	12.0	2.760	4.400	0.720	0.120
30 PPM	P1R4745	7.45	15.4	45	60.4027	20.6711	34.2222	6.2	0.682	5.332	0.124	0.062
30 PPM	P1R4747	7.05	13.5	39	55.3191	19.1489	34.6154	12.6	5.418	6.426	0.756	0.000
30 PPM	P1R4752	7.82	16.4	45	57.5448	20.4719	36.4444	6.6	2.706	3.762	0.066	0.066
30 PPM	P1R4754	5.76	12.8	36	62.5000	22.2222	35.5556	15.7	11.775	3.611	0.314	0.000

TABLE 14

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN BLOOD CHEMISTRY VALUES WITH STANDARD DEVIATIONS

	N	GLUCOSE (MG/DL)		BLOOD UREA NITROGEN (MG/DL)		ALT (IU/L)		AST (IU/L)	
		MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE -----									
MONTH 3 -----									
0 PPM	15	120.6	13.74	16.3	1.84	21.4	2.67	45.3	7.26
300 PPM	15	129.5*	8.38	19.4*	2.06	21.9#	21.94	58.2	27.23
30 PPM	15	134.6*	8.83	17.1	1.46	24.5#	15.33	59.7	22.47
MONTH 6 -----									
0 PPM	15	119.0	13.29	17.5	1.36	24.1	3.75	49.7	14.98
300 PPM	15	123.7	11.17	20.7*	1.40	54.8#	29.26	87.8#	34.83
30 PPM	15	134.9*	10.33	15.9*	1.44	53.3#	29.34	92.1#	45.60
MONTH 12 -----									
0 PPM	14	154.3	26.17	16.4	2.50	83.5	19.45	79.1	44.61
300 PPM	15	138.7	8.85	17.5	1.73	106.1#	70.00	132.7	76.84
30 PPM	15	131.1#	8.70	16.2	1.15	77.6#	56.59	124.4	94.04
MONTH 18 -----									
0 PPM	15	123.4	26.39	18.1	3.38	84.1	10.68	99.1	68.14
300 PPM	15	139.3	16.14	17.6	1.88	84.3#	55.95	123.3	62.98
30 PPM	15	120.6	27.62	16.5#	6.48	69.7#	33.41	116.4	57.99
MONTH 24 -----									
0 PPM	15	122.5	23.07	16.5	3.16	83.4	0.10	64.9	25.76
300 PPM	15	147.1*	13.26	17.2	5.03	61.8*	20.13	95.7*	29.76
30 PPM	14	121.3	13.72	16.6	6.70	42.5	10.00	68.0	17.64

* : P < .05. TWO TAILED DUNNETT T ON RAW DATA.

: P < .05. TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 14

TWO YEAR UHAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
 MEAN BLOOD CHEMISTRY VALUES (TBILI, ALB, TPROT, ALKPPOS, CPK, QA) WITH STANDARD DEVIATIONS

	N	TOTAL BILIRUBIN (MG/DL)		ALBUMIN (GM/DL)		TOTAL PROTEIN (GM/DL)		ALKALINE PHOSPHATASE (IU/L)		CREATINE PHOSPHOKINASE (IU/L)		CALCIUM (MG/DL)	
		MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV
MALE													
MONTH 3													
0 PPM	15	0.6	0.16	4.4	0.34	6.8	0.34	91.1	26.23	100.7	26.46	11.1	0.68
300 PPM	15	0.8	0.40	5.1*	0.29	6.5	0.31	153.5*	51.86	67.0*	24.24	10.8	0.50
30 PPM	15	0.7	0.09	4.7*	0.37	6.6	0.34	138.7*	53.16	66.5*	12.65	11.0	0.78
MONTH 6													
0 PPM	15	0.8	0.19	4.6	0.20	7.0	0.36	97.1	40.41	89.9	41.32	11.5	0.40
300 PPM	15	0.7	0.22	5.4*	0.31	6.6*	0.28	147.3*	54.85	81.4	26.66	11.1*	0.22
30 PPM	15	0.5*	0.14	5.0*	0.40	6.7*	0.33	146.9*	57.18	58.3*	31.23	10.9*	0.33
MONTH 12													
0 PPM	14	0.7	0.20	3.7	0.20	6.8	0.27	105.8	43.94	79.7	47.61	10.5	0.30
300 PPM	15	0.6	0.12	4.4*	0.34	6.8	0.31	166.5*	59.20	68.3	23.65	10.6	0.24
30 PPM	15	0.8	0.22	3.9	0.26	6.9	0.33	128.3	41.75	67.6	19.45	10.6	0.29
MONTH 18													
0 PPM	15	0.9	0.35	3.2	0.38	7.1	0.61	85.2	53.76	79.9	74.52	11.1	0.93
300 PPM	15	0.7	0.31	3.7*	0.34	6.9	0.42	184.4*	73.37	82.5	45.87	10.8	1.10
30 PPM	15	0.7	0.25	3.2	0.29	7.2	0.45	112.5	52.61	106.5	69.23	10.4	0.80*
MONTH 24													
0 PPM	15	0.4	0.25	2.8	0.23	6.9	0.44	70.1	25.58	111.1	68.04	10.9	0.43
300 PPM	15	0.2*	0.06	3.1*	0.27	6.9	0.50	113.5*	22.84	88.3	37.33	10.8	0.25
30 PPM	14	0.4	0.12	2.8	0.30	6.8	0.39	61.2	26.20	71.1*	20.55	10.5*	0.31

* 1 P < .05. TWO TAILED DUNNETT T ON RAW DATA.

1 P < .05. TWO TAILED DUNNETT T ON RANKED DATA.

- N NUMBER IS 14 FOR THIS MEAN.

**TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES**

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TABLE 14

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

MONTH=6											
DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	AIR3519	133	19	18	39	0.6	4.3	6.4	123	70	10.6
0 PPM	AIR3524	139	17	21	54	0.8	4.4	7.3	109	82	11.6
0 PPM	AIR3529	130	16	20	25	0.6	4.7	6.7	72	51	11.3
0 PPM	AIR3533	124	19	28	41	0.8	4.8	7.5	85	119	11.7
0 PPM	AIR3537	109	16	27	58	1.1	4.9	7.0	110	204	11.6
0 PPM	AIR3541	124	18	19	35	0.7	4.5	7.2	65	58	11.3
0 PPM	AIR3547	115	19	29	28	1.1	4.8	7.5	114	62	12.2
0 PPM	AIR3550	128	15	25	43	0.6	4.7	7.0	213	57	11.6
0 PPM	AIR3553	99	20	29	53	0.7	4.6	7.1	62	57	11.9
0 PPM	AIR3557	109	17	22	74	1.1	4.7	7.3	120	119	11.6
0 PPM	AIR3559	100	17	21	51	0.9	4.5	6.7	50	85	11.4
0 PPM	AIR3562	133	18	28	55	0.6	4.7	6.6	69	79	10.9
0 PPM	AIR3567	124	18	23	49	0.8	4.6	6.8	69	85	11.4
0 PPM	AIR3573	102	17	26	74	1.0	5.0	7.5	118	144	11.7
0 PPM	AIR3575	111	17	25	67	0.7	4.4	6.7	78	77	11.0
300 PPM	BIR3583	119	21	29	57	0.7	5.7	6.4	162	77	11.0
300 PPM	AIR3584	152	23	84	112	1.2	5.1	6.7	178	76	11.2
300 PPM	AIR3596	119	21	21	47	0.9	5.3	6.6	156	80	11.4
300 PPM	AIR3598	121	21	92	122	0.8	6.0	7.2	183	106	11.5
300 PPM	9IR3600	110	22	27	47	1.1	5.1	6.3	97	75	10.9
300 PPM	AIR3604	144	21	60	86	0.5	5.4	7.0	123	46	11.4
300 PPM	AIR3608	117	19	73	80	0.7	5.3	6.3	160	61	11.2
300 PPM	HIR3609	123	21	37	89	1.0	5.5	6.7	127	142	11.1
300 PPM	AIR3613	112	20	85	174	0.6	5.0	6.5	109	55	11.0
300 PPM	AIR3617	122	23	35	73	0.6	5.5	7.0	162	58	11.2
300 PPM	AIR3628	120	21	73	95	0.6	5.8	6.9	172	110	11.3
300 PPM	AIR3629	122	20	37	79	0.6	4.9	6.3	102	63	10.7
300 PPM	AIR3631	117	19	34	70	0.5	5.5	6.6	166	65	10.9
300 PPM	AIR3633	129	20	111	130	0.6	5.2	6.5	211	115	11.0
300 PPM	AIR3642	128	18	24	56	0.6	5.7	6.6	102	92	11.1
30 PPM	CIR3646	146	19	35	64	0.6	5.0	6.5	94	50	11.0
30 PPM	CIR3650	151	16	53	83	0.4	4.9	6.5	163	91	10.6
30 PPM	CIR3656	149	15	131	212	0.5	4.8	6.5	188	64	10.6
30 PPM	CIR3658	137	15	48	65	0.4	4.7	6.4	165	42	10.9
30 PPM	CIR3660	138	15	25	49	0.4	4.9	6.7	79	43	10.6
30 PPM	CIR3664	138	16	81	118	0.4	4.5	6.5	121	28	10.9
30 PPM	CIR3665	133	16	87	148	0.4	4.9	6.8	185	40	11.2
30 PPM	CIR3667	133	17	39	72	0.4	5.0	6.7	172	41	10.8
30 PPM	CIR3679	144	16	39	77	0.6	5.8	7.6	97	157	11.4
30 PPM	CIR3680	130	15	49	77	0.4	5.6	7.1	135	38	11.3
30 PPM	CIR3682	122	16	75	139	0.4	4.4	6.9	209	58	11.0
30 PPM	CIR3687	112	18	30	74	0.9	5.3	7.1	158	63	11.5
30 PPM	CIR3689	128	13	20	39	0.4	5.2	6.6	156	51	10.7
30 PPM	CIR3691	134	15	53	105	0.3	4.4	6.4	134	45	10.4
30 PPM	CIR3694	129	17	28	59	0.5	5.1	6.7	148	63	10.7

TWO YEAR ORAL (WJET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

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TABLE 14

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

DOSE	ANIMAL	GLU	HUN	ALT	AST	TRILL	ALR	TPROT	ALKPHOS	CPK	CA
0 PPM	AIR3519	151	19	41	94	0.7	3.2	6.8	128	37	10.6
0 PPM	AIR3521	125	29	59	317	0.2	2.1	5.5	164	79	10.5
0 PPM	AIR3528	148	19	24	55	0.6	3.2	7.0	57	39	11.9
0 PPM	AIR3531	143	18	42	98	1.0	3.4	7.4	56	34	12.0
0 PPM	AIR3538	129	15	38	93	0.7	3.3	6.8	113	96	10.9
0 PPM	AIR3539	132	16	24	54	0.9	3.7	8.1	82	35	11.8
0 PPM	AIR3542	107	18	30	61	1.1	3.4	7.2	41	49	11.5
0 PPM	AIR3552	117	21	23	54	1.1	3.3	7.4	55	41	12.0
0 PPM	AIR3553	127	17	44	74	0.9	3.4	7.5	65	83	11.9
0 PPM	AIR3555	140	17	35	84	1.1	3.3	7.3	124	108	11.1
0 PPM	AIR3561	135	17	28	61	0.9	3.4	7.6	90	59	10.2
0 PPM	AIR3565	126	15	23	62	0.9	3.3	6.6	87	41	9.0
0 PPM	AIR3567	134	17	34	133	0.9	3.2	7.7	66	77	10.9
0 PPM	AIR3574	91	17	24	79	0.2	2.6	6.7	82	87	10.1
0 PPM	AIR3577	46	17	45	168	1.6	3.4	7.3	68	334	12.4
300 PPM	AIR3583	135	19	31	42	0.4	3.8	5.8	148	59	11.3
300 PPM	AIR3593	124	17	85	109	0.9	3.8	7.5	214	45	10.9
300 PPM	AIR3596	137	19	39	68	1.0	3.4	7.4	113	67	11.5
300 PPM	AIR3600	140	19	92	139	0.4	4.0	6.9	142	54	11.3
300 PPM	AIR3601	138	14	96	132	0.6	3.8	7.0	213	83	11.5
300 PPM	AIR3605	136	20	51	68	0.6	3.9	7.0	172	57	10.3
300 PPM	AIR3608	124	14	124	163	0.4	3.2	6.5	177	64	7.8
300 PPM	AIR3610	150	19	75	117	0.7	3.9	7.0	202	55	11.7
300 PPM	AIR3612	148	19	118	205	0.8	3.4	6.6	168	212	11.7
300 PPM	AIR3615	117	17	63	101	0.8	4.1	7.4	129	104	11.4
300 PPM	AIR3624	118	18	42	95	0.4	2.9	7.0	106	152	9.9
300 PPM	AIR3632	168	19	91	142	1.1	4.0	7.3	233	53	12.0
300 PPM	AIR3641	145	16	47	78	0.9	3.6	6.9	156	52	9.9
300 PPM	AIR3644	173	18	258	295	1.5	3.7	7.0	413	109	9.8
300 PPM	AIR3645	136	16	53	95	0.7	4.0	6.8	180	71	11.1
30 PPM	CIR3647	116	12	40	117	0.3	2.4	7.8	105	73	10.4
30 PPM	CIR3651	142	13	37	60	0.6	3.4	7.0	138	46	9.3
30 PPM	CIR3654	134	16	43	100	0.8	3.2	7.1	92	86	10.7
30 PPM	CIR3658	156	16	71	104	0.6	3.3	6.7	134	71	9.8
30 PPM	CIR3662	31	39	53	161	0.1	2.9	8.3	100	327	12.5
30 PPM	CIR3663	121	18	58	120	0.7	3.1	7.1	69	186	10.8
30 PPM	CIR3664	125	16	97	153	0.8	3.4	6.9	133	71	9.8
30 PPM	CIR3667	134	15	82	156	0.8	3.4	7.2	124	79	10.6
30 PPM	CIR3668	128	15	160	289	0.7	3.5	7.1	186	115	11.0
30 PPM	CIR3676	110	17	34	60	1.1	3.0	7.6	105	80	9.8
30 PPM	CIR3679	123	13	41	89	1.0	3.5	7.5	68	110	10.5
30 PPM	CIR3681	136	12	45	87	0.7	3.2	7.2	82	89	9.8
30 PPM	CIR3685	113	16	34	64	0.8	3.2	6.9	95	108	9.8
30 PPM	CIR3689	126	15	62	95	0.7	3.4	6.7	156	56	10.5
30 PPM	CIR3695	114	14	39	87	0.5	3.4	6.7	101	100	9.6

TABLE 14

TWO YEAR OMAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

MONTH-24											
DOSE	ANIMAL	GLU	RUN	ALT	AST	THLI	ALH	TPROT	ALKPHOS	CPK	CA
0 PPM	AIR3518	130	14	20	52	0.2	2.6	6.6	118	87	10.5
0 PPM	AIR3524	138	23	29	42	0.6	2.7	7.1	74	51	11.5
0 PPM	AIR3528	141	15	28	47	0.2	3.0	6.8	39	63	10.8
0 PPM	AIR3531	109	14	36	60	0.3	3.1	7.1	55	72	11.0
0 PPM	AIR3534	67	20	21	142	0.3	2.7	5.9	61	190	11.1
0 PPM	AIR3538	147	12	38	69	0.2	2.8	6.4	66	69	10.5
0 PPM	AIR3542	96	15	35	50	0.0	3.0	7.0	37	54	11.6
0 PPM	AIR3548	122	15	32	48	0.4	2.9	7.0	97	108	10.9
0 PPM	AIR3554	158	17	43	74	0.2	3.0	6.6	29	73	11.0
0 PPM	AIR3557	117	16	42	66	0.6	3.0	7.3	109	90	11.2
0 PPM	AIR3562	134	17	33	53	0.1	2.4	6.8	68	76	10.1
0 PPM	AIR3564	116	19	27	50	0.5	2.5	6.9	77	187	10.5
0 PPM	AIR3569	143	22	29	74	1.0	2.7	7.4	58	299	10.3
0 PPM	AIR3573	105	14	29	50	0.7	3.1	7.7	86	101	11.3
0 PPM	AIR3578	115	15	53	97	0.4	2.6	7.3	77	146	10.9
300 PPM	AIR3581	120	15	41	57	0.2	3.4	6.6	97	82	10.8
300 PPM	AIR3585	155	17	111	133	0.2	3.2	6.8	122	57	10.5
300 PPM	AIR3591	147	17	88	130	0.3	2.9	7.9	132	79	10.5
300 PPM	AIR3594	159	16	75	109	0.3	3.4	7.1	162	176	10.8
300 PPM	AIR3597	143	15	64	117	0.2	2.9	6.4	74	95	10.6
300 PPM	AIR3601	146	16	47	68	0.2	3.0	6.2	127	85	10.7
300 PPM	AIR3605	157	14	43	59	0.1	3.3	7.4	99	83	10.5
300 PPM	AIR3608	136	14	41	75	0.2	2.8	6.5	108	86	10.7
300 PPM	AIR3611	128	19	41	56	0.3	3.5	6.8	133	57	11.2
300 PPM	AIR3618	169	17	82	152	0.2	3.1	6.9	105	54	10.8
300 PPM	AIR3623	142	14	60	95	0.3	3.6	7.3	107	162	10.9
300 PPM	AIR3630	137	17	61	101	0.3	3.4	7.8	111	114	11.3
300 PPM	AIR3633	163	34	62	110	0.2	2.7	6.7	121	51	11.0
300 PPM	AIR3636	153	13	52	91	0.2	3.0	6.4	75	86	10.6
300 PPM	AIR3641	152	20	59	83	0.3	3.0	6.9	129	57	11.0
30 PPM	AIR3646	144	17	47	70	0.4	3.1	6.6	62	64	11.4
30 PPM	CIR3650	147	14	35	51	0.3	2.8	7.1	100	71	10.4
30 PPM	CIR3654	133	13	64	89	0.3	3.2	6.7	102	74	10.2
30 PPM	CIR3658	123	15	43	66	0.3	3.2	6.8	102	47	10.8
30 PPM	CIR3663	115	14	27	43	0.6	2.6	6.8	47	51	10.5
30 PPM	CIR3667	107	15	45	72	0.4	2.3	6.8	103	76	10.5
30 PPM	CIR3670	110	21	46	105	0.3	2.3	6.4	75	44	10.6
30 PPM	CIR3672	107	10	29	44	0.2	2.6	7.7	20	47	10.1
30 PPM	CIR3676	125	39	33	52	0.6	2.2	6.6	91	77	10.7
30 PPM	CIR3679	122	16	41	54	0.4	2.9	7.1	64	57	10.5
30 PPM	CIR3682	116	18	39	64	0.3	3.0	7.0	104	105	10.7
30 PPM	CIR3684	132	12	60	92	0.4	3.1	6.5	77	86	10.4
30 PPM	CIR3689	126	15	43	64	0.2	2.9	6.3	118	114	10.2
30 PPM	CIR3691	99	15	41	74	0.3	3.0	6.3	65	73	10.4
30 PPM	CIR3694	113	15	45	75	0.4	3.1	7.3	88	60	10.6

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-UNCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
 MEAN BLOOD CHEMISTRY VALUES WITH STANDARD DEVIATIONS

	N	GLUCOSE (MG/DL)		BLOOD UREA NITROGEN (MG/DL)		ALT (IU/L)		AST (IU/L)	
		MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE -----									
MONTH 3 -----									
0 PPM	15	138.9	9.74	19.7	1.62	22.6	4.87	40.0	9.20
300 PPM	15	132.9	10.96	24.5*	3.91	26.2	6.72	51.6	13.42
30 PPM	15	132.1	12.06	16.5	2.07	19.4	3.18	44.9	5.79
MONTH 6 -----									
0 PPM	15	154.8	14.98	21.6	3.22	23.5	17.20	49.7	38.56
300 PPM	15	133.6*	9.61	20.7	2.96	24.3	20.46	59.2	29.11
30 PPM	15	128.6*	13.41	19.1*	2.00	25.7	14.55	59.9	28.60
MONTH 12 -----									
0 PPM	15	134.9	10.51	19.8	2.14	24.1	15.17	68.1	38.77
300 PPM	15	135.3	8.18	21.2	5.21	28.6	21.59	66.2	30.37
30 PPM	15	135.4	10.25	19.9	2.83	27.1	12.94	72.6	36.65
MONTH 18 -----									
0 PPM	15	123.5	15.51	18.1	2.49	28.7	11.60	70.1	24.40
300 PPM	15	120.0	9.34	18.7	3.37	26.4	6.36	63.5	18.97
30 PPM	15	122.2	15.34	20.1	4.02	29.4	14.31	63.5	25.21
MONTH 24 -----									
0 PPM	15	122.2	13.75	17.9	4.10	20.0	10.11	67.8	30.03
300 PPM	15	115.3	18.72	16.2	3.76	23.1	25.27	87.0	35.26
30 PPM	15	114.4	15.23	15.3	3.35	28.6	9.61	63.5	12.95

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.

: P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN BLOOD CHEMISTRY VALUES (TBILI, ALB, TPOT, ALKPPOS, CPK, CA) WITH STANDARD DEVIATIONS

	TOTAL BILIRUBIN (MG/DL)		ALBUMIN (GM/DL)		TOTAL PROTEIN (GM/DL)		ALKALINE PHOSPHATASE (IU/L)		CREATINE PHOSPHOKINASE (IU/L)		CALCIUM (MG/DL)		
	N	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV
FEMALE													
MONTH 3													
0 PPM	15	0.6	0.18	5.3	0.45	7.2	0.41	83.7	32.29	93.9	51.44	11.0	0.55
300 PPM	15	0.5*	0.11	5.0	0.52	6.9*	0.41	89.1	25.36	87.7	37.12	11.1	0.52
30 PPM	15	0.6	0.09	5.0	0.41	7.0	0.32	69.9	25.98	86.7	21.06	10.5*	0.69
MONTH 6													
0 PPM	15	0.6	0.14	5.9	0.65	7.4	0.64	77.8	30.58	56.5	14.79	11.7	0.53
300 PPM	15	0.5	0.09	5.6	0.46	7.4	0.34	82.1	22.06	66.7	21.17	11.7	0.43
30 PPM	15	0.6	0.10	5.5	0.66	7.3	0.57	80.9	25.76	89.2	45.03	11.8	0.45
MONTH 12													
0 PPM	15	0.8	0.38	4.3	0.26	7.3	0.52	76.5	30.01	54.6	20.02	11.2	0.60
300 PPM	15	0.6	0.21	4.2	0.32	7.1	0.46	91.1	42.86	41.3	11.52	11.1	0.33
30 PPM	15	0.8	0.21	4.4	0.26	7.5	0.46	89.4	29.87	78.7	78.42	11.0	0.43
MONTH 18													
0 PPM	15	0.6	0.26	3.9	0.23	7.9	0.57	65.5	32.10	37.3	9.81	11.4	0.53
300 PPM	15	0.6	0.23	3.9	0.28	7.8	0.47	76.1	28.36	35.1	9.64	11.1	0.43
30 PPM	15	0.6	0.24	3.8	0.26	8.3	0.73	39.7*	13.47	27.6	19.18	10.6*	1.01
MONTH 24													
0 PPM	15	0.6	0.31	3.4	0.21	7.6	0.69	68.7	33.39	68.4	32.23	11.5	0.64
300 PPM	15	0.4	0.17	3.4	0.28	7.4	0.56	63.1	19.69	67.7	27.06	11.2	0.46
30 PPM	15	0.5	0.21	3.3	0.38	7.2	0.75	56.7	19.98	71.3	35.73	11.3	0.45

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
: P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

MONTH=3											
DOSE	ANIMAL	GLU	BUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4576	143	22	20	47	0.5	4.8	6.8	120	71	10.1
0 PPM	N1R4578	150	22	18	49	0.8	5.1	7.0	61	95	10.7
0 PPM	N1R4582	129	20	17	55	0.8	5.9	7.8	152	150	11.7
0 PPM	N1R4583	147	18	19	41	0.5	4.9	7.1	61	58	10.6
0 PPM	N1R4584	129	19	29	66	0.5	4.8	7.1	95	234	11.2
0 PPM	N1R4592	134	17	25	62	0.6	5.2	7.0	128	168	11.3
0 PPM	N1R4610	143	21	32	57	0.7	5.9	7.8	68	60	12.2
0 PPM	N1R4612	147	20	19	39	0.5	4.8	6.6	89	58	10.8
0 PPM	N1R4613	129	19	19	41	0.5	4.9	7.0	61	50	10.6
0 PPM	N1R4619	139	18	22	51	1.0	5.3	6.9	65	94	11.2
0 PPM	N1R4621	131	19	23	49	0.5	4.9	7.1	67	80	10.7
0 PPM	N1R4626	163	20	28	44	0.4	5.3	7.1	120	58	10.6
0 PPM	N1R4627	133	18	16	43	0.5	5.7	7.0	40	66	10.9
0 PPM	N1R4633	134	22	25	32	0.8	5.9	8.0	70	90	11.4
0 PPM	N1R4640	133	21	27	40	0.9	5.9	7.6	58	76	11.7
300 PPM	N1R4645	126	28	29	37	0.4	4.7	6.2	51	72	10.1
300 PPM	N1R4654	129	19	35	47	0.5	5.3	7.2	65	63	10.8
300 PPM	N1R4660	119	29	32	45	0.5	3.6	6.2	73	57	10.5
300 PPM	N1R4664	122	26	25	59	0.4	5.1	7.1	125	90	10.9
300 PPM	N1R4668	130	20	32	70	0.6	5.5	7.3	54	136	11.2
300 PPM	N1R4669	138	27	20	39	0.5	5.1	7.0	86	84	10.6
300 PPM	N1R4672	136	19	21	40	0.5	5.3	7.1	118	46	11.3
300 PPM	N1R4673	129	26	31	77	0.3	5.0	6.8	106	123	11.1
300 PPM	N1R4674	124	25	31	72	0.4	5.0	7.1	111	186	11.9
300 PPM	N1R4679	154	23	26	49	0.3	5.0	7.0	82	90	11.5
300 PPM	N1R4680	139	25	15	33	0.4	4.8	6.8	55	56	11.6
300 PPM	N1R4693	145	28	19	49	0.6	5.1	6.8	95	100	10.8
300 PPM	N1R4698	130	31	20	56	0.5	5.0	6.7	124	68	11.8
300 PPM	N1R4700	152	20	21	43	0.7	6.1	7.4	93	57	11.6
300 PPM	N1R4701	120	21	29	58	0.5	4.7	6.1	99	88	11.4
30 PPM	N1R4708	148	20	19	44	0.6	5.3	6.6	75	74	11.8
30 PPM	N1R4710	121	19	19	32	0.5	4.9	7.0	104	65	9.8
30 PPM	N1R4720	135	18	26	50	0.7	5.7	7.5	45	99	9.6
30 PPM	N1R4721	142	18	22	47	0.6	4.9	7.0	97	89	10.7
30 PPM	N1R4730	140	16	18	39	0.6	5.1	7.3	53	63	10.9
30 PPM	N1R4731	145	21	22	40	0.7	4.4	6.7	99	84	10.8
30 PPM	N1R4734	137	18	21	50	0.7	5.5	7.4	61	114	11.5
30 PPM	N1R4735	117	21	14	42	0.6	5.2	7.0	47	109	11.1
30 PPM	N1R4736	106	22	20	53	0.6	5.3	7.1	33	111	11.0
30 PPM	N1R4737	125	16	15	50	0.6	4.6	6.9	33	69	9.8
30 PPM	N1R4738	141	16	17	45	0.6	4.6	6.7	55	83	9.9
30 PPM	N1R4744	118	18	23	46	0.6	5.4	7.3	99	98	10.6
30 PPM	N1R4749	133	21	16	38	0.6	4.9	6.9	58	58	9.8
30 PPM	N1R4752	140	18	20	46	0.8	5.2	7.4	91	121	10.7
30 PPM	N1R4753	133	16	19	51	0.4	4.3	6.4	98	63	9.9

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

MONTHS											
DOSE	ANIMAL	GLU	HUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4582	178	21	21	37	0.9	7.2	7.7	137	71	12.9
0 PPM	N1R4584	172	22	55	114	0.6	5.8	8.9	125	55	11.2
0 PPM	N1R4586	159	23	88	183	0.5	6.5	7.9	85	41	12.2
0 PPM	N1R4590	183	22	26	48	0.6	5.6	7.2	101	69	11.8
0 PPM	N1R4598	141	20	20	48	0.6	5.8	7.2	51	33	11.6
0 PPM	N1R4603	161	22	32	71	0.4	6.1	7.5	39	85	11.6
0 PPM	N1R4607	147	23	35	96	0.5	5.5	7.0	61	49	11.4
0 PPM	N1R4616	150	18	25	56	0.4	5.2	6.9	55	52	11.0
0 PPM	N1R4619	140	18	26	57	0.6	6.0	7.2	57	66	11.8
0 PPM	N1R4621	154	20	26	47	0.7	6.9	8.1	51	73	12.2
0 PPM	N1R4622	160	18	34	79	0.5	5.6	7.2	108	50	11.0
0 PPM	N1R4629	130	20	33	54	0.4	4.9	6.3	98	55	11.4
0 PPM	N1R4631	137	22	25	55	0.4	5.2	6.7	90	32	11.3
0 PPM	N1R4632	154	24	27	30	0.7	6.4	8.0	50	59	12.3
0 PPM	N1R4639	156	31	30	62	0.6	6.4	7.6	59	57	11.8
300 PPM	N1R4650	133	18	76	122	0.6	6.2	7.4	7.4	52	12.3
300 PPM	N1R4653	128	19	30	50	0.6	6.2	7.6	111	63	11.7
300 PPM	N1R4657	123	19	75	115	0.5	5.2	7.5	76	60	11.5
300 PPM	N1R4660	136	25	22	61	0.6	5.1	7.3	78	126	11.4
300 PPM	N1R4663	125	17	16	43	0.4	4.9	7.0	88	84	11.0
300 PPM	N1R4670	151	19	14	30	0.6	6.0	7.9	41	80	12.3
300 PPM	N1R4673	125	24	66	100	0.4	5.7	7.5	97	54	11.9
300 PPM	N1R4681	125	21	34	40	0.5	5.4	7.5	81	51	11.9
300 PPM	N1R4682	118	22	26	44	0.5	5.8	7.7	56	51	12.1
300 PPM	N1R4692	142	22	23	42	0.4	5.1	7.4	57	53	11.6
300 PPM	N1R4693	137	24	23	41	0.6	5.1	7.0	97	40	11.5
300 PPM	N1R4694	144	17	23	34	0.6	5.2	6.8	73	83	11.3
300 PPM	N1R4698	135	26	24	53	0.6	5.6	7.3	100	69	11.4
300 PPM	N1R4699	147	18	27	45	0.5	5.5	7.0	116	58	11.5
300 PPM	N1R4700	135	20	31	64	0.7	6.3	8.0	101	77	12.5
30 PPM	P1R4710	109	19	25	54	0.5	4.6	6.7	110	134	11.6
30 PPM	P1R4711	152	22	41	70	0.6	6.0	8.1	140	52	12.1
30 PPM	P1R4717	144	17	32	33	0.7	6.1	7.8	95	49	11.8
30 PPM	P1R4719	116	20	40	63	0.7	6.0	7.7	78	117	12.1
30 PPM	P1R4729	144	18	59	61	0.7	6.3	8.0	93	103	12.3
30 PPM	P1R4731	140	19	27	42	0.5	4.4	6.3	100	34	11.1
30 PPM	P1R4732	122	20	26	34	0.6	5.7	7.3	68	74	12.3
30 PPM	P1R4733	127	18	22	40	0.7	5.0	6.6	57	78	11.3
30 PPM	P1R4737	140	18	25	40	0.5	5.3	7.4	94	45	11.9
30 PPM	P1R4740	133	21	28	53	0.6	5.4	7.0	94	51	12.0
30 PPM	P1R4743	112	19	27	41	0.5	4.6	7.1	42	133	11.6
30 PPM	P1R4745	133	14	23	75	0.5	4.8	6.7	50	205	10.8
30 PPM	P1R4746	117	21	54	102	0.5	6.1	7.9	81	107	12.3
30 PPM	P1R4749	125	21	35	47	0.8	6.2	7.7	61	60	12.0
30 PPM	P1R4750	115	20	67	140	0.7	5.8	7.6	65	72	11.8

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES

MONTH=12											
DOSE	ANIMAL	GLU	RUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	NIR4578	146	24	27	48	1.2	4.1	7.3	71	62	11.7
0 PPM	NIR4582	124	18	22	42	1.5	4.7	8.6	134	82	12.5
0 PPM	NIR4585	132	24	33	60	0.8	4.5	7.6	84	42	11.5
0 PPM	NIR4588	137	20	23	47	0.5	4.4	7.0	44	56	10.8
0 PPM	NIR4589	132	19	67	183	0.7	4.6	7.7	104	50	11.7
0 PPM	NIR4590	136	19	24	46	0.6	4.5	7.3	84	38	11.3
0 PPM	NIR4601	143	20	40	54	0.6	4.1	7.3	127	41	10.8
0 PPM	NIR4608	131	18	24	51	1.1	4.2	7.2	39	60	11.1
0 PPM	NIR4610	127	21	25	62	1.0	4.1	7.1	72	104	10.7
0 PPM	NIR4620	146	19	31	51	0.6	4.1	7.0	71	55	10.9
0 PPM	NIR4629	136	18	67	119	0.4	3.9	6.7	80	40	10.9
0 PPM	NIR4630	157	22	42	79	0.5	3.8	6.6	54	37	10.5
0 PPM	NIR4631	128	20	41	94	0.5	4.4	7.4	99	29	10.8
0 PPM	NIR4632	113	18	19	33	1.4	4.3	8.2	43	76	12.4
0 PPM	NIR4640	135	17	26	47	0.2	4.4	7.2	42	47	11.1
300 PPM	NIR4642	137	18	24	51	0.5	4.5	7.7	39	31	11.1
300 PPM	NIR4652	124	20	112	163	0.6	4.6	7.8	115	42	11.7
300 PPM	NIR4655	132	24	28	51	0.7	4.6	7.5	137	36	11.5
300 PPM	NIR4656	136	22	32	56	0.6	4.6	7.4	46	41	11.4
300 PPM	NIR4664	127	25	29	54	0.6	4.3	7.0	99	40	11.2
300 PPM	NIR4666	125	15	26	57	0.4	3.7	6.6	44	51	10.7
300 PPM	NIR4669	129	23	23	48	0.6	4.3	7.0	101	37	10.9
300 PPM	NIR4671	139	18	34	59	1.0	4.3	7.1	56	67	11.5
300 PPM	NIR4674	125	22	40	79	0.4	4.0	6.7	155	58	10.7
300 PPM	NIR4676	134	17	41	65	0.9	4.3	7.0	132	40	10.9
300 PPM	NIR4687	132	37	26	52	0.3	3.5	6.6	124	41	10.5
300 PPM	NIR4689	148	22	35	52	0.4	4.2	6.9	96	16	11.1
300 PPM	NIR4692	146	18	32	50	0.6	4.2	7.2	39	44	11.2
300 PPM	NIR4699	149	19	38	53	0.9	4.5	7.8	142	38	11.2
300 PPM	NIR4704	143	18	51	103	0.4	4.1	6.3	41	38	11.0
30 PPM	PIR4711	141	17	38	62	1.2	4.7	8.1	121	52	12.1
30 PPM	PIR4714	121	17	29	57	0.6	4.7	8.3	94	38	11.3
30 PPM	PIR4715	142	19	49	85	0.8	4.1	7.2	86	271	10.9
30 PPM	PIR4716	124	19	36	55	0.6	4.0	6.9	102	35	10.5
30 PPM	PIR4717	134	22	31	51	0.8	4.2	7.7	131	42	10.5
30 PPM	PIR4721	124	19	39	72	1.0	4.7	7.9	122	248	11.1
30 PPM	PIR4725	159	19	76	94	0.4	4.1	6.9	102	42	10.4
30 PPM	PIR4727	149	19	33	44	0.5	4.7	7.7	108	26	11.0
30 PPM	PIR4729	131	14	37	54	0.7	4.4	7.4	85	48	11.2
30 PPM	PIR4734	135	19	36	54	0.7	4.3	7.3	76	39	10.9
30 PPM	PIR4742	135	25	30	55	0.8	4.0	6.9	87	59	10.8
30 PPM	PIR4743	125	21	26	194	1.0	4.5	8.2	46	46	11.5
30 PPM	PIR4749	146	27	42	83	0.4	4.6	7.5	53	45	11.1
30 PPM	PIR4750	130	18	36	74	0.8	4.4	7.5	48	145	11.2
30 PPM	PIR4755	131	19	14	43	0.9	4.4	7.6	104	44	11.2

**TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE MICE
INDIVIDUAL SEMUM CHEMISTRY VALUES**

76.
000463

**TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
INDIVIDUAL SERUM CHEMISTRY VALUES**

77.

000464

TABLE 16

Two Year Oral (Diet) Toxicity-Oncogenicity Study of Fluorocarbon FC-143 in Rats
0281CR0012

Ranges of Urinalysis Values at 3 and 6 Months

Dose Group	Specific Gravity	pH	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
<u>3 Mo. Male</u>							
Control	1.025-1.062	7-9	N-Tr	N-N	N-N	N-4+	N-N
300 PPM	1.030-1.046	7-9	N-1+	N-N	N-N	N-N	N-N
30 PPM	1.018-1.090	7-8	N-Tr	N-N	N-N	N-3+	N-N
<u>3 Mo. Female</u>							
Control	1.011-1.052	7-8	N-1+	N-N	N-N	N-N	N-N
300 PPM	1.015-1.052	7-9	N-N	N-N	N-N	N-N	N-N
30 PPM	1.016-1.056	7-8	N-N	N-N	N-N	N-N	N-N
<u>6 Mo. Male</u>							
Control	1.021-1.066	6-8	N-3+	N-N	N-N	N-3+	N-N
300 PPM	1.022-1.054	7-8	N-Tr	N-N	N-N	N-1+	N-1+
30 PPM	1.018-1.070	6-8	N-Tr	N-N	N-N	N-1+	N-N
<u>6 Mo. Female</u>							
Control	1.028-1.072	6-7	N-3+	N-N	N-N	N-1+	N-1+
300 PPM	1.018-1.046	6-8	N-3+	N-N	N-N	N-2+	N-1+
30 PPM	1.024-1.050	6-8	N-Tr	N-N	N-N	N-Tr	N-1+

Code: N - negative
Tr - trace1+ - slight
2+ - slight to moderate3+ - moderate marked
4+ - marked

TABLE 16

Two Year Oral (Diet) Toxicity-Oncogenicity Study of Fluorocarbon FC-143 in Rats
0281CR0012

Ranges of Urinalysis Values at 12 and 18 Months

Dose Group	Specific Gravity	pH	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
<u>12 Mo. Male</u>							
Control	1.040-1.093	7.0-8.5	N-4+	N-N	N-N	N-3+	N-Tr
300 PPM	1.015-1.054	7.0-8.5	N-3+	N-N	N-N	N-Tr	N-Tr
30 PPM	1.029-1.063	7.5-8.5	N-4+	N-N	N-N	N-3+	N-N
<u>12 Mo. Female</u>							
Control	1.023-1.070	6.5-7.5	N-3+	N-N	N-N	N-N	N-N
300 PPM	1.012-1.059	6.5-9.0	N-3+	N-N	N-N	N-2+	N-N
30 PPM	1.008-1.048	6.5-7.5	N-2+	N-N	N-N	N-2+	N-N
<u>18 Mo. Male</u>							
Control	1.016-1.064	6.5-8.0	N-3+	N-N	N-N	N-2+	N-N
300 PPM	1.024-1.050	7.0-8.5	N-4+	N-N	N-N	N-N	N-N
30 PPM	1.022-1.066	6.5-8.0	N-4+	N-N	N-N	N-3+	N-N
<u>18 Mo. Female</u>							
Control	1.016-1.058	7.0-7.5	N-3+	N-N	N-N	N-Tr	N-N
300 PPM	1.011-1.034	6.5-8.0	N-2+	N-N	N-N	N-Tr	N-N
30 PPM	1.016-1.050	6.0-7.5	N-3+	N-N	N-Tr	N-4+	N-N

Code: N - negative 1+ - slight 3+ - moderate to marked
Tr - trace 2+ - slight to moderate 4+ - marked

TABLE 16

Two Year Oral (Diet) Toxicity-Oncogenicity Study of Fluorocarbon FC-143 in Rats
0281CR0012

Ranges of Urinalysis Values at 24 Months

Dose Group	Specific Gravity	pH	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
<u>24 Mo. Male</u>							
Control	1.018-1.054	6.5-8.5	N-4+	N-N	N-N	N-4+	N-N
300 PPM	1.023-1.043	6.5-8.5	N-4+	N-N	N-N	N-N	N-N
30 PPM	1.018-1.056	6.0-8.0	N-4+	N-N	N-N	N-4+	N-N
<u>24 Mo. Female</u>							
Control	1.012-1.034	7.0-8.5	N-2+	N-N	N-N	N-N	N-N
300 PPM	1.009-1.037	5.0-8.0	N-2+	N-N	N-N	N-N	N-N
30 PPM	1.014-1.030	7.0-8.0	N-1+	N-N	N-N	N-4+	N-N

Code: N - negative 1+ - slight 3+ - moderate to marked
Tr - trace 2+ - slight to moderate 4+ - marked

TABLE 17

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS
ONE YEAR INTERIM

ABSOLUTE ORGAN WEIGHTS (GRAMS)

MALE	ORGAN	0 PPM		300 PPM	
		N = 15		N = 15	
		WT	SD	WT	SD
BODY		625.5+-65.905		580.8+-51.153	
LIVER		19.15+-3.212		21.33+-2.497	
HEART		1.629+-0.157		1.452+-0.053*	
SPLEEN		0.894+-0.144		0.800+-0.109	
KIDNEYS		3.854+-0.507		4.047+-0.419	
ADRENALS		.0679+-0.013		.0553+-0.008*	
TESTES		3.553+-0.419		3.459+-0.325	
BRAIN		2.113+-0.111		2.064+-0.067	
PITUITARY		.0205+-0.006		.0115+-0.004*	

FEMALE	ORGAN	N = 15		N = 15	
		WT	SD	WT	SD
BODY		401.1+-77.172		403.1+-66.702	
LIVER		12.28+-1.904		12.90+-1.781	
HEART		1.117+-0.134		1.086+-0.121	
SPLEEN		0.663+-0.123		0.613+-0.120	
KIDNEYS		2.533+-0.383		2.599+-0.283 A	
ADRENALS		.0761+-0.012		.0796+-0.019	
UTERUS		0.775+-0.247		0.702+-0.221	
BRAIN		1.963+-0.128		1.970+-0.119	
PITUITARY		.0227+-0.006		.0195+-0.007	

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
 A : N = 14.

TABLE 17

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS
ONE YEAR INTERIM

		ORGAN WEIGHT/BODY WEIGHT (%)			
		0 PPM		300 PPM	
MALE		N = 15		N = 15	
ORGAN		%	SD	%	SD
LIVER		3.053+-0.318		3.696+-0.504*	
HEART		0.262+-0.021		0.252+-0.024	
SPLEEN		0.144+-0.025		0.138+-0.018	
KIDNEYS		0.617+-0.057		0.701+-0.090*	
ADRENALS		0.011+-0.002		0.010+-0.001	
TESTES		0.570+-0.057		0.598+-0.064	
BRAIN		0.340+-0.026		0.358+-0.029	
PITUITARY		0.003+-0.001		0.002+-0.001*	
FEMALE					
		N = 15		N = 15	
ORGAN		%	SD	%	SD
LIVER		3.090+-0.293		3.239+-0.423	
HEART		0.284+-0.038		0.274+-0.040	
SPLEEN		0.168+-0.031		0.158+-0.048	
KIDNEYS		0.642+-0.091		0.649+-0.111 A	
ADRENALS		0.020+-0.005		0.020+-0.006	
UTERUS		0.201+-0.077		0.181+-0.074	
BRAIN		0.507+-0.105		0.499+-0.077	
PITUITARY		0.006+-0.002		0.005+-0.002	

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
 A : N = 14.

TABLE 17

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS
ONE YEAR INTERIM

ORGAN WEIGHT/BRAIN WEIGHT (GRAMS)				
		0 PPM	300 PPM	
MALE		N = 15		
ORGAN		RATIO	SD	RATIO SD
LIVER		9.049+-1.321		10.339+-1.187*
HEART		0.772+-0.071		0.705+-0.036*
SPLEEN		0.424+-0.070		0.389+-0.058
KIDNEYS		1.821+-0.192		1.964+-0.227
ADRENALS		0.032+-0.006		0.027+-0.004*
TESTES		1.678+-0.150		1.675+-0.129
PITUITARY		0.010+-0.003		0.005+-0.002*
FEMALE		N = 15		
ORGAN		RATIO	SD	RATIO SD
LIVER		6.273+-1.001		6.550+-0.826
HEART		0.571+-0.073		0.552+-0.065
SPLEEN		0.337+-0.056		0.312+-0.064
KIDNEYS		1.294+-0.197		1.323+-0.123A
ADRENALS		0.039+-0.006		0.041+-0.010
UTERUS		0.397+-0.130		0.356+-0.111
PITUITARY		0.012+-0.004		0.010+-0.003

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
 A : N = 14.

TABLE 17

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
ONE YEAR INTERIM INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS ^a	TESTES	HYPH	PITUITARY ^a
0 PPM	AIR-3516	720	23.88	1.786	1.079	3.970	44	3.727	2.330	9
0 PPM	AIR-3517	651	21.74	1.565	0.874	4.043	66	4.147	2.111	14
0 PPM	AIR-3520	655	20.87	1.719	0.772	4.352	62	3.467	2.204	14
0 PPM	AIR-3522	627	16.18	1.675	0.776	4.241	67	3.744	2.227	20
0 PPM	AIR-3527	634	16.71	1.517	0.658	3.356	57	3.316	2.088	33
0 PPM	AIR-3535	594	18.12	1.654	0.895	3.474	87	3.238	1.453	27
0 PPM	AIR-3543	747	24.96	1.783	0.904	4.365	54	3.704	2.194	16
0 PPM	AIR-3546	656	17.61	2.018	0.905	3.958	77	3.460	2.074	24
0 PPM	AIR-3550	566	15.14	1.476	0.704	3.656	41	3.411	2.150	15
0 PPM	AIR-3551	494	13.96	1.361	0.751	2.657	59	2.581	1.420	24
0 PPM	AIR-3559	627	19.53	1.536	0.672	3.548	78	3.331	2.074	23
0 PPM	AIR-3568	688	22.31	1.629	1.091	4.674	64	3.870	2.207	14
0 PPM	AIR-3570	575	16.55	1.526	0.491	3.525	64	3.503	2.114	25
0 PPM	AIR-3575	551	19.88	1.636	1.113	3.741	67	2.944	1.471	15
0 PPM	AIR-3580	544	19.77	1.556	1.028	4.170	76	3.405	2.071	15
300 PPM	AIR-3584	547	18.56	1.487	0.603	3.845	53	3.226	1.981	6
300 PPM	AIR-3588	564	25.31	1.516	0.593	4.584	63	3.995	2.147	15
300 PPM	AIR-3589	552	24.34	1.506	0.794	3.852	55	3.700	2.076	11
300 PPM	AIR-3592	657	18.67	1.402	0.820	3.654	65	3.839	2.165	20
300 PPM	AIR-3598	565	22.98	1.448	0.742	4.396	61	3.264	2.054	10
300 PPM	AIR-3604	554	21.43	1.503	0.854	4.826	62	3.228	1.947	10
300 PPM	AIR-3613	686	18.07	1.368	0.963	3.593	70	3.376	2.046	4
300 PPM	AIR-3617	552	20.50	1.445	0.875	3.915	44	3.404	2.033	10
300 PPM	AIR-3620	641	22.91	1.499	0.859	4.096	54	3.464	2.104	11
300 PPM	AIR-3622	487	17.88	1.357	0.780	3.442	61	2.700	1.994	16
300 PPM	AIR-3626	603	25.32	1.395	0.813	4.542	47	3.205	2.066	12
300 PPM	AIR-3627	595	20.94	1.481	0.715	3.743	47	3.381	2.124	11
300 PPM	AIR-3638	554	20.30	1.412	0.746	3.793	47	3.822	2.124	6
300 PPM	AIR-3642	543	20.35	1.434	0.887	3.886	44	3.649	2.101	14
300 PPM	AIR-3643	607	22.38	1.489	0.958	4.446	43	3.418	1.938	11

NOTES: Body weights and organ weights in grams.

^a - indicates organ weights in mg.

TABLE 17

TWO YEAR OMAL (DIFT) TOXICITY-INCONGENICITY
STUDY OF FLUOROCARBON PC-143 IN FEMALE RATS
ONE YEAR INTERIM INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS ^a	UTERUS	BRAIN	PITUITARY ^a
0 PPM	NIR-4570	540	15.34	1.390	0.751	3.279	80	0.696	2.044	22
0 PPM	NIR-4582	385	12.26	1.185	0.418	2.405	81	0.870	1.674	27
0 PPM	NIR-4585	353	12.90	1.035	0.626	2.223	56	0.674	1.912	14
0 PPM	NIR-4588	386	11.99	1.117	0.679	2.535	87	0.654	2.073	14
0 PPM	NIR-4589	375	13.14	1.095	0.651	3.106	78	1.032	1.963	24
0 PPM	NIR-4590	373	10.52	1.037	0.571	2.308	78	1.033	1.875	17
0 PPM	NIR-4601	470	13.34	1.164	0.868	3.115	62	0.407	1.928	25
0 PPM	NIR-4608	429	13.00	1.021	0.688	2.356	85	0.963	2.124	14
0 PPM	NIR-4610	345	11.31	0.982	0.681	2.435	87	1.371	1.949	30
0 PPM	NIR-4620	320	11.45	1.176	0.780	2.470	89	0.868	2.135	14
0 PPM	NIR-4629	401	11.33	1.084	0.663	2.176	65	0.523	1.967	14
0 PPM	NIR-4630	466	13.03	1.280	0.725	2.616	80	0.520	2.154	17
0 PPM	NIR-4631	248	7.37	0.830	0.414	1.844	62	0.520	1.883	20
0 PPM	NIR-4632	531	14.70	1.128	0.723	2.620	59	0.890	1.848	40
0 PPM	NIR-4640	395	11.64	1.238	0.731	2.512	92	0.813	1.843	24
300 PPM	OIR-4642	323	10.85	0.920	0.732	2.679	76	1.150	1.945	24
300 PPM	OIR-4652	383	13.12	1.114	0.809	2.972	64	0.766	2.265	25
300 PPM	OIR-4655	372	12.16	1.045	0.603	2.527	71	0.563	1.740	6
300 PPM	OIR-4656	447	13.44	1.160	0.805	3.020	74	0.888	2.011	6
300 PPM	OIR-4664	399	14.26	1.156	0.685	2.384	75	0.557	1.948	21
300 PPM	OIR-4666	339	12.28	1.066	0.618	2.788	106	0.863	1.966	22
300 PPM	OIR-4669	385	12.10	0.952	0.470	2.396	59	0.756	1.856	16
300 PPM	OIR-4671	447	17.67	1.181	0.663	2.852	114	0.835	2.008	17
300 PPM	OIR-4674	355	13.59	0.927	0.594	2.240	64	0.648	2.004	24
300 PPM	OIR-4676	519	14.36	1.206	0.630	2.888 ^b	90	0.704	2.048	30
300 PPM	OIR-4687	329	12.56	1.108	0.837	2.647	88	0.924	2.047	17
300 PPM	OIR-4689	363	11.72	1.312	0.798	2.488	115	0.668	1.837	21
300 PPM	OIR-4692	531	13.54	1.210	0.468	2.488	60	0.355	1.941	22
300 PPM	OIR-4699	395	11.59	0.942	0.561	2.384	70	0.708	1.830	20
300 PPM	OIR-4704	409	10.18	0.943	0.527	2.067	64	0.358	1.648	14

NOTES: Body weights and organ weights in grams.

^a Indicates organ weights in mg.

^b Kidney weights not recorded due to marked hydronephrosis.

TABLE 18

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARRON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS

ABSOLUTE ORGAN WEIGHT (GRAMS)

MALE	ORGAN	0 PPM			300 PPM			30 PPM		
		N = 15			N = 15			N = 15		
		WT	SD		WT	SD		WT	SD	
	BODY	6667+-996761			63256+-91.947			649.2+-104.96		
	LIVER	18.15+-3.074			19.12+-3.037			18.81+-3.427		
	HEART	1.720+-0.225			1.665+-0.295			1.806+-0.313		
	SPLEEN	1.217+-0.339			1.158+-0.310			1.105+-0.206		
	KIDNEYS	4.404+-0.746			4.590+-0.525			5.185+-1.782		
	ADRENALS	.0801+-0.018			.0866+-0.018			.0900+-0.027		
	TESTES	3.478+-0.702			3.626+-0.643			3.696+-0.727		
	BRAIN	2.105+-0.133			2.185+-0.072			2.203+-0.130*		

FEMALE	ORGAN	N = 15			N = 15			N = 15		
		WT	SD		WT	SD		WT	SD	
	BODY	51265+-82.585			45152+-68.116			533.3+-82.486		
	LIVER	15.11+-3.752			14.05+-2.735A			17.06+-3.847		
	HEART	1.306+-0.199			1.310+-0.170			1.489+-0.192		
	SPLEEN	0.797+-0.140			0.698+-0.195			1.153+-0.681*		
	KIDNEYS	3.129+-0.287			3.155+-0.465			3.475+-0.446*		
	ADRENALS	.1030+-0.046A			.1126+-0.039			.1365+-0.044		
	UTERUS	0.814+-0.290			0.819+-0.391			0.858+-0.487		
	BRAIN	2.034+-0.102			2.049+-0.111			2.030+-0.131		

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA;

N : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.

A : N = 14 ANIMALS.

TABLE 18

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS

ORGAN WEIGHT/BODY WEIGHT (%)					
0 PPM			300 PPM		
N = 15			N = 15		
MALE	ORGAN	%	SD	%	SD
	LIVER	2.733+-0.939		3.043+-0.400	2.934+-0.531
	HEART	0.261+-0.037		0.267+-0.054	0.283+-0.055
	SPLEEN	0.187+-0.059		0.184+-0.047	0.174+-0.042
	KIDNEYS	0.686+-0.101		0.736+-0.109	0.821+-0.350
	ADRENALS	0.012+-0.003		0.014+-0.003	0.014+-0.005
	TESTES	0.536+-0.144		0.578+-0.100	0.574+-0.093
	BRAIN	0.322+-0.049		0.353+-0.054	0.347+-0.056
FEMALE					
N = 15			N = 15		
ORGAN	%	SD	ORGAN	%	SD
LIVER	2.941+-0.465		LIVER	3.125+-0.417A	3.196+-0.550
HEART	0.269+-0.036		HEART	0.296+-0.056	0.283+-0.046
SPLEEN	0.158+-0.033		SPLEEN	0.197+-0.046	0.210+-0.078*
KIDNEYS	0.621+-0.080		KIDNEYS	0.709+-0.120*	0.662+-0.102
ADRENALS	0.020+-0.008A		ADRENALS	0.025+-0.010	0.026+-0.007
UTERUS	0.161+-0.055		UTERUS	0.183+-0.076	0.163+-0.092
BRAIN	0.408+-0.077		BRAIN	0.465+-0.079	0.388+-0.056

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA;
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
 A : N = 14 ANIMALS.

TABLE 18

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARRON FC-143 IN RATS
ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS

ORGAN WEIGHT/BRAIN WEIGHT (GRAMS)

MALE	ORGAN	0 PPM		300 PPM		30 PPM	
		RATIO	SD	RATIO	SD	RATIO	SD
		N = 15		N = 15		N = 15	
LIVER		8.648	+1.587	8.756	+1.424	8.544	+1.485
HEART		0.819	+0.103	0.760	+0.119	0.821	+0.141
SPLEEN		0.578	+0.155	0.531	+0.149	0.501	+0.086
KIDNEYS		2.099	+0.977	2.101	+0.232	2.360	+0.827
ADRENALS		0.038	+0.010	0.040	+0.008	0.041	+0.013
TESTES		1.658	+0.336	1.699	+0.287	1.675	+0.297

FEMALE	ORGAN	N = 15		N = 15		N = 15	
		RATIO	SD	RATIO	SD	RATIO	SD
LIVER		7.456	+1.918	6.883	+1.508A	8.460	+2.162
HEART		0.673	+0.100	0.642	+0.097	0.738	+0.117
SPLEEN		0.394	+0.078	0.343	+0.100	0.568	+0.325*
KIDNEYS		1.543	+0.166	1.545	+0.255	1.716	+0.231
ADRENALS		0.050	+0.022A	0.055	+0.019	0.068	+0.023
UTERUS		0.404	+0.156	0.400	+0.173	0.419	+0.226

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA
 # : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
 A : N = 14 ANIMALS.

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TABLE 18

TWO YEAR UMAL (U1ET) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN MALE RATS
TWO YEAR INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS ^a	TESTES	UVAIN
0 PPM	AIR3518	556	15.12	1.623	1.318	3.913	60	4.523	2.154
0 PPM	AIR3524	638	23.45	1.511	1.415	4.845	57	3.919	2.046
0 PPM	AIR3528	812	19.67	1.744	1.111	4.424	87	4.082	2.076
0 PPM	AIR3531	733	17.52	1.871	0.870	3.842	75	3.574	2.127
0 PPM	AIR3533	765	18.07	1.575	0.991	4.128	100	2.946	2.080
0 PPM	AIR3538	788	21.72	2.251	1.893	4.535	94	3.774	2.143
0 PPM	AIR3542	733	17.60	1.556	0.728	4.233	54	1.434	2.200
0 PPM	AIR3548	786	18.44	1.667	1.148	4.670	73	3.526	2.329
0 PPM	AIR3554	517	14.19	1.547	1.135	3.461	88	3.628	1.990
0 PPM	AIR3557	612	17.71	1.746	1.106	4.718	70	4.123	2.252
0 PPM	AIR3562	588	15.14	1.616	1.754	3.988	61	3.475	2.061
0 PPM	AIR3564	576	16.20	1.679	1.396	3.745	93	3.324	2.223
0 PPM	AIR3569	696	21.44	2.172	1.586	6.410	100	3.203	2.046
0 PPM	AIR3573	759	22.41	1.825	0.907	5.011	113	3.561	1.861
0 PPM	AIR3578	521	13.52	1.538	0.900	3.641	77	3.015	1.450
0 PPM	81R3581	734	18.42	1.786	1.227	4.472	92	4.177	2.240
0 PPM	81R3585	656	21.42	1.465	1.447	4.641	84	3.944	2.074
300 PPM	81R3591	440	14.04	1.427	0.662	3.831	62	2.631	2.091
300 PPM	81R3594	774	23.83	1.486	1.237	5.013	76	3.967	2.210
300 PPM	81R3597	634	14.99	1.582	0.992	4.032	97	4.056	2.134
300 PPM	81R3601	643	21.09	2.530	1.023	5.680	89	3.943	2.272
300 PPM	81R3605	626	20.04	1.523	0.995	4.160	92	2.867	2.141
300 PPM	81R3608	606	18.66	1.345	1.650	4.787	84	3.254	2.095
300 PPM	81R3611	641	18.83	1.642	1.320	4.271	107	3.777	2.282
300 PPM	81R3618	801	18.91	1.574	0.790	4.342	77	3.844	2.123
300 PPM	81R3623	622	20.26	1.803	1.217	4.057	91	3.543	2.212
300 PPM	81R3630	507	15.62	1.443	0.824	4.081	78	3.886	2.210
300 PPM	81R3633	632	24.41	1.666	1.800	5.125	135	3.434	2.130
300 PPM	81R3636	564	16.44	1.585	1.067	4.222	68	2.114	2.247
300 PPM	81R3641	609	19.45	2.032	1.124	5.133	67	4.444	2.231
30 PPM	81R3646	680	18.71	1.409	1.042	3.748	66	3.199	2.214
30 PPM	81R3650	586	18.17	1.605	1.417	4.367	94	4.083	2.473
30 PPM	81R3654	704	21.44	2.020	1.108	4.309	83	5.371	2.317
30 PPM	81R3658	628	16.67	1.293	0.837	4.197	60	4.001	2.164
30 PPM	81R3663	713	25.66	2.172	1.178	5.023	99	3.794	2.220
30 PPM	81R3667	583	17.03	1.872	0.979	4.562	74	3.305	2.111
30 PPM	81R3670	653	19.03	2.010	1.417	7.178	124	3.205	2.286
30 PPM	81R3672	616	16.77	1.825	1.082	4.468	73	2.452	2.060
30 PPM	81R3676	539	24.00	2.326	1.414	10.404	143	3.209	2.150
30 PPM	81R3679	921	23.86	2.120	0.962	5.664	90	4.544	2.304
30 PPM	81R3682	545	16.02	1.464	0.905	4.147	64	3.040	1.934
30 PPM	81R3684	772	16.98	2.022	1.151	5.550	91	4.104	2.144
30 PPM	81R3689	491	13.94	1.416	0.773	4.170	62	3.044	2.312
30 PPM	81R3691	595	16.89	1.707	1.277	3.948	81	3.412	2.244
30 PPM	81R3694	697	16.58	1.631	1.033	4.626	142	4.179	2.090

NOTES: Body weights and organ weights in grams.

^a Indicates adrenal weight in mg.

TABLE 18

TWO YEAR ORAL (DIFT) TOXICITY-ONCOGENICITY
STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS
TWO YEAR INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS ^a	UTERUS	BRAIN
0 PPM	N1R4583	494	15.99	1.174	1.032	3.368	9H	0.443	2.045
0 PPM	N1R4586	480	11.86	1.215	0.983	2.824	63	1.065	2.064
0 PPM	N1R4591	516	14.21	1.322	0.749	3.161	84	0.884	1.960
0 PPM	N1R4595	455	11.98	1.415	0.740	2.768	10H ^b	0.729	2.089
0 PPM	N1R4598	471	13.45	1.538	0.983	3.466	c	1.155	1.928
0 PPM	N1R4603	481	14.37	1.465	0.657	3.218	84	0.725	2.174
0 PPM	N1R4606	592	14.99	1.601	0.757	3.374	114	1.541	1.927
0 PPM	N1R4611	604	24.88	1.567	0.721	3.318	253	0.566	2.115
0 PPM	N1R4614	518	14.40	1.498	0.697	3.356	91	0.570	2.055
0 PPM	N1R4616	347	11.77	1.254	0.717	3.012	122	0.803	2.140
0 PPM	N1R4626	353	10.28	0.949	0.581	2.464	78	0.354	2.032
0 PPM	N1R4628	535	13.34	1.182	0.938	3.082	79	0.812	1.971
0 PPM	N1R4634	567	14.23	1.523	0.665	2.878	108	0.738	1.919
0 PPM	N1R4636	560	19.57	1.180	0.933	3.261	85	0.746	1.874
0 PPM	N1R4638	675	16.28	1.612	0.798	3.340	75	0.636	2.218
0 PPM	N1R4644	468	14.35	1.208	0.608	2.832	76	0.466	1.968
300 PPM	N1R4646	539	17.04	1.258	0.946	3.688	89	0.767	2.236
300 PPM	N1R4649	378	11.32	1.056	0.495	2.806	38	0.588	2.195
300 PPM	N1R4657	418	14.58	1.179	0.677	2.844	131	0.596	2.043
300 PPM	N1R4659	519	15.84	1.308	1.134	2.293	102	1.465	2.016
300 PPM	N1R4661	459	12.22	1.153	0.630	2.398	64	0.424	2.045
300 PPM	N1R4663	480	14.01	1.452	0.688	3.275	138	1.076	2.024
300 PPM	N1R4672	380	10.92	1.403	0.944	2.430	100	0.665	1.934
300 PPM	N1R4679	551	21.34	1.521	0.717	4.125	128	0.424	1.847
300 PPM	N1R4683	376	13.96	1.575	0.841	3.490	183	0.438	2.065
300 PPM	N1R4688	375	13.32	1.334	0.454	3.143	137	1.043	2.264
300 PPM	N1R4693	480	12.13	1.187	0.557	2.592	129	0.926	2.046
300 PPM	N1R4695	449	c	1.610	0.471	3.737	175	1.532	2.031
300 PPM	N1R4697	354	11.60	1.122	0.722	2.937	87	0.803	1.933
300 PPM	N1R4701	542	13.98	1.288	0.549	3.194	112	0.529	1.958
30 PPM	N1R4708	526	17.63	1.375	0.857	3.804	173	0.944	1.975
30 PPM	N1R4711	559	22.66	1.456	1.016	3.085	123	0.517	1.927
30 PPM	N1R4714	545	23.62	1.693	1.027	3.904	202	0.612	1.854
30 PPM	N1R4716	404	10.44	1.594	0.484	2.722	105	0.408	1.840
30 PPM	N1R4720	539	19.74	1.411	1.296	3.748	185	0.610	2.010
30 PPM	N1R4723	542	16.73	1.432	1.084	4.066	118	2.450	2.127
30 PPM	N1R4726	606	16.46	1.864	1.057	3.878	103	1.064	2.117
30 PPM	N1R4729	502	19.16	1.693	0.947	3.608	169	1.035	1.841
30 PPM	N1R4733	452	12.22	1.217	0.707	2.997	94	0.811	2.103
30 PPM	N1R4736	533	13.87	1.394	0.920	3.216	73	0.540	2.001
30 PPM	N1R4739	756	22.13	1.708	3.561	3.113	210	0.522	2.044
30 PPM	N1R4745	428	14.03	1.464	0.824	3.670	111	0.974	2.047
30 PPM	N1R4747	545	16.57	1.274	0.943	3.407	125	0.846	2.351
30 PPM	N1R4752	575	15.04	1.538	0.854	4.012	164	0.864	2.106
30 PPM	N1R4754	487	14.88	1.210	1.157	2.856	89	0.614	1.967

NOTES:

Body weights and organ weights in grams.

^a Indicates adrenal weights in mg.^b Indicates adrenal weight not recorded; left adrenal greatly enlarged.^c Indicates liver weight not recorded due to mass.

TABLE 19

Two Year Oral (Diet) Toxicity - Oncogenicity Study of
Fluorocarbon FC-143 in Rats

Summary of Major Microscopic Findings - Percent Incidence at 2 Years

		NEOPLASTIC LESIONS					
Organ/Lesion	n = 1	Controls		High		Low	
		Male 50	Female 50	Male 50	Female 50	Male 50	Female 50
Adrenal							
Pheochromocytoma, benign		4	4	8	0	8	0
Pheochromocytoma, malig.		0	0	0	2	2	0
Liver							
Hepatocellular Carcinoma		6	0	10	2	2	0
Mammary Gland							
Adenocarcinoma		-	15	-	11	-	31
Adenoma		-	7	-	0	-	0
Carcinoma		-	2	-	0	-	0
Fibroadenoma		-	22	-	48*	-	42
Lymphangiosarcoma		-	0	-	2	-	0
Pituitary							
Adenoma		35	72	28	72	36	83
Testes/Epididymis							
Leydig Cell Adenoma		0	-	14*	-	4	-
Thyroid							
C-cell Adenoma		0	2	9	0	4	0
C-cell Carcinoma		5	0	0	0	0	0

1 = 50 rats/sex/group were at risk, % values derived from actual tissues examined

* = Significantly different ($p = 0.05$) from controls

TABLE 20

Two Year Oral (Diet) Toxicity - Oncogenicity Study of
Fluorocarbon FC-143 in Rats

Summary of Major Microscopic Findings - Percent Incidence at 2 Years

		<u>NON-NEOPLASTIC LESIONS</u>					
<u>Organ/Lesion</u>	n = 1	<u>Controls</u>		<u>High</u>		<u>Low</u>	
		Male 50	Female 50	Male 50	Female 50	Male 50	Female 50
Adrenal							
Nodular Hyperplasia		4	0	18	2	2	6
Sinusoidal Ectasis		22	84	32	82	26	86
Heart							
Myocarditis, Chronic		28	32	34	20	36	10*
Liver							
Cystoid Degeneration		8	0	56*	2	14	2
Hepatocellular Alt. Basophil.		4	16	12	4	2	16
Hyperplastic Nodule		0	2	6	4	0	0
Megalocytosis		0	0	80*	16*	12	2
Portal Mononuclear Cell Infil.		74	38	96*	38	64	22
Necrosis		6	10	10	4	10	12
Lung							
Alveolar Macrophages		20	28	62*	38	32	20
Hemorrhage		20	28	44*	38	28	26
Perivas. Mono. Infil.		42	26	14*	28	6*	4*
Vascular Mineralization		86	44	94	52	86	76*
Pneumonia, Interstitial		32	14	14	18	10*	6
Testis/Epididymis							
Tubular Atrophy		14	-	22	-	20	-
Vascular Mineralization		0	-	18*	-	6	-
Ovary							
Cyst		-	13	-	11	-	18
Tubular Hyperplasia		-	0	-	32*	-	14*
Thyroid							
C-Cell Hyperplasia		2	0	2	7	13	2
Uterus							
Cystic Glands		-	14	-	10	-	24
Pancreas							
Acinar Atrophy		13	12	22	9	20	12
Salivary Gland							
Sialadenitis, Chronic		2	2	30*	5	27*	2
Spleen							
Hemosiderosis		32	50	44	24*	8*	6*

1 = 50 rats/sex/group were at risk, % values derived from actual tissues examined

* = Significantly different ($p = 0.05$) from controls

FIGURE 1

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN BODY WEIGHTS (G) OF MALES

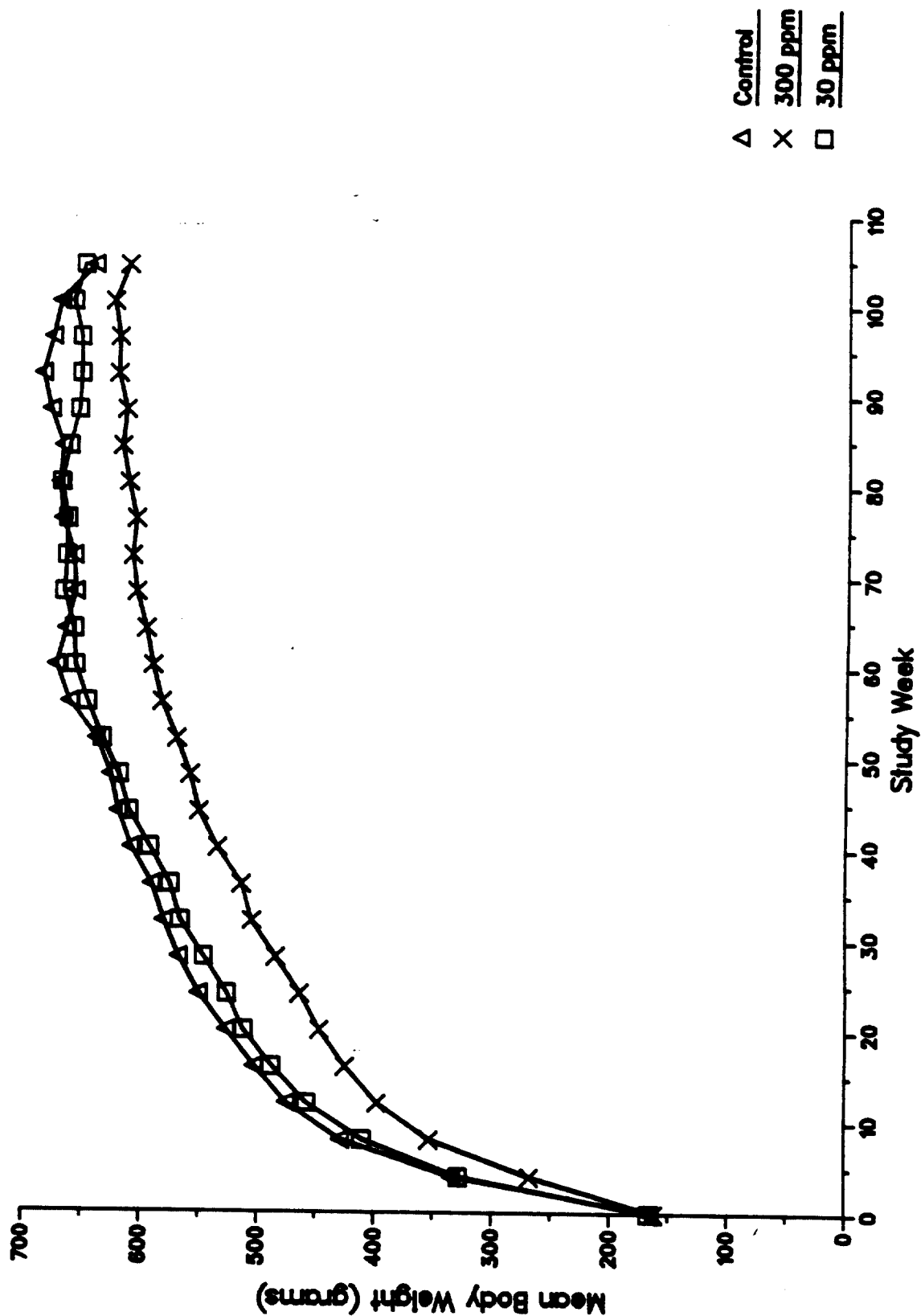


FIGURE 2

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN BODY WEIGHTS (G) OF FEMALES

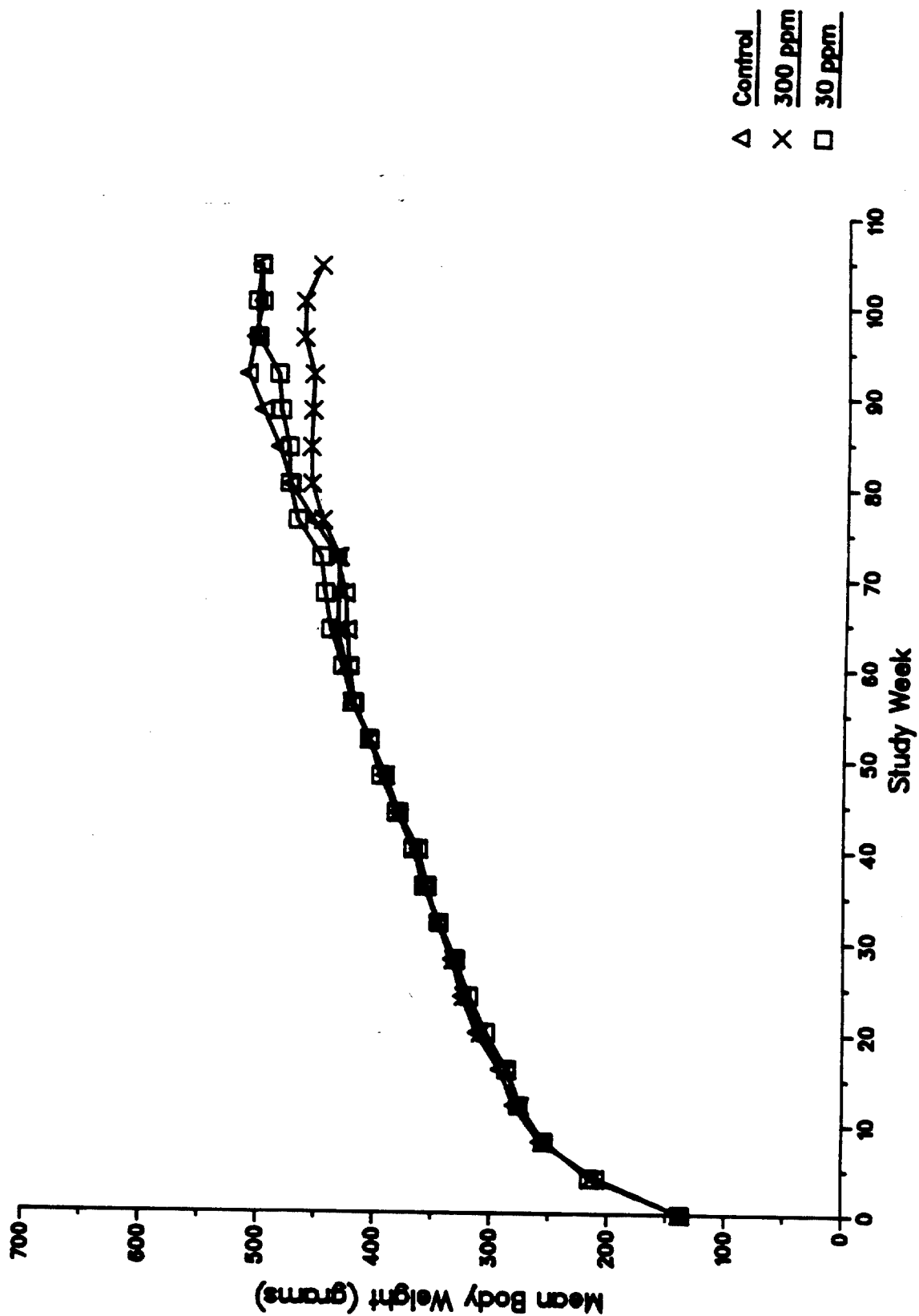


FIGURE 3

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN FOOD CONSUMPTION (G/KG OF MEAN BODY WEIGHT) OF MALES

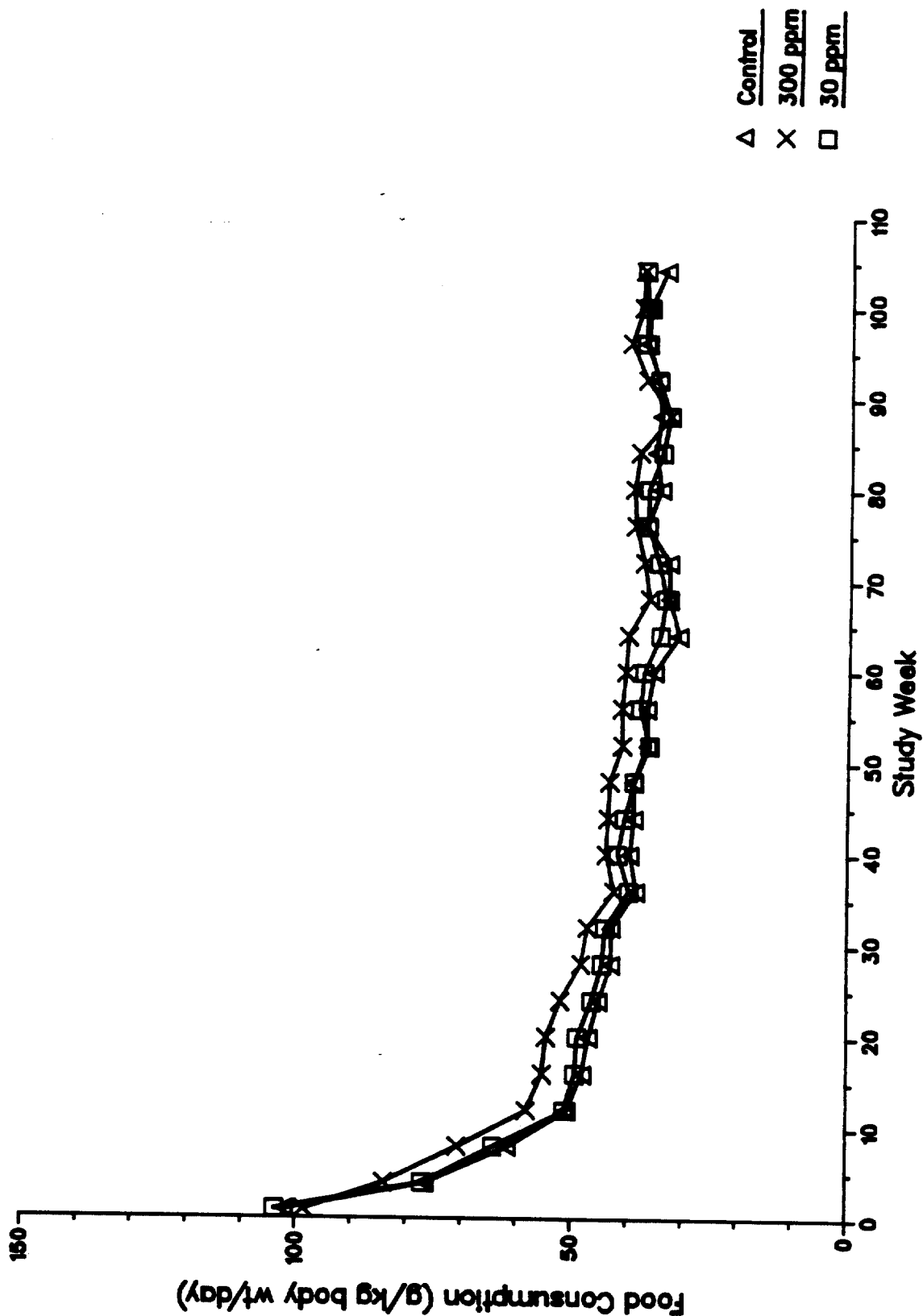
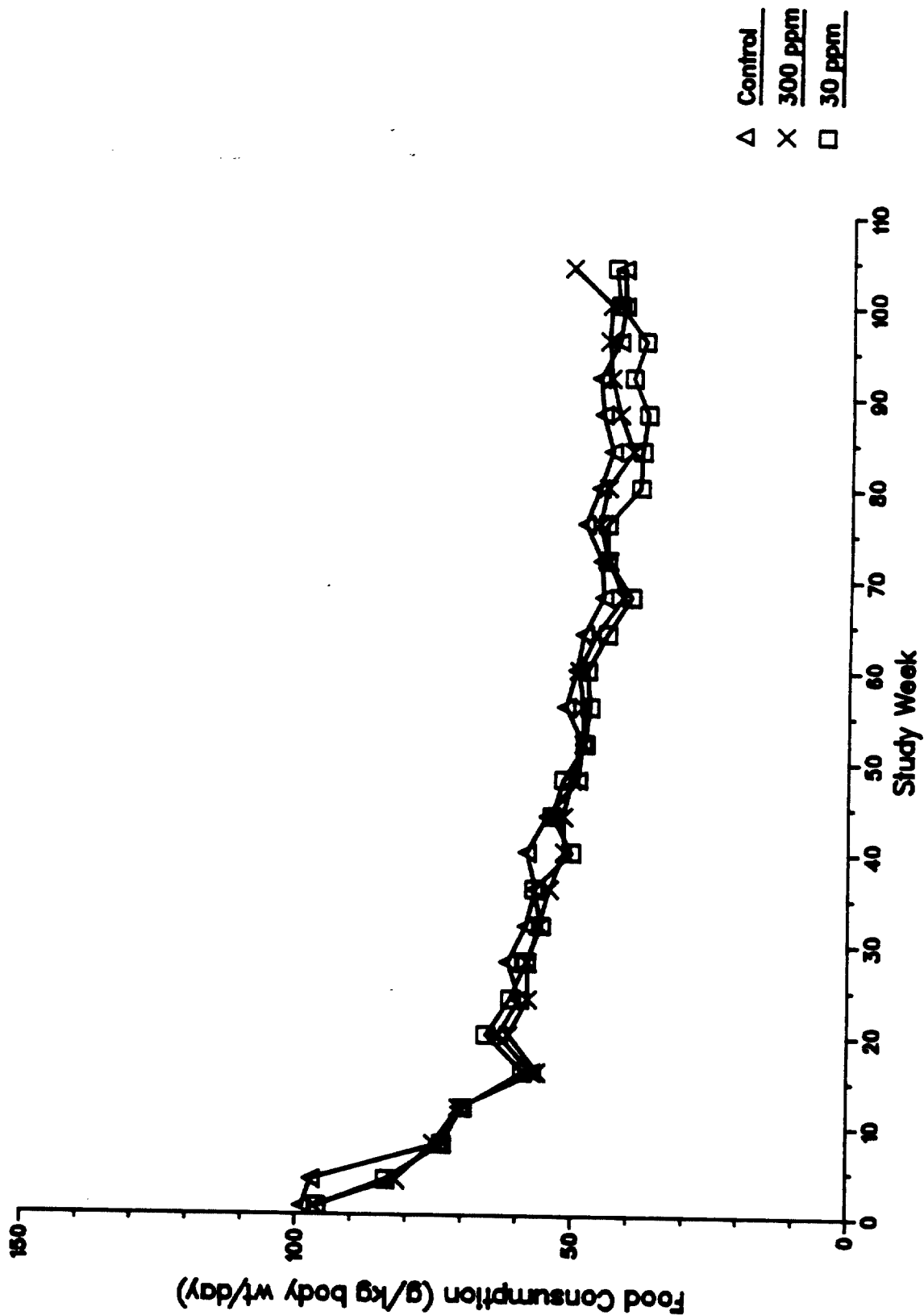


FIGURE 4

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS
MEAN FOOD CONSUMPTION (G/KG OF MEAN BODY WEIGHT) OF FEMALES



TWO YEAR ORAL (DIET) TOXICITY / CARCINOGENICITY
STUDY OF FLUOROCHEMICAL FC-143 IN RATS

APPENDIX ITEMS

Internal Correspondence

Appendix Item A

cc: F. D. Griffith - 220-2E-02
W. C. McCormick - 220-2E-02

rc: J. K. Sugg - 220-2E-02
F. A. Ubel, M.D. - 220-2E-02

To: M. T. CASE - RIKER LABORATORIES - 218-3S
From: S. D. SORENSON - MEDICAL, IND. HYG. SERV. - 220-2E-02
Subject: Air Monitoring, Project 89003107
Date: August 27, 1981

3M

Summary

Air monitoring has been conducted in three animal treatment rooms used in fluorochemical studies. The purpose of the monitoring was to evaluate possible airborne contaminants.

The sample results indicate that fluorochemical exposures, if any, were below detectable amounts.

Detail

Air sampling was conducted in the three animal treatment rooms used in the two year animal feeding study of FM-3924 and FC-143. The study has been in progress since April 21, 1981.

Area samples were collected in each of the several treatment rooms by means of either impingers with methanol media or SKC® silica gel sampling tubes. With one exception, samples were located on top of the animal racks. The one exception was an air sampler located near the room air exhaust near the floor. The periods sampled are judged representative of "usual" or steady state conditions.

The flow rate of the sample pumps was checked approximately every 30 minutes throughout the sampling period.

The samples were analyzed by the Analytical Section of the 3M Central Research Laboratory. This laboratory has full accreditation as an Industrial Hygiene Laboratory by the American Industrial Hygiene Association.

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Appendix Item A

M. T. Case

-2-

August 27, 1981

The sample results indicate that airborne concentrations of the test fluorochemicals, if any, were below detectable limits. On this basis, it is judged that cross contamination potential by airborne means is unlikely.

Please call if there are any questions.


SDS:cr

APPENDIX ITEM A

M. T. Case

-3-

August 27, 1981

Sample Data
Building 218-3
Project #89003107
August 7, 1981

<u>Sample Number</u>	<u>Description</u>	<u>Time</u>	<u>Compound</u>	<u>Concentration, mg/m³</u>
CCL81-20	D-340. Control Room, top of rack.	922-1225	FM-3924	< 0.003
CCL81-23	Same as above	922-1225	FC-143	< 0.001
CCL81-21	D-332. FM-3924, dose Room. Sampler on top of high dose rack.	926-1236	FM-3924	< 0.003
CCL81-25	D-332. Sampler at rear room air exhaust about 18 inches above floor.	1055-1236	FM-3924	< 0.025
CCL81-22	D-338. FC-143, dose Room. Sampler on top of high dose rack.	925-1228	FC-143	< 0.001
CCL81-24	Same as CCL81-22, duplicate sample using silica gel tube.	931-1228	FC-143	< 0.002

SAMPLING METHOD: FM-3924 SKC silica gel sampling tubes.
FC-143 Impinger - methanol.

ANALYTICAL METHOD: FM-3924 - gas chromatography, electron capture detector.
FC-143 - derivatization; gas chromatography, electron capture
detector.

ANALYTICAL REQUEST: #A80248.

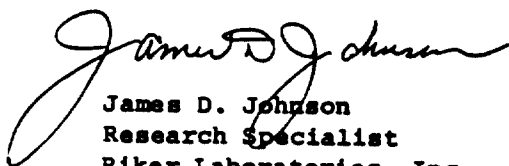
Internal Correspondence

APPENDIX ITEM A

To: L. J. Sibinski
From: J. D. Johnson
Subject: Analysis of Plasma Samples from Sentinal Rats Housed in Room
with Two Year Tox Study-Rats (Riker Study No. 0281CR0012)
Date: October 7, 1985

3M

I have attached the one page protocol attachment for the use of sentinal rats in Riker Study No. 0281CR0012. These samples were collected as described. On July 15, 1981, forty plasma samples (see attached) were transferred to V. Pothapragada (Dr. V) in Commercial Chemicals for analysis of organic fluorine. The results were sent back by Dr. V 8/24/81. All samples were less than one part per million. From this, it can be concluded that there was no airborne fluorine present that was interfering with this study. These data are in SJG Notebook 56531, p 53.


James D. Johnson
Research Specialist
Riker Laboratories, Inc.

Internal Correspondence

cc: M.T. Case
F.D. Griffith
R.E. Ober
W.H. Pearlson
R.A. Prokop

~~_____~~ 218-3

To: V. Pothapragada

From: J.D. Johnson

Subject: Analysis of Plasma Samples from Sentinal Rats Housed in Room
with Two Year Tox Study Rats (Riker Study No. 0281 CR 0012).

Date: July 15, 1981

3M

Forty plasma samples from sentinal rats are submitted for fluorine analysis. These samples include 5 male (IR 3861, IR 3862, IR 3863, IR 3864, and IR 3865) and 5 female (IR 4921, IR 4922, IR 4923, IR 4924, and IR 4925) which were sacrificed before dosing was initiated. The other thirty plasma samples were collected at 30 days after dosing started. There are 5 rats of each sex from the control room, from the room in which study rats are receiving FC-143, and from the room in which study rats are receiving FM-3924.

The numbers for these rats are as follows:

5 male Control Room (IR 3866, IR 3867, IR 3868, IR 3869, IR 3870)

5 female Control Room (IR 4926, IR 4927, IR 4928, IR 4929, IR 4930)

5 male FC-143 Room (IR 3876, IR 3877, IR 3878, IR 3879, IR 3880)

5 female FC-143 Room (IR 4936, IR 4937, IR 3838, IR 3839, IR 3840)

5 male FM-3924 Room (IR 3886, IR 3887, IR 3888, IR 3889, IR 3890)

5 female FM-3924 Room (IR 4946, IR 4947, IR 4948, IR 4949, IR 4950)

Please get back to us with the data. It may be that interpretation of the results will lead to specific analysis or to analysis of tissue.


J.D. Johnson/mho

Appendix Item B

To ~~XXXXXXXXXXXX~~
 From P. J. Colbert - 236-2B
 Subject GLC Analysis of FM-3924 (T-2999CoC) FC-143 (T-2998CoC) Blended
 into Ground Lab Chow. (Riker Study #0281CR0012)
 Date April 29, 1981

Reference: Commercial Chemicals Analytical Laboratory
 Requests #17079, 17080, 17096

Commercial Chemicals Analytical Laboratory
 Method #'s G30-0481, G31-0481

The samples of FM-3924 (W.R. EtFOSE) blended into Ground Lab Chow, along with four blank Ground Lab Chow samples, were received from L. J. Sibinski on 4-20-81 for analysis. All samples were run in triplicate. The results are:

<u>Compound</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>ug/g FM-3924</u>
Blank for concentrate	0	0
FM-3924 Concentrate (blended 4-17-81)	200	214
FM-3924 Top Sample	100	105
Mid Sample	100	105
Bottom Sample	100	111
FM-3924 Top Sample	30	29
Mid Sample	30	27
Bottom Sample	30	30
FM-3924 Top Sample	10	11
Mid Sample	10	9
Bottom Sample	10	10

APPENDIX ITEM B

L. J. Sibinski
CCD Analytical Report #213
April 29, 1981
Page 2

<u>Compound</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>(ug/g) FM-3924</u>
Blank for 100 ppm level	0	0
Blank for 30 ppm level	0	0
Blank for 10 ppm level	0	0

The level of ethanol in FM-3924 Concentrate (blended 4-17-78) was also checked and found to be less than 1 ppm (ug/g).

Six samples of FC-143 blended into Ground Lab Chow, along with two blank Ground Lab Chow samples were received from L. J. Sibinski on 4/20/81 for analysis. All samples were run in triplicate. The results are:

<u>Compound</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>(ug/g) FC-143</u>
FC-143 Top Sample	300	326
Mid Sample	300	282
Bottom Sample	300	297
Blank for 300 ppm level	0	0
FC-143 Top Sample	30	24
Mid Sample	30	23
Bottom Sample	30	28
Blank for 30 ppm level	0	0

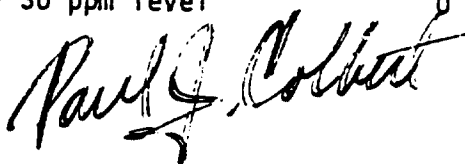
Because two of the three 30 ppm level samples were low, another set of samples were received from L. J. Sibinski on 4/27/81 for analysis. The results are:

APPENDIX ITEM B

L. J. Sibinski
CCD Analytical Report #213
April 29, 1981
Page 3

<u>Compound</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>(ug/g) FC-143</u>
FC-143 Top Sample	30	31
Mid Sample	30	28
Bottom Sample	30	30
Blank for 30 ppm level	0	0

LJS/mao



cc: M. T. Case - 218-2
E. G. Lamprecht - 218-3
W. C. McCormick - 220-2E-02
J. D. LaZerte - 236-1L
R. A. Prokop - 236-2B
V. Pothapragada - 236-3A

APPENDIX ITEM B

Internal Correspondence

dc: M. T. Case 218-2
E. G. Lamprecht 218-3
J. D. LaZerte 236-1
W. C. McCormick 220-2E-02
V. Pothapragada 236-3A
R. A. Prokop 236-2B
L. D. Winter 236-2B

Commercial Chemicals
Analytical Report
#229

To: L. J. Sibinski 218-3-3

From: P. J. Colbert 236-2B

Subject: GLC Analysis of FM-3924 (T-2999 CoC) FC-143 (T-2998 CoC) Blended
Into Ground Lab Chow (Riker Study #0281CR0012)

Date: June 15, 1981

3M

Six samples of FC-143 blended into Ground Lab Chow, along with two blank Ground Lab Chow samples, were received from L. J. Sibinski on 5-18-81 for analysis. All samples were run in triplicate. The results are:

<u>Sample</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>µg/g FC-143</u>
Blank for 300 ppm	0	0
FC-143 Top	300	303
Mid	300	305
Bottom	300	295
Blank for 30 ppm	0	0
FC-143 Top	30	31
Mid	30	31
Bottom	30	29

The next set of Ground Lab Chow Samples will be submitted for analysis on August 17, 1981.

Paul J. Colbert

PJC:da

G00493

Internal Correspondence

APPENDIX ITEM B

Commercial Chemicals
Analytical Report #250

To: L. J. Sibinski - 218-3-3
From: P. J. Colbert - 236-2B
Subject: GLC Analysis of FC-143 (T-2993CoC) Blended into Ground Lab Chow (Riker Study #0281CR0012)
Date: August 20, 1981

3M

Reference: Commercial Chemicals Analytical Laboratory
Request #17449, and CCD Method G31-0481

Six samples of FC-143 blended into Ground Lab Chow, along with two Blank Ground Lab Chow samples, were received from L. J. Sibinski on August 17, 1981, for analysis. All samples were run in triplicate. The results are:

<u>Sample</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>ug/g FC-143</u>
Blank for 300 ppm	0	0
FC-143 Top	300	308
Mid	300	310
Bottom	300	328
Blank for 30 ppm	0	0
FC-143 Top	30	28
Mid	30	30
Bottom	30	30

-2.3%

PJC/mao *Paul J. Colbert*

cc: M. T. Case - 218-2
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1L
W. C. McCormick - 220-2E-02
V. Pothapragada - 236-3A
R. A. Prokop - 236-2B
L. D. Winter - 236-2B
R. M. Payfer - 236-2B
G. W. Kirsch - 236-3A

G00494

Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #289

To: L. J. SIBINSKI - 218-3-3
From: R. M. PAYFER - 236-2B
Subject: GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND
LAB CHOW (RIKER STUDY #2081cR0012)
Date: November 30, 1981

3M

References: Commercial Chemicals Analytical Laboratory
Request #17779

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on November 16, 1981 for analysis. All samples were run in triplicate with the following results:

<u>Sample</u>	<u>Theoretical PPM</u>	<u>Actual PPM</u> <u>ug/g FC-143</u>
Blank for 300	0	0
PPM FC-143 Top	300	278
Middle	300	310
Bottom	300	323
Blank for 30 PPM	0	0
FC-143 Top	30	29
Middle	30	28
Bottom	30	33

RMP/hc

Richard M. Payfer

dc: M. T. Case - 218-2
G. W. Kirsch - 236-3A
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1
W. C. McCormick - 220-2E-02
V. Pothapragada - 236-3A
R. A. Prokop - 236-2B
L. D. Winter - 236-2B (2 copies)

000495

APPENDIX ITEM B

Internal Correspondence:

dc: M.T. Case - 218-2
 G.W. Kirsch - 236-2
 E.G. Lamprecht - 218-3
 J.D. LaZerte - 236-1
 W.C. McCormick - 220-2E-02
 V. Pothapragada - 236-3A
 L.D. Winter - 236-2B

COMMERCIAL CHEMICALS
 ANALYTICAL REPORT #319

To: L. J. SIBINSKI - 218-3-3

From: R. M. PAYFER - 236-2B

Subject: GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND
 LAB CHOW (RIKER STUDY #2081 CR 0012)

Date: MARCH 5, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18069

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on February 15, 1982. These samples were analyzed in triplicate for FC-143 with the following results:

Sample	Theoretical PPM	Actual PPM ug/g FC-143
Blank for 300 PPM	0	0
300 PPM Top	300	165
300 PPM Middle	300	215
300 PPM Bottom	300	215
Blank for 30 PPM	0	0
30 PPM Top	30	27
30 PPM Middle	30	33
30 PPM Bottom	30	24

Richard M. Payfer
 RMP:df

*incorrect carbon counts
 faulty detector in per
 communication with R.M. Payfer
 on 3/14/82 J. Sibinski*

*Re-analyze 4 samples
 done J. Sibinski*

Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #328

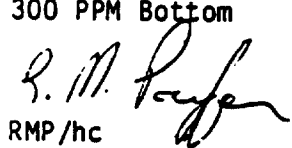
To: L. J. SIBINSKI - 218-3-3 -
From: R. M. PAYFER - 236-2B
Subject: GLC RE-ANALYSIS OF FC-143 (T-2998 COC) BLENDED INTO
GROUND LAB CHOW (RIKER STUDY #2081 CRO012)
Date: March 31, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18100

Three samples of FC-143 blended into ground lab chow, along with one blank ground lab chow sample, were received from L. J. Sibinski on March 8, 1982. These samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical PPM</u>	<u>Actual PPM ug/g FC-143</u>
Blank for 300 PPM	0	0
300 PPM Top	300	278
300 PPM Middle	300	283
300 PPM Bottom	300	284


RMP/hc

cc: M. T. Case - 218-2
G. W. Kirsch - 236-3A
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1
W. C. McCormick - 220-2E-02
V. Pothapragada - 236-3A
L. D. Winter - 236-2B

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Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #340

To: L. J. SIBINSKI - 218-3-3
From: R. M. PAYFER - 236-2B
Subject: GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND
LAB CHOW (RIKER STUDY #0281 CRO012)
Date: May 28, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18320

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on May 17, 1982. These samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical PPM</u>	<u>Actual PPM</u> <u>ug/g FC-143</u>
Blank for 300 PPM	0	0
300 PPM Top	300	310
300 PPM Middle	300	280
300 PPM Bottom	300	289
Blank for 30 PPM	0	0
30 PPM Top	30	31
30 PPM Middle	30	33
30 PPM Bottom	30	33

Richard M. Payfer
RMP/hc

dc: M. T. Case - 218-2
G. W. Kirsch - 236-GB
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1
W. C. McCormick - 220-2E-D2
V. Pothapragada - 236-GB
L. D. Winter - 236-2B

G00498

111

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #366

To L. J. SIBINSKI - 218-3-3
From R. M. PAYFER - 236-2B
Subject GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND
LAB CHOW (RIKER STUDY #0281 CR0012)
Date Sept. 13, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18609

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on Aug. 16, 1982. These samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical PPM</u>	<u>Actual PPM</u> <u>ug/g FC-143</u>
Blank for 300 PPM	0	0
300 PPM Top	300	300
300 PPM Middle	300	319
300 PPM Bottom	300	304
Blank for 30 PPM	0	0
30 PPM Top	30	29.5
30 PPM Middle	30	35
30 PPM Bottom	30	29.5

Richard Payfer
RMP/hc

dc: M. T. Case - 218-2
G. W. Kirsch - 236-GB
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1
W. C. McCormick - 220-2E-D2
V. Pothapragada - 236-GB
L. D. Winter - 236-2B

Internal CorrespondenceAPPENDIX ITEM B

To: J. L. Sibinski - 218-3
From: G. W. Kirsch - 236-2B
Subject: GLC Analysis of FC-143 (T-2998 CoC) Blended into Ground
Lab Chow (Riker Study #0281 CR0012)
Date: December 8, 1982

Commercial Chemicals
Analytical Report #384

3M

Reference: Commercial Chemicals Analytical Laboratory
Request #18855.

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on December 5, 1982. These samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>µg/g FC-143</u>
Blank for 300 ppm	0	0
300 ppm Top	300	323
300 ppm Middle	300	292
300 ppm Bottom	300	303
Blank for 30 ppm	0	0
30 ppm Top	30	28
30 ppm Middle	30	32
30 ppm Bottom	30	32

Handwritten notes:
For 300 ppm: 306 ppm + 2%
For 30 ppm: 31.6 ppm + 2%

G. W. Kirsch

GWK:ch

cc: M. T. Case - 218-2
E. G. Lamprecht - 218-3
J. D. LaZerte - 236-1L
W. C. McCormick - 220-2E
R. M. Payfer - 236-2B
V. Prothapragada - 236-GB
L. D. Winter - 236-2B

Internal Correspondence

APPENDIX ITEM BCommercial Chemicals
Analytical Report #395

To: L. J. SIBINSKI - 218-3
 From: G. W. KIRSCH - 236-2B
 Subject: GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND
 RODENT CHOW (RIKER STUDY #0281-CR0012)
 Date: MARCH 7, 1983

3M

 Reference: Commercial Chemicals Analytical Laboratory Request #19121

Six samples of FC-143 blended into ground lab chow, along with two blank ground lab chow samples, were received from L. J. Sibinski on February 16, 1983. These samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>ug/g FC-143</u>
Blank for 300 ppm	0	0
300 ppm Top	300	317
300 ppm Middle	300	286
300 ppm Bottom	300	323
Blank for 30 ppm	0	0
30 ppm Top	30	32
30 ppm Middle	30	30
30 ppm Bottom	30	31

GWK/hc J. Kimb

dc: M. T. Case - 218-2
 E. G. Lamprechts - 218-3
 J. D. LaZerte - 236-1

W. C. McCormick - 220-2E
 R. M. Payfer - 236-2B
 W. H. Pearlson - 223-6SE
 L. D. Winter - 236-2B

Internal Correspondence

APPENDIX ITEM BCommercial Chemicals
Analytical Report #404

To L. J. SIBINSKI - 218-3
 From G. W. KIRSCH - 236-2B
 Subject GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND
 RODENT CHOW (RIKER STUDY #0281-CR0012)
 Date MAY 2, 1983

3M

Reference: Commercial Chemicals Analytical Laboratory Request #19333

Six samples of FC-143 blended into ground rat chow, along with two blank ground rat chow samples, were received from L. J. Sibinski on April 13, 1983. All samples were analyzed in triplicate for FC-143 with the following results:

<u>Sample</u>	<u>Theoretical ppm</u>	<u>Actual ppm</u> <u>ug/g FC-143</u>
Blank for 300 ppm	0	0
300 ppm Top	300	326
300 ppm Middle	300	331
300 ppm Bottom	300	328
Blank for 30 ppm	0	0
30 ppm Top	30	33
30 ppm Middle	30	34
30 ppm Bottom	30	32

GWK/hc G. Kirsch

dc: M. T. Case - 218-2 R. M. Payfer - 236-2B
 J. D. LaZerte - 236-1 W. H. Pearlson - 223-6SE
 W. C. McCormick - 220-2E L. D. Winter - 236-2B

Appendix Item C

Two Year Oral (Diet) Toxicity-Oncogenicity Study of Fluorocarbon
FC-143 in Rats

Normal Ranges for Hematologic and Blood Chemistry Values of Rats
at Riker Laboratories, Inc., St. Paul, MN

Erythrocytes	5,000,000-8,000,000 cells/cu mm
Hemoglobin	11-17 g/dl
Hematocrit	36-52%
Mean Corpuscular Volume (MCV)	57-77 microns ³
Mean Corpuscular Hemoglobin (MCH)	18-24 picograms
Mean Corpuscular Hemoglobin Concentration (MCHC)	30-34%
Leukocytes	6,000-15,000 cells/cu mm
Neutrophils 2-22%	500-4,000 cells/cu mm
Lymphocytes 65-95%	5,000-14,000 cells/cu mm
Monocytes 0-5%	0-500 cells/cu mm
Eosinophils 0-6%	0-500 cells/cu mm
Blood Urea Nitrogen (BUN)	10-30 mg/dl
Glucose	120-160 mg/dl
Total Bilirubin	0.1-1.0 mg/dl
Total Protein	5.5-7.5 g/dl
Albumin	3.5-5.5 g/dl
Calcium	10.2-12.5 mg/dl
Alanine Aminotransferase (ALT)	10-40 International Units/l
Aspartate Aminotransferase (AST)	20-60 International Units/l
Alkaline Phosphatase	50-200 International Units/l
Creatine Phosphokinase (CPK)	50-150 International Units/l

Appendix Item C

Methods Used for Hematology On Bleedings at 3 and 6 Months

Parameters	Units	Methods
<u>Hematology</u>		
Total Erythrocytes & Leukocytes	cells/cubic mm	Coulter Counter Model FN Coulter Electronics
Hemoglobin	g/dl	Hemoglobinometer, Model 231, Instrumentation Laboratories
Hematocrit	% packed cells	Microhematocrit Centrifuge, Model MB International Equipment Co.
Differential	%/100 WBC	Microscope slide

APPENDIX ITEM C

METHODS USED FOR HEMATOLOGY DETERMINATIONS FOR 12, 18 AND 24 MONTHS

METHODS USED FOR CLINICAL CHEMISTRY DETERMINATIONS FOR 3, 6, 12, 18 AND 24 MONTHS

Parameters	Units	Methods and Techniques
<u>Hematology</u>		
Erythrocytes	cells($10^6/\text{mm}^3$)	UltraLogic 800 Hematology Analyzer Clay Adams, Division of Becton, Dickinson & Co.
Leukocytes	cells($10^3/\text{mm}^3$)	
Hemoglobin	g/dl	
Hematocrit	%	
Differential	%/100 WBC	Microscope slide
<u>Chemistry</u>		
Total Bilirubin, Glucose	mg/dl	Rotochem 36 IIA Travenol Laboratories, Inc.
Blood Urea Nitrogen		
Albumin, Total Protein	g/dl	
Alkaline Phosphatase	International	
AST, ALT, CPK	Units/l	
<u>Urinalysis</u>		
Specific Gravity		TS Meter, AO Instrument Co.
pH, Albumin, Bilirubin, Glucose, Occult Blood and Ketones		BiliLabstix Ames Company

APPENDIX ITEM D

PATHOLOGY REPORT OF RATS
RECEIVING FLUOROCHEMICAL FC-143
IN DIET FOR TWO YEARS

METHODS

Gross Pathology

All rats which were sacrificed at the 1 year interim or the 2 year terminal sacrifice or which died or were sacrificed in extremis during the course of study were necropsied. At necropsy, an examination was made of the external body surface and body orifices. The carcass was then opened and the contents of the abdomen, thorax and cranium were examined in situ and after removal from the carcass. Representative tissues and organs from each rat were fixed in 10% buffered neutral formalin for subsequent histologic processing. At the 1 and 2 year sacrifices, wet weights were obtained on adrenals, brain, testes, heart, kidneys, liver, spleen and uterus from 15 randomly selected rats/sex/group. Body weights were obtained prior to necropsy from the same rats for calculation of relative organ weights.

Histopathology

Microscopic examination was made of hematoxylin and eosin stained paraffin tissue sections of the following tissues and organs, where available, from all rats from the control group (0 ppm) and the 300 ppm group which were sacrificed at 1 and 2 years or which died or were sacrificed in extremis during the course of study.

aorta	liver (2 sections)
adrenals (2)	lung (2 sections)
brain (3 sections including	lymph node (mesenteric)
frontal cortex and basal	mammary gland (females)
ganglia, parietal cortex	pancreas
and thalamus; cerebellum	pituitary
and pons)	salivary gland
eyes	spinal cord/bone marrow (vertebrae)
gonads	spleen
ovaries (2)	stomach
testes/epididymides (2)	thyroid/parathyroid/trachea/esophagus
heart	urinary bladder
small intestine (3 sections)	uterus or prostate
large intestine	any tissue masses (suspected tumors)
kidneys (2 sections)	any other gross lesions

Microscopic examination of tissues from the 30 ppm group included all the above listed tissues except aorta, brain, eyes, small and large intestine, lymph node and spinal cord/bone marrow.

RESULTS

Gross Pathology

There were no gross findings suggestive of a compound effect in any rats from the 300 ppm group which were sacrificed at the 1 year interim. At the 2 year terminal sacrifice and in rats which died or were sacrificed in extremis during the course of study (TS/DOS), possible compound related lesions included an increased incidence of masses, nodules or raised lesions in the liver, an increased incidence of yellow or pale liver foci or lesions and an increased incidence of mottled livers and testicular masses in male rats from the 300 ppm group. There were no findings suggestive of a compound effect in TS/DOS female rats from the 300 or 30 ppm groups or in male rats from the 30 ppm group.

Other gross pathologic findings were typical of findings in ageing rats of this strain. These included mammary masses, pituitary foci and masses, ulcers on the hind footpads, pale livers and pale, pitted and enlarged kidneys.

Organ Weights

There were statistically significant ($p < 0.05$) variations in absolute and relative weights (organ:body or organ:brain weight ratios) of a number of organs in 300 ppm group male rats sacrificed at the 1 year interim. Except for an increase in the liver:body weight ratio, these variations were not considered toxicologically significant. The increase in liver:body weight ratio correlated with compound related morphologic liver changes. The mean absolute liver weight and the liver:brain weight ratio in these rats also were increased but not to a statistically significant degree. There were no statistically significant variations in organ weights in 300 ppm females sacrificed at the 1 year interim.

None of the several statistically significant organ weight variations in rats sacrificed at the 2 year termination occurred in target organs or showed a dose response; none was considered toxicologically significant.

Histopathology

Compound related microscopic changes were observed in the liver of male rats from the 300 ppm group at the 1 year interim sacrifice and in liver of male and female TS/DOS rats at both the 300 and 30 ppm levels. The principal compound related liver change was megalocytosis, which was characterized by an increase in size of liver parenchymal cells due to increased cytoplasmic volume. The increased cytoplasm was of a finely granular "ground glass" appearance. The coarser cytoplasmic organelles were relatively decreased and were displaced

to the cell membrane. The nucleus:cytoplasm ratio was decreased by the increase in cytoplasm in affected cells. In affected livers, most or all lobules were involved and the centrilobular cells were more severely affected. At the 1 year interim, megalocytosis occurred to a minimal to moderate degree in 12/15 males from the 300 ppm group. No females were affected at the 1 year interim. In TS/DOS rats, megalocytosis to a minimal to moderate degree occurred in 40/50 males at the 300 ppm level and to a minimal to mild degree in 8/50 females at the same level. At the 30 ppm level in TS/DOS rats, megalocytosis to a minimal degree occurred in 6/50 males and in 1/50 females. In more markedly involved livers, the megalocytic hepatocytes were frequently vacuolated with multiple small spherical cytoplasmic vacuoles which in life probably contained lipid. Livers which had appreciable involvement with megalocytosis and cytoplasmic vacuolation also commonly had focal areas of necrosis. This association of hepatocyte vacuolation and necrosis with megalocytosis suggests that the progression of lesions is megalocytosis to fatty degeneration to necrosis. Incidence of hyperplastic nodules was also increased at 300 ppm, indicating regeneration also occurred. The association of hepatocyte vacuolation and focal necrosis with megalocytosis was more clear-cut at the 1 year interim than in TS/DOS rats because of the normally higher background incidence of the former in older rats. Cystoid degeneration, characterized by areas of multilocular microcysts in the liver parenchyma, also was increased in male TS/DOS rats from the 300 ppm group. Incidence of this lesion was 4/50, 28/50 and 7/50 in the 0, 300 and 30 ppm males, respectively. The increased incidence of cystoid degeneration, megalocytosis and portal mononuclear cell infiltration in the 300 ppm dosage group was statistically significant at the 5% level in male rats. In females from the 300 ppm level, only the increased incidence of megalocytosis was statistically significant.

Occurrence of these histomorphologic changes in the liver correlates with elevation of alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase levels observed in male rats. The markedly reduced incidence and severity of histomorphologic liver changes in females parallels the absence of alterations in liver specific serum biochemical values in females.

There was no direct or indirect compound effect in tissues other than liver at the 1 year interim sacrifice. In TS/DOS rats, changes which were considered secondarily compound related, probably through to FC-143 altered liver metabolism of endogenous steroids, were observed in the adrenals, ovaries and

testes. In the adrenals, an increased incidence of nodular hyperplasia of the cortex occurred in males at the 300 ppm level. Incidence of this finding in males was 2/49, 9/50 and 1/50 in 0, 300 and 30 ppm males, respectively. The increased incidence of nodular hyperplasia in males at the 300 ppm level was not statistically significant, however. In females, tubular hyperplasia of the ovarian stroma occurred in 0/48, 15/47 and 7/50 rats from the 0, 300 and 30 ppm groups, respectively. This incidence was statistically significant at both the 300 and 30 ppm levels. Tubular hyperplasia of the stroma was a non-neoplastic diffuse increase in tubular elements of the ovarian stroma which was usually bilateral and associated with absent or markedly reduced follicular development.

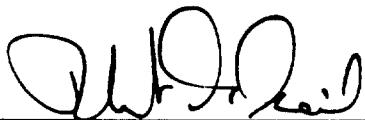
In male rats, there was a statistically significant, compound related occurrence of benign Leydig cell tumors of the testes at the 300 ppm level. Incidence of Leydig cell tumors was 0/49, 7/50 and 2/50 at the 0, 300 and 30 ppm levels, respectively. Although occurrence of 2 Leydig cell tumors at 30 ppm is also suggestive of a compound effect, these neoplasms are not uncommon in untreated rats, although none were found in control rats from this study. The occurrence of Leydig cell tumors correlated with the observations of testicular masses at necropsy. Testes which contained Leydig cell tumors were usually totally aspermic. Mineralization of vessels within the testes occurred in 0/49, 9/50 and 3/50 rats from the 0, 300 and 30 ppm groups respectively. The increased incidence of testicular vascular mineralization at 300 ppm was statistically significant. In female rats, there was a statistically significant increased incidence in mammary fibroadenomas at the 300 ppm level. Incidence of this tumor was 10/46, 21/44 and 19/45 at the 0, 300 and 30 ppm levels, respectively.

An increased incidence of focal accumulations of foamy alveolar macrophages occurred in the lungs of males from the 300 and 30 ppm groups. The incidence of this finding was 10/50, 31/50 and 16/50 at the 0, 300 and 30 ppm levels respectively. The increased incidence of alveolar macrophages at 300 ppm was statistically significant. In females, the incidence of 14/50, 19/50 and 10/50 at the 0, 300 and 30 ppm levels did not have a statistically significant increase in treated animals. Other microscopic lesions in tissues from FC-143 treated rats were typical of naturally occurring inflammatory, degenerative and neoplastic lesions in an ageing population of Charles River CD rats. Commonly occurring inflammatory lesions included chronic nonsuppurative myocarditis, with associated myocardial fibrosis, mononuclear inflammatory cell infiltrate into the portal

triads of the liver which was frequently associated with portal bile duct proliferation and perivascular mononuclear inflammatory cell infiltrate and multifocal chronic interstitial pneumonia in the lung. A high incidence of chronic sialadenitis occurred in male rats from the 300 and 30 ppm groups sacrificed at termination. The appearance of the salivary glands in these animals was typical of glands in the recovery stages of dacryosialadenitis, a common, highly contagious disease of laboratory rats. Its peculiar incidence in this study was attributed to the housing arrangement. Both affected groups were housed in the same room and the unaffected groups were housed in other rooms. Although the incidence of sialadenitis in male rats from the 300 and 30 ppm groups was statistically significant, this increase was not considered compound related since it was explainable by the housing arrangement. Other statistically significant variations in incidence of non-neoplastic lesions which were not considered of toxicological significance included decreased chronic myocarditis in females from the 30 ppm group, increased lung hemorrhage in males from the 300 ppm group, decreased perivascular mononuclear cell infiltrate in the lung in males from the 300 ppm group and in males and females from the 30 ppm group and decreased splenic hemosiderosis in females from the 300 ppm group and in males and females from the 30 ppm group.

Some of the more commonly occurring degenerative lesions in this study included adrenal cortical vacuolation and sinusoidal ectasia, focal mineralization in large pulmonary artery branches in the lung, focal acinar atrophy in the pancreas and chronic progressive nephropathy. Pituitary adenomas were the most common neoplasm in male and female rats.

Overall, the health of the rats in this study was excellent, with organs free of lesions of common infectious diseases which would have had an impact upon survival or the validity of the study.



Robert G. Geil, D.V.M.
Diplomate, American College
of Veterinary Pathologists

9/27/81
Date

TABLE OF CONTENTS

<u>Table Number</u>		<u>Page</u>
1	Macroscopic Incidence for Males - 1 Year Interim.....	1
2	Macroscopic Incidence for Females - 1 Year Interim.....	2
3	Macroscopic Incidence for Males.....	3-5
4	Macroscopic Incidence for Females.....	6-7
5	Non-neoplastic Incidence for Males - 1 Year Interim.....	8-11
6	Non-neoplastic Incidence for Females - 1 Year Interim.....	12-15
7	Non-neoplastic Incidence for Males.....	16-24
8	Non-neoplastic Incidence for Females.....	25-33
9	Neoplastic Incidence for Males - 1 Year Interim.....	34
10	Neoplastic Incidence for Females - 1 Year Interim.....	35 -
11	Neoplastic Incidence for Males.....	36-37
12	Neoplastic Incidence for Females.....	38-39

Appendix

<u>Table Number</u>		<u>Page</u>
1	Single Tabulated Animal Report - 1 Year Interim.....	1-27
2	Single Tabulated Animal Report.....	28-214
3	Tissue Inventory - 1 Year Interim.....	215-218
4	Tissue Inventory.....	21 ⁰ -242

Macroscopic Incidence for Males
 Riker Laboratories, Inc. SM

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Project Number: 0201CR0012 Species: Rat

Site/ Description	Group 1	Group 5
No visible lesions	0	0
Eye		
opacity		1
Pituitary		
mass		1
Liver		
pale/tan color	2	0
Mesentery		
fat necrosis	1	
Kidney		
hydronephrosis	1	
cystic lesion	1	
depressed area		1
Testis		
small		1
Spleen		
nodule		1
Soft Tissue (leg)		
swollen foot	1	

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Project Number: 0201CR0012 Species: Rat

Site/ Description	Group 1	Group 5
No visible lesions	5	9
Eye		
atrophy	1	2
Pituitary		
enlarged	3	
Adrenal		
enlarged	1	
Liver		
pale/tan*	1	1
Lymph Node (mesenteric)		
hemorrhagic		1
Mesentery		
mass	1	
Kidney		
hydronephrosis	1	1
calculi		1
Ureter		
dilatation, calculi		1
Urinary Bladder		
distended, calculi		1
Uterus		
cystic lesion	1	
enlarged	1	
dilated, fluid filled		1
Mammary Gland		
mass	1	3
Skin		
hair loss	2	

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 200 ppm

* includes "possibly"

Macroscopic Incidence for Males
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

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Table: 3

Project Number: 0231CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
No visible lesions	11	12	18
Brain			
dark area	1		
Eye			
opacity/cloudy		1	4
hypopyon		1	
Pituitary			
mass/enlarged/raised lesion	7	3	11
dark/hemorrhagic/red foci	4	2	2
Thyroid			
enlarged*	1	1	1
Adrenal			
enlarged/mass	2	2	3
Throat (internal)			
fluid filled	1		
Thymus			
enlarged*	1	2	
hemorrhagic/hemorrhagic lesion		1	
mass			1
Lung			
mottled	1		
frothy tracheal exudate	1		
consolidation*			1
mass/raised lesion		1	
multiple white lesions			1
Heart			
flaccid/flabby	1		
enlarged*			1
pale	1		
Abdomen (internal)			
gas, gastrointestinal tract	1	1	
stomach empty of food	1		
mass, omentum	1		
fatty tumor			1
Stomach			
edema/thickened wall	1		1
erosions/ulcerations*	1		2
Small Intestine			
enlarged, reddened Peyer's patches		1	
Large Intestine			
enlarged, reddened Peyer's patches		1	
impaction			1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

* includes "possibly"

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Project Number: 0201CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
Pancreas			
mass/nodule	2		
Liver			
pale/pale lobes*	10	3	7
mass/nodule/raised lesion	3	7	1
mottled*		6	5
yellow/pale foci/lesion	1	9	
enlarged	1	1	
possible congestion			1
Spleen			
enlarged	3	2	3
raised lesion	1		
pale foci	2		
pale, depressed area	1		
small*		1	
Lymph node (mesenteric/abdominal)			
enlarged	2	2	2
greenish color			1
Mesentery			
nodular/enlarged/thickened vessels	1		2
mass		1	1
Kidney			
enlarged, pale, pitted	3	1	2
enlarged, pitted		1	
pale, pitted	2	1	1
pale, enlarged*	1		3
pale		1	
pale area	1		
hydronephrosis, pelvic dilatation	2	3	
cystic/polycystic	3		2
Urinary Bladder			
distended	1	2	
hematuria/filled with reddish/dark fluid		1	
hemorrhagic wall	1		
Testis/Epididymis			
small	4	5	6
mass		6	1
Penis			
swollen		1	
Mammary Gland			
mass		1	2

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

* includes "possibly"

Macroscopic Incidence for Males
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 3

Project Number: 0201CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
Skin			
ulcers/inflamed/circular/raised lesions, hind footpads	7	1	4
dermatitis/ulcer/lesion/inflamed area*	1		2
moist area	1		
hair loss	1		1
mass/thickening	4	1	1
abscess	1		1
inflamed fat			1
Soft Tissue (neck)			
mass		1	1
Soft Tissue (thorax)			
mass	1		
Soft Tissue (leg)			
swollen paws/feet	1		2
Bone			
swollen joints	1	1	

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 5 FC-143 30 ppm

* includes "possibly"

Macroscopic Incidence for Females
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

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Project Number: 0271CROC12 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
No visible lesions	4	3	3
Eye			
opacity/cloudy	3		
inflammation	1		
atrophy	1		
Pituitary			
mass/enlarged/raised lesion	25	25	25
hemorrhagic/dark lesion		2	3
Adrenal			
enlarged	8	3	7
mass/raised lesion			1
pale	1		
small		1	
Lung			
mottled	1		
consolidation	2	1	1
nodule	1		1
pale	1		
Lymph Node (bronchial)			
enlarged	1		
Heart			
enlarged*		1	1
Abdomen (internal)			
gas, gastrointestinal tract			1
bloody fluid filled			2
nodular tissue, omentum, mesentery			1
Stomach			
ulcerations/erosions	1		
red mucosal areas/reddened	2		
Small Intestine			
inflamed	1		
ulceration/ulcerated outpouching			2
Large Intestine			
impaction	1		
Pancreas			
mass/nodule	1		1
Liver			
pale*	10	3	6
mass/nodule/raised lesion	2	2	
mottled	4	1	1
circular lesion/pale foci/			
pale lesion/yellowish lesion		1	2
enlarged*	2	1	2

Titles:

Group 1 CONTROL 0 ppm
Group 5 FC-143 300 ppm
Group 6 FC-143 30 ppm

* includes "possibly"

Macroscopic Incidence for Females
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 4

Project Number: 0281CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
Liver (continued)			
dark red area/lobe	1		
rough/irregular surface	1		
Spleen			
enlarged*	5		2
Lymph node (mesenteric/abdominal)			
enlarged	2	1	1
reddened	1		
cystic		1	
Kidney			
enlarged, pale, pitted	2		
enlarged*	1		
pale, pitted	1	2	1
pitted	2		
pale*			1
cyst	3		1
Urinary Bladder			
enlarged	1		
calculi	1		
thickened walls	1	1	
Ovary			
mass	1		
Uterus			
enlarged			1
filled with dark/bloody fluid			1
mass	1		1
dark area/lesion	2		1
hemorrhagic lesion			1
Mammary Gland			
mass/nodule	27	26	37
milk cyst		3	3
Skin			
raised/inflamed/ulcerated lesion, footpad		1	
mass	1	1	
raised lesion	1		
hair loss/thinning	2		3
circular lesion	1		
Soft Tissues (neck)			
mass			1
reddened, gland like structures	1		
Soft Tissues (leg)			
swollen foot	1		

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 20 ppm

* includes "possibly"

Non-Neoplastic Incidence for Males
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 5

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Adrenal	(15)	(15)
Within normal limits	12	15
Cortical vacuolation	1	0
mild	1	0
Nodular hyperplasia, cortex	1	0
moderate	1	0
Sinusoidal ectasia, cortex	1	0
moderate	1	0
Aorta	(15)	(11)
Within normal limits	15	11
Bone Marrow	(14)	(15)
Within normal limits	14	15
Brain	(15)	(15)
Within normal limits	15	15
Esophagus	(15)	(15)
Within normal limits	15	15
Eye	(15)	(15)
Within normal limits	15	13
Cataract	0	1
Retinal atrophy	0	1
minimal	0	1
Heart	(15)	(15)
Within normal limits	14	12
Myocardial fibrosis	0	2
minimal	0	1
mild	0	1
Myocarditis, chronic nonsuppurative	1	2
minimal	0	2
mild	1	0
Kidney	(15)	(15)
Within normal limits	5	4
Calculus	1	0
Chronic progressive nephropathy	8	10
minimal	5	6
mild	3	4
Cyst	1	0
Hydronephrosis	1	0
moderate	1	0
Mineralization	0	1
Nephritis, interstitial, chronic	1	0
mild	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

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 Table: 5

Project Number: 0201CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1	Group 5
Kidney (continued)		
Pyelitis, acute	1	1
minimal	1	0
mild	0	1
Large Intestine	(15)	(15)
Within normal limits	15	14
Nematodiasis	0	1
Liver	(15)	(15)
Within normal limits	7	0
Hepatocyte alteration, vacuolated	2	0
minimal	1	0
mild	1	0
Hepatocyte vacuolation	0	2
minimal	0	1
mild	0	1
Megalocytosis	0	12
minimal	0	7
mild	0	3
moderate	0	2
Necrosis	0	0
minimal	0	2
mild	0	4
Pigment, Kupfer cell	0	2
minimal	0	1
mild	0	1
Portal bile duct proliferation	5	1
minimal	1	0
mild	4	1
Portal mononuclear cell infiltrate	7	13
minimal	1	4
mild	6	9
Lung	(15)	(15)
Within normal limits	1	2
Alveolar macrophages	3	6
mild	3	6
Atelectasis	1	0
mild	1	0
Hemorrhage	6	3
mild	6	2
moderate	0	1
Hyperplasia, septal cell	1	0
mild	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

() = Total Examined

Project Number: 0261CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1	Group 5
Lung (continued)		
Perivascular mononuclear infiltrate	2	1
mild	2	1
Pneumonia, interstitial, chronic	3	2
minimal	1	0
mild	2	2
Vascular mineralization	7	8
minimal	4	1
mild	3	7
Lymph Node (mesenteric)	(13)	(13)
Within normal limits	13	11
Hemorrhage	0	2
minimal	0	1
mild	0	1
Mammary Gland	(3)	(0)
Within normal limits	3	0
Mesentery	(1)	(0)
Necrosis, fat	1	0
marked	1	0
Steatitis, chronic	1	0
moderate	1	0
Pancreas	(15)	(15)
Within normal limits	11	15
Acinar atrophy	3	0
mild	2	0
moderate	1	0
Pancreatitis, chronic	3	0
mild	3	0
Parathyroid	(7)	(3)
Within normal limits	7	3
Pituitary	(14)	(12)
Within normal limits	13	12
Cyst	1	0
Prostate	(15)	(13)
Within normal limits	15	12
Prostatitis, chronic	0	1
minimal	0	1
Salivary Gland	(15)	(14)
Within normal limits	15	14
Small Intestine	(15)	(15)
Within normal limits	15	15

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Males (continued)

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 5

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Spinal Cord	(14)	(15)
Within normal limits	14	15
Spleen	(15)	(15)
Within normal limits	15	14
Hemosiderosis	0	1
mild	0	1
Stomach	(14)	(15)
Within normal limits	14	15
Testis/Epididymis	(15)	(15)
Within normal limits	15	13
Tubule atrophy, aspermatogenesis	0	2
marked	0	2
Thyroid	(11)	(13)
Within normal limits	11	13
Trachea	(15)	(15)
Within normal limits	15	15
Urinary Bladder	(15)	(13)
Within normal limits	15	13

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Females
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 6

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Adrenal	(15)	(15)
Within normal limits	10	11
Cortical degeneration	2	1
mild	2	1
Sinusoidal ectasia, cortex	4	3
mild	3	3
marked	1	0
Aorta	(14)	(13)
Within normal limits	14	13
Bone Marrow	(15)	(15)
Within normal limits	15	15
Brain	(15)	(15)
Within normal limits	15	15
Esophagus	(15)	(13)
Within normal limits	15	13
Eye	(15)	(15)
Within normal limits	14	13
Atrophy	1	2
marked	1	2
Panophthalmitis	1	2
marked	1	2
Heart	(15)	(15)
Within normal limits	14	14
Myocarditis, chronic nonsuppurative	1	1
minimal	1	0
mild	0	1
Kidney	(15)	(15)
Within normal limits	6	9
Calculus	4	2
mild	1	1
moderate	1	0
Chronic progressive nephropathy	1	3
mild	1	3
Cyst	1	0
mild	1	0
Hydronephrosis	1	1
moderate	1	0
marked	0	1
Hyperplasia, pelvic epithelium	1	0
mild	1	0
Mineralization	0	1
mild	0	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 6

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Kidney (continued)		
Pelvic mineralization	4	1
minimal	4	0
mild	0	1
Pyelitis, chronic	0	1
moderate	0	1
Large Intestine	(14)	(14)
Within normal limits	12	12
Nematodiasis	2	2
Liver	(15)	(15)
Within normal limits	6	3
Hepatocyte alteration, vacuolated	1	0
mild	1	0
Hepatocyte vacuolation	5	11
minimal	3	1
mild	2	10
Portal bile duct proliferation	2	1
mild	2	1
Portal mononuclear cell infiltrate	2	2
minimal	1	0
mild	1	2
Lung	(15)	(15)
Within normal limits	3	5
Alveolar macrophages	1	1
mild	1	1
Hemorrhage	11	9
mild	9	7
moderate	2	2
Perivascular mononuclear infiltrate	1	0
mild	1	0
Pneumonia, interstitial, chronic	1	0
mild	1	0
Vascular mineralization	1	1
mild	1	1
Lymph Node (mesenteric)	(12)	(13)
Within normal limits	12	12
Hemorrhage	0	1
marked	0	1
Mammary Gland	(15)	(13)
Within normal limits	13	10
Galactoceles	2	1

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 5

Project Number: 0231CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1	Group 5
Mesentery	(1)	(0)
Macrosis, fat	1	0
moderate	1	0
Steatitis, chronic	1	0
moderate	1	0
Ovary	(15)	(15)
Within normal limits	14	15
Cyst	1	0
Pancreas	(15)	(15)
Within normal limits	14	15
Pancreatitis, chronic	1	0
mild	1	0
Parathyroid	(6)	(9)
Within normal limits	6	9
Pituitary	(15)	(14)
Within normal limits	14	14
Salivary Gland	(15)	(15)
Within normal limits	15	15
Skin	(2)	(0)
Within normal limits	2	0
Small Intestine	(15)	(15)
Within normal limits	15	15
Spinal Cord	(14)	(15)
Within normal limits	14	15
Spleen	(15)	(15)
Within normal limits	14	15
Hemosiderosis	1	0
mild	1	0
Stomach	(15)	(15)
Within normal limits	15	15
Thyroid	(14)	(13)
Within normal limits	14	13
Trachea	(15)	(15)
Within normal limits	15	15
Ureter	(6)	(1)
Calculus	0	1
Dilatation	0	1
marked	0	1
Inflammation, chronic	0	1
moderate	0	1

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Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Females (continued)

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 6

Project Number: 0281CRO012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Urinary Bladder	(12)	(15)
Within normal limits	12	14
Cystitis, chronic	0	1
moderate	0	1
Epithelial hyperplasia, simple	0	1
mild	0	1
Uterus	(15)	(15)
Within normal limits	12	13
Cystic glands	1	0
marked	1	0
Endometritis, chronic	0	1
mild	0	1
Hydrometra	0	2
moderate	0	1
Hyperplasia, glandular epithelium	2	0
mild	2	0
Metaplasia, squamous	2	0
mild	2	0

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

() = Total Examined

Non-Neoplastic Incidence for Males
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0231CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Adrenal	(15)	(34)	(6)	(44)	(14)	(36)
Within normal limits	6	13	2	12	8	18
Cortical degeneration	0	0	0	0	0	2
moderate	0	0	0	0	0	2
Cortical vacuolation	7	17	2	11	4	5
minimal	0	2	1	2	0	0
mild	4	13	1	5	3	5
moderate	3	2	0	4	0	0
marked	0	0	0	0	1	0
Medullary cell hyperplasia	2	6	1	6	0	3
minimal	0	0	0	2	0	0
mild	1	4	1	4	0	3
moderate	1	2	0	0	0	0
Nodular hyperplasia, cortex	0	2	1	5	0	1
minimal	0	0	1	0	0	0
mild	0	1	0	7	0	0
moderate	0	1	0	1	0	1
Sinusoidal ectasia, cortex	4	7	0	16	5	8
minimal	0	2	0	2	0	1
mild	2	3	0	10	4	5
moderate	2	2	0	3	1	2
marked	0	0	0	1	0	0
Aorta	(15)	(34)	(6)	(43)	(0)	(0)
Within normal limits	13	34	6	43	0	0
Mineralization	1	0	0	0	0	0
mild	1	0	0	0	0	0
Necrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Bone	(0)	(2)	(0)	(1)	(0)	(1)
Arthritis, synovitis; joints	0	2	0	1	0	1
moderate	0	0	0	1	0	1
marked	0	2	0	0	0	0
Bone Marrow	(15)	(32)	(6)	(42)	(0)	(0)
Within normal limits	15	32	5	42	0	0
Brain	(16)	(34)	(6)	(44)	(0)	(1)
Within normal limits	14	33	5	44	0	0
Abscess	1	0	0	0	0	0
mild	1	0	0	0	0	0
Hemorrhage	1	0	0	0	0	0
moderate	1	0	0	0	0	0

Titles:

Group 1 CONTROL 0 ppm
Group 5 FC-143 300 ppm
Group 6 FC-143 30 ppm

() = Total Examined
DOS= Unscheduled Death(s)
SAC= Protocol Scheduled Sacrifice(s)

141

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Esophagus	(15)	(33)	(6)	(41)	(13)	(32)
Within normal limits	15	33	5	41	13	32
Eye	(12)	(33)	(6)	(44)	(2)	(3)
Within normal limits	12	32	4	41	1	0
Cataract	0	0	0	0	1	2
Keratitis, acute	0	0	1	0	0	0
marked	0	0	1	0	0	0
Keratitis, chronic	0	0	0	1	0	1
mild	0	0	0	0	0	1
moderate	0	0	0	1	0	0
Phthisis bulbi	0	0	0	1	0	0
marked	0	0	0	1	0	0
Retinal atrophy	0	1	0	1	0	1
mild	0	1	0	0	0	0
marked	0	0	0	1	0	0
Heart	(16)	(34)	(6)	(44)	(14)	(36)
Within normal limits	8	23	6	27	9	19
Endocarditis, chronic	0	0	0	0	0	1
marked	0	0	0	0	0	1
Myocardial fibrosis	3	2	0	1	1	6
mild	3	2	0	1	1	6
Myocarditis, chronic nonsuppurative	4	10	0	17	5	13
minimal	0	2	0	5	0	1
mild	4	7	0	12	4	12
moderate	0	1	0	0	1	0
Kidney	(16)	(34)	(6)	(44)	(14)	(36)
Within normal limits	4	0	1	2	3	2
Calculus	0	1	1	0	0	1
minimal	0	1	0	0	0	0
mild	0	0	1	0	0	0
Chronic progressive nephropathy	10	34	3	40	9	34
minimal	1	4	1	9	2	2
mild	5	16	0	23	3	22
moderate	2	11	1	6	2	7
marked	2	3	1	2	2	3
Cyst	1	3	0	1	1	1
moderate	0	1	0	1	1	0
marked	1	2	0	0	0	0
Hydronephrosis	1	2	0	1	0	0
mild	1	0	0	1	0	0
moderate	0	2	0	0	0	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0221CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Kidney (continued)						
Hyperplasia, pelvic epithelium	0	0	0	3	0	0
mild	0	0	0	2	0	0
moderate	0	0	0	1	0	0
Mineralization	0	0	0	1	0	0
mild	0	0	0	1	0	0
Nephrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Papillary necrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Pelvic mineralization	1	3	0	3	4	6
minimal	0	1	0	1	0	1
mild	1	2	0	2	3	3
moderate	0	0	0	0	0	2
marked	0	0	0	0	1	0
Protein resorption droplets	0	0	0	0	1	0
mild	0	0	0	0	1	0
Pyelitis, acute	0	0	0	0	1	2
mild	0	0	0	0	1	2
Pyelonephritis, acute	1	0	0	3	0	0
mild	1	0	0	2	0	0
moderate	0	0	0	1	0	0
Vacuolation, conv. tub. epitheium	0	0	0	0	1	0
minimal	0	0	0	0	1	0
Large Intestine	(14)	(34)	(6)	(44)	(1)	(0)
Within normal limits	14	28	6	44	1	0
Nematodiasis	0	6	0	0	0	0
Liver	(16)	(34)	(6)	(44)	(14)	(36)
Within normal limits	2	0	0	0	1	6
Cystoid degeneration	0	4	1	27	2	5
minimal	0	1	0	2	0	1
mild	0	2	1	22	2	4
moderate	0	1	0	3	0	0
Hematopoiesis, extramedullary	0	0	0	0	1	0
mild	0	0	0	0	1	0
Hepatocyte alteration, basophilic	0	2	0	6	0	1
minimal	0	0	0	1	0	0
mild	0	1	0	2	0	1
moderate	0	1	0	3	0	0
Hepatocyte alteration, vacuolated	1	9	0	10	1	10
mild	1	7	0	8	1	9
moderate	0	2	0	2	0	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

143

000530

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Liver (continued)						
Hepatocyte vacuolation	8	14	2	10	6	2
minimal	0	1	1	1	0	1
mild	4	13	0	8	3	1
moderate	2	0	1	1	3	0
marked	2	0	0	0	0	0
Hyperplasia, Kupffer cell	0	0	0	0	0	1
moderate	0	0	0	0	0	1
Hyperplastic nodule	0	0	0	3	0	0
Megalocytosis	0	0	2	33	0	6
minimal	0	0	2	24	0	6
mild	0	0	0	10	0	0
moderate	0	0	0	4	0	0
Mononuclear cell infiltration	0	0	0	0	0	1
mild	0	0	0	0	0	1
Necrosis	2	1	2	3	2	3
minimal	0	0	0	1	0	1
mild	1	0	1	1	1	2
moderate	1	1	1	1	1	0
Portal bile duct proliferation	6	21	1	14	5	10
minimal	0	0	0	1	0	0
mild	5	21	1	13	5	10
moderate	1	0	0	0	0	0
Portal mononuclear cell infiltrate	7	30	5	43	7	25
minimal	0	2	0	2	0	0
mild	7	28	5	41	7	25
Lung	(15)	(34)	(5)	(44)	(14)	(35)
Within normal limits	0	1	0	0	1	2
Alveolar macrophages	5	5	4	27	6	10
minimal	1	2	0	0	0	0
mild	4	2	3	25	6	8
moderate	0	1	0	2	0	2
marked	0	0	1	0	0	0
Atelectasis	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Edema	3	0	0	0	0	0
mild	1	0	0	0	0	0
moderate	1	0	0	0	0	0
marked	1	0	0	0	0	0
Fibrosis	1	0	0	1	0	0
mild	1	0	0	0	0	0
moderate	0	0	0	1	0	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

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Table: 7

Project Number: 0201CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Lung (continued)						
Granuloma	0	0	1	1	0	0
Hemorrhage	0	4	2	20	3	5
mild	2	1	0	5	3	4
moderate	1	0	1	13	0	2
marked	3	1	1	2	0	0
Medial hypertrophy, arteries	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Necrosis	1	0	0	0	0	0
marked	1	0	0	0	0	0
Peribronchial lymphoid hyperplasia	0	1	0	0	0	0
mild	0	1	0	0	0	0
Perivascular mononuclear infiltrate	2	10	0	7	0	3
minimal	0	2	0	4	0	0
mild	2	14	0	2	0	3
moderate	0	3	0	1	0	0
Pneumonia, interstitial, acute	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Pneumonia, interstitial, chronic	2	14	1	5	0	5
mild	1	11	1	5	0	5
moderate	1	3	0	0	0	0
Thrombus	1	0	1	0	0	0
Vascular mineralization	10	33	4	43	11	32
minimal	0	2	0	0	0	0
mild	10	31	4	41	11	32
moderate	0	0	0	2	0	0
Lymph Node (mesenteric)	(12)	(33)	(6)	(44)	(0)	(1)
Within normal limits	10	29	5	33	0	1
Granuloma	0	0	0	1	0	0
moderate	0	0	0	1	0	0
Hemorrhage	2	4	0	4	0	0
minimal	1	2	0	1	0	0
mild	1	1	0	3	0	0
Sinusoidal ectasia	0	0	0	1	0	0
mild	0	0	0	1	0	0
Mammary Gland	(0)	(0)	(0)	(0)	(1)	(0)
Within normal limits	0	0	0	0	1	0
Mesentery	(0)	(2)	(0)	(0)	(1)	(1)
Polyarteritis	0	2	0	0	1	1
marked	0	2	0	0	1	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

145

000532

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Pancreas	(13)	(33)	(6)	(43)	(12)	(34)
Within normal limits	10	24	4	27	10	21
Acinar atrophy	2	4	0	11	1	8
minimal	0	0	0	1	1	1
mild	1	2	0	6	0	5
moderate	1	1	0	4	0	2
marked	0	1	0	0	0	0
Hyperplasia, acinar cell	0	0	1	1	0	2
mild	0	0	0	1	0	1
moderate	0	0	1	0	0	1
Hyperplasia, islet cell	0	2	1	3	1	1
mild	0	0	0	0	1	1
moderate	0	2	1	3	0	0
Polyarteritis	0	4	0	2	0	3
minimal	0	0	0	0	0	1
moderate	0	2	0	2	0	2
marked	0	2	0	0	0	0
Parathyroid	(6)	(16)	(5)	(31)	(7)	(26)
Within normal limits	6	16	5	29	7	26
Pituitary	(15)	(33)	(5)	(41)	(13)	(34)
Within normal limits	7	13	3	28	3	20
Cyst	2	2	0	2	1	4
Hyperplasia	0	2	0	0	0	2
mild	0	2	0	0	0	1
Prostate	(13)	(33)	(6)	(43)	(13)	(35)
Within normal limits	10	27	5	40	11	35
Edema	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Prostatitis, acute	3	6	1	3	2	1
minimal	0	0	0	1	0	0
mild	1	2	0	0	1	1
moderate	1	3	0	1	0	0
marked	1	1	1	1	1	0
Salivary Gland	(12)	(32)	(5)	(41)	(10)	(34)
Within normal limits	12	31	4	25	10	21
Sialadenitis, acute	0	0	0	1	0	1
moderate	0	0	0	1	0	0
marked	0	0	0	0	0	1
Sialadenitis, chronic	0	1	0	14	0	12
minimal	0	1	0	0	0	0
mild	0	0	0	0	0	1
moderate	0	0	0	7	0	6

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Salivary Gland (continued)						
Sialadenitis, chronic						
marked	0	0	0	7	0	5
Skin	(3)	(7)	(0)	(2)	(5)	(4)
Abscess	0	0	0	0	1	0
Pododermatitis, ulcerative	3	5	0	1	2	2
marked	3	5	0	1	2	2
Ulcer	1	0	0	0	0	1
marked	1	0	0	0	0	1
Small Intestine	(14)	(34)	(6)	(44)	(1)	(0)
Within normal limits	13	32	5	44	1	0
Polyarteritis	0	2	0	0	0	0
moderate	0	1	0	0	0	0
marked	0	1	0	0	0	0
Spinal Cord	(15)	(32)	(6)	(42)	(0)	(0)
Within normal limits	15	32	5	42	0	0
Spleen	(16)	(34)	(6)	(44)	(14)	(35)
Within normal limits	5	20	1	25	8	35
Atrophy	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Fibrosis	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Hematopoiesis, extramedullary, increased	4	0	1	1	1	0
mild	2	0	0	1	0	0
moderate	1	0	1	0	0	0
marked	1	0	0	0	1	0
Hemosiderosis	5	11	3	19	4	0
mild	5	11	3	19	4	0
Necrosis	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Polyarteritis	0	0	0	0	0	1
moderate	0	0	0	0	0	1
Stomach	(16)	(33)	(6)	(44)	(14)	(35)
Within normal limits	11	33	5	43	11	35
Edema	3	0	0	0	0	0
moderate	2	0	0	0	0	0
marked	1	0	0	0	0	0
Gastritis, acute	0	0	1	0	0	0
mild	0	0	1	0	0	0
Ulcer	1	0	0	0	3	0
marked	1	0	0	0	3	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Testis/Epididymis	(16)	(33)	(6)	(44)	(14)	(35)
Within normal limits	13	26	5	23	7	25
Granuloma, spermatic	0	0	0	0	1	0
Leydig cell hyperplasia	0	0	0	1	1	1
mild	0	0	0	1	0	1
moderate	0	0	0	0	1	0
Mineralization	0	1	0	2	0	0
mild	0	1	0	2	0	0
Polyarteritis	1	5	0	2	1	5
mild	1	1	0	0	0	2
moderate	0	1	0	2	1	2
marked	0	3	0	0	0	1
Tubule atrophy, aspermatogenesis	3	4	1	10	5	5
mild	1	1	0	1	3	0
moderate	1	1	0	3	1	1
marked	1	2	1	6	1	4
Vascular mineralization	0	0	0	9	3	0
mild	0	0	0	7	3	0
moderate	0	0	0	2	0	0
Thymus	(1)	(0)	(1)	(1)	(1)	(0)
Hemorrhage	0	0	0	1	0	0
marked	0	0	0	1	0	0
Thyroid	(12)	(31)	(5)	(42)	(12)	(35)
Within normal limits	11	25	4	33	10	26
Cyst, colloid	0	1	1	1	0	1
mild	0	1	1	0	0	0
Follicular hyperplasia, cystic	0	1	0	1	1	1
moderate	0	1	0	1	0	0
marked	0	0	0	0	1	1
Hyperplasia, C cell	0	1	0	1	1	5
mild	0	1	0	1	1	3
moderate	0	0	0	0	0	2
Ultimobranchial cyst	1	1	0	3	1	2
Trachea	(15)	(34)	(6)	(42)	(13)	(35)
Within normal limits	15	34	6	42	13	35
Urinary Bladder	(13)	(33)	(6)	(44)	(14)	(35)
Within normal limits	10	32	5	41	11	35
Calculus	0	0	0	0	1	0
Cystitis, acute	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Cystitis, chronic	0	0	0	0	1	0
minimal	0	0	0	0	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

148

000535

Non-Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 *FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Urinary Bladder (continued)						
Epithelial hyperplasia, papillary	0	0	0	0	1	0
mild	0	0	0	0	1	0
Epithelial hyperplasia, simple	2	1	1	3	3	0
minimal	0	0	0	1	0	0
mild	2	1	1	2	3	0
Hemorrhage	1	0	0	1	0	0
minimal	0	0	0	1	0	0
marked	1	0	0	0	0	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

149

Non-Neoplastic Incidence for Females
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 9

Project Number: 0291CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Adrenal	(25)	(25)	(20)	(29)	(26)	(24)
Within normal limits	2	0	4	2	3	1
Cortical atrophy	0	0	1	2	0	0
moderate	0	0	1	2	0	0
Cortical degeneration	2	5	1	0	4	4
mild	1	0	0	0	1	2
moderate	1	3	0	0	3	2
marked	0	2	1	0	0	0
Cortical vacuolation	3	2	1	3	4	1
mild	2	1	1	2	1	1
moderate	1	1	0	1	3	0
Hematopoiesis, extramedullary	4	0	0	0	1	1
mild	3	0	0	0	0	0
moderate	1	0	0	0	0	1
marked	0	0	0	0	1	0
Hemosiderosis	0	0	0	0	1	0
mild	0	0	0	0	1	0
Medullary cell hyperplasia	1	2	2	0	0	2
mild	1	2	1	0	0	2
moderate	0	0	1	0	0	0
Necrosis	3	0	0	0	0	0
moderate	1	0	0	0	0	0
marked	2	0	0	0	0	0
Nodular hyperplasia, cortex	0	0	0	1	1	2
moderate	0	0	0	1	1	2
Sinusoidal ectasia, cortex	19	23	16	25	21	22
minimal	0	1	0	1	1	0
mild	3	4	9	6	7	3
moderate	5	8	3	7	7	13
marked	5	9	4	11	6	0
Aorta	(21)	(23)	(19)	(27)	(0)	(0)
Within normal limits	17	23	10	27	0	0
Mineralization	2	0	0	0	0	0
mild	2	0	0	0	0	0
Bone Marrow	(25)	(25)	(21)	(29)	(0)	(0)
Within normal limits	23	25	21	29	0	0
Brain	(25)	(25)	(21)	(29)	(0)	(0)
Within normal limits	25	24	21	29	0	0
Esophagus	(15)	(21)	(9)	(15)	(23)	(22)
Within normal limits	14	21	9	15	23	22

Titles:

Group 1 CONTROL 0 ppm
Group 5 FC-143 300 ppm
Group 6 FC-143 30 ppm

() = Total Examined
DOS= Unscheduled Death(s)
SAC= Protocol Scheduled Sacrifice(s)

150

000537

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Eye	(20)	(23)	(16)	(28)	(2)	(1)
Within normal limits	17	21	16	28	1	1
Cataract	1	0	0	0	0	0
Keratitis, acute	1	0	0	0	1	0
marked	1	0	0	0	1	0
Panophthalmitis	0	1	0	0	0	0
marked	0	1	0	0	0	0
Phthisis bulbi	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Heart	(25)	(25)	(21)	(29)	(26)	(24)
Within normal limits	19	14	15	24	25	20
Myocardial fibrosis	0	2	1	1	0	0
minimal	0	0	0	1	0	0
mild	0	2	1	0	0	0
Myocarditis, chronic nonsuppurative	6	10	5	5	1	4
minimal	0	0	1	1	0	0
mild	4	10	4	4	1	4
moderate	2	0	0	0	0	0
Kidney	(25)	(25)	(21)	(29)	(26)	(24)
Within normal limits	3	3	7	4	5	5
Chronic progressive nephropathy	12	18	7	19	12	9
minimal	3	4	5	4	4	5
mild	5	10	1	12	8	4
moderate	2	3	0	2	0	0
marked	2	1	1	1	0	0
Cyst	2	1	0	0	0	0
moderate	2	0	0	0	0	0
Hydronephrosis	1	0	0	1	0	0
moderate	1	0	0	0	0	0
Hyperplasia, pelvic epithelium	4	1	0	0	0	0
mild	4	1	0	0	0	0
Mineralization	2	0	0	0	1	0
mild	2	0	0	0	0	0
moderate	0	0	0	0	1	0
Nephrosis	7	0	0	0	1	2
mild	1	0	0	0	0	1
moderate	3	0	0	0	0	1
marked	2	0	0	0	1	0
Pelvic mineralization	14	16	10	14	12	15
minimal	4	6	4	6	4	6
mild	8	8	4	7	6	6
moderate	1	2	1	0	0	2

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined

DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 3

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Kidney (continued)						
Pelvic mineralization						
marked	1	0	1	1	2	1
Pigment, conv. tub. epithelium	0	0	0	1	0	2
minimal	0	0	0	1	0	0
moderate	0	0	0	0	0	2
Polyarteritis	0	0	0	0	0	1
minimal	0	0	0	0	0	1
Protein resorption droplets	0	0	1	0	1	1
mild	0	0	0	0	0	1
marked	0	0	1	0	1	0
Pyelitis, acute	0	0	2	0	0	0
mild	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Pyelonephritis, acute	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Vacuolation, conv. tub. epithelium	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Large Intestine	(24)	(23)	(17)	(29)	(0)	(0)
Within normal limits	22	22	17	27	0	0
Nematodiasis	1	1	0	2	0	0
Liver	(25)	(25)	(21)	(23)	(25)	(24)
Within normal limits	1	0	4	4	7	7
Atrophy	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Cystoid degeneration	0	0	0	1	1	0
minimal	0	0	0	1	0	0
mild	0	0	0	0	1	0
Hematopoiesis, extramedullary	3	0	1	0	5	2
minimal	0	0	0	0	3	1
mild	3	0	0	0	2	1
moderate	0	0	1	0	0	0
Hepatocyte alteration, basophilic	1	7	0	2	5	3
minimal	0	0	0	1	0	0
mild	1	5	0	1	5	3
moderate	0	2	0	0	0	0
Hepatocyte alteration, eosinophilic	1	2	0	0	0	0
mild	0	2	0	0	0	0
moderate	1	0	0	0	0	0
Hepatocyte alteration, vacuolated	2	11	2	4	1	5
minimal	0	0	1	0	0	1
mild	2	11	1	4	0	4

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Table: 8

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Liver (continued)						
Hepatocyte alteration, vacuolated						
marked	0	0	0	0	1	0
Hepatocyte vacuolation	15	15	8	13	7	9
minimal	1	1	0	3	2	2
mild	0	13	5	10	2	7
moderate	3	1	2	0	2	0
marked	2	0	1	0	1	0
Hyperplastic nodule	0	1	0	2	0	0
Megalocytosis	0	0	1	7	0	1
minimal	0	0	1	6	0	1
mild	0	0	0	1	0	0
Mitotic activity, increased	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Mononuclear cell infiltration	0	0	1	0	0	0
mild	0	0	1	0	0	0
Necrosis	4	1	2	0	6	0
minimal	0	0	0	0	1	0
mild	1	1	1	0	3	0
moderate	1	0	0	0	0	0
marked	2	0	1	0	2	0
Pigment, Kupfer cell	0	0	1	0	0	0
mild	0	0	1	0	0	0
Portal bile duct proliferation	4	13	5	9	1	4
mild	3	12	5	8	1	4
moderate	0	1	0	1	0	0
marked	1	0	0	0	0	0
Portal mononuclear cell infiltrate	10	9	4	15	5	5
minimal	1	0	0	2	0	2
mild	8	9	4	12	5	4
moderate	1	0	0	1	0	0
Telangiectasis	1	0	0	0	0	0
mild	1	0	0	0	0	0
Lung	(25)	(25)	(21)	(29)	(26)	(24)
Within normal limits	2	3	1	3	2	2
Abscess	1	0	0	0	0	0
Alveolar macrophages	5	9	6	13	3	7
minimal	1	0	2	0	0	1
mild	4	9	4	12	3	6
moderate	0	0	0	1	0	0
Atelectasis	0	0	0	0	1	0
mild	0	0	0	0	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 3

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Lung (continued)						
Edema	0	0	0	0	1	0
mild	0	0	0	0	1	0
Granuloma	0	0	0	4	0	1
mild	0	0	0	2	0	1
marked	0	0	0	1	0	0
Hemorrhage	9	5	9	10	9	4
minimal	0	0	0	0	0	1
mild	8	3	6	6	8	0
moderate	1	1	2	4	0	2
marked	0	1	1	0	1	1
Hyperplasia, septal cell	0	0	0	0	0	1
mild	0	0	0	0	0	1
Perivascular mononuclear infiltrate	4	9	5	9	0	2
minimal	0	1	3	4	0	0
mild	4	7	2	5	0	2
moderate	0	1	0	0	0	0
Pigment	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Pneumonia, acute exudative	1	0	0	0	1	0
mild	0	0	0	0	1	0
moderate	1	0	0	0	0	0
Pneumonia, foreign body	0	0	0	0	1	0
marked	0	0	0	0	1	0
Pneumonia, interstitial, chronic	4	3	3	6	0	3
minimal	0	0	1	1	0	0
mild	4	3	1	5	0	3
marked	0	0	1	0	0	0
Vascular mineralization	12	10	15	11	18	20
minimal	0	0	0	0	7	8
mild	12	10	15	10	11	12
moderate	0	0	0	1	0	0
Lymph Node	(0)	(0)	(0)	(0)	(1)	(1)
Hyperplasia, reactive	0	0	0	0	1	1
moderate	0	0	0	0	1	1
Lymph Node (mesenteric)	(19)	(23)	(14)	(29)	(0)	(0)
Within normal limits	14	22	14	21	0	0
Granuloma	0	0	0	1	0	0
Hemorrhage	2	1	0	2	0	0
mild	1	1	0	0	0	0
moderate	1	0	0	1	0	0
marked	0	0	0	1	0	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 8

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Lymph Node (mesenteric) (continued)						
Pigment, brown	0	0	0	5	0	0
minimal	0	0	0	1	0	0
mild	0	0	0	2	0	0
moderate	0	0	0	2	0	0
Sinusoidal ectasia	1	0	0	2	0	0
moderate	1	0	0	1	0	0
marked	0	0	0	1	0	0
Mammary Gland	(23)	(23)	(17)	(27)	(23)	(22)
Within normal limits	4	9	7	9	4	7
Fibrosis	0	0	0	1	0	0
mild	0	0	0	1	0	0
Galactoceles	5	4	2	1	7	2
Lobular hyperplasia	4	3	2	1	2	1
moderate	1	0	2	0	0	0
Ovary	(25)	(23)	(18)	(29)	(26)	(24)
Within normal limits	19	17	11	16	23	11
Cyst	3	3	0	5	2	7
Tubular hyperplasia	0	0	7	8	0	7
mild	0	0	0	2	0	1
moderate	0	0	6	6	0	6
marked	0	0	1	0	0	0
Pancreas	(24)	(25)	(19)	(23)	(22)	(21)
Within normal limits	22	16	15	24	18	17
Acinar atrophy	0	6	2	2	3	2
minimal	0	1	0	1	1	1
mild	0	2	2	1	1	0
moderate	0	3	0	0	0	1
marked	0	0	0	0	1	0
Cyst	0	1	0	0	0	0
Edema	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Hyperplasia, islet cell	0	0	0	1	0	1
mild	0	0	0	1	0	1
Pancreatitis, chronic	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Polyarteritis	0	0	0	0	0	1
minimal	0	0	0	0	0	1
Parathyroid	(5)	(0)	(9)	(14)	(15)	(15)
Within normal limits	5	0	9	14	15	15

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 3

Project Number: 0201CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Pituitary	(22)	(24)	(21)	(29)	(23)	(24)
Within normal limits	5	7	7	7	3	4
Cyst	0	0	0	0	0	1
Hemorrhage	1	0	0	0	0	0
marked	1	0	0	0	0	0
Necrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Salivary Gland	(19)	(24)	(15)	(25)	(22)	(24)
Within normal limits	13	24	15	23	22	23
Sialadenitis, chronic	1	0	0	2	0	1
mild	0	0	0	0	0	1
moderate	1	0	0	2	0	0
Skin	(3)	(3)	(2)	(0)	(6)	(4)
Within normal limits	0	0	0	0	2	2
Acanthosis	0	1	0	0	0	0
mild	0	1	0	0	0	0
Pododermatitis, ulcerative	0	0	1	0	0	0
marked	0	0	1	0	0	0
Ulcer	2	0	0	0	0	0
moderate	1	0	0	0	0	0
marked	1	0	0	0	0	0
Small Intestine	(24)	(25)	(15)	(29)	(1)	(1)
Within normal limits	24	25	17	28	0	0
Edema	0	0	1	0	0	0
mild	0	0	1	0	0	0
Granuloma	0	0	0	1	0	0
Ulcer	0	0	0	0	1	0
marked	0	0	0	0	1	0
Spinal Cord	(25)	(23)	(21)	(29)	(0)	(0)
Within normal limits	23	23	21	29	0	0
Malacia	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Spleen	(25)	(25)	(21)	(29)	(24)	(23)
Within normal limits	4	11	12	23	10	17
Hematopoiesis, extramedullary, increased	7	2	2	1	11	5
mild	1	1	1	0	5	2
moderate	4	1	1	0	4	2
marked	2	0	0	1	2	1
Hemosiderosis	12	13	7	5	2	1
minimal	0	0	0	1	0	0
mild	8	13	6	3	0	1
moderate	4	0	1	1	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 9

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Spleen (continued)						
Hemosiderosis						
marked	0	0	0	0	1	0
Stomach	(25)	(25)	(20)	(29)	(25)	(24)
Within normal limits	20	25	13	29	20	24
Edema	0	0	2	0	0	0
moderate	0	0	2	0	0	0
Hemorrhage	1	0	0	0	1	0
mild	0	0	0	0	1	0
moderate	1	0	0	0	0	0
Mineralization	1	0	0	0	0	0
mild	1	0	0	0	0	0
Necrosis	2	0	0	0	1	0
mild	1	0	0	0	1	0
moderate	1	0	0	0	0	0
Ulcer	1	0	0	0	4	0
mild	0	0	0	0	2	0
Thyroid	(25)	(25)	(15)	(26)	(23)	(22)
Within normal limits	20	23	14	22	22	21
Follicular hyperplasia, cystic	1	0	0	0	0	0
mild	1	0	0	0	0	0
Hyperplasia, C cell	0	0	1	2	1	0
mild	0	0	1	2	1	0
Ultimobranchial cyst	2	1	0	2	0	1
Trachea	(25)	(25)	(20)	(25)	(24)	(23)
Within normal limits	25	25	20	25	24	23
Urinary Bladder	(25)	(25)	(16)	(26)	(25)	(22)
Within normal limits	17	25	15	25	22	22
Calculus	1	0	0	0	0	0
Epithelial hyperplasia, papillary	1	0	0	0	0	0
marked	1	0	0	0	0	0
Epithelial hyperplasia, simple	7	0	0	1	2	0
mild	6	0	0	1	2	0
moderate	1	0	0	0	0	0
Hypertrophy	0	0	0	1	0	0
mild	0	0	0	1	0	0
Uterus	(25)	(25)	(19)	(29)	(26)	(23)
Within normal limits	21	17	17	24	17	17
Cystic glands	2	5	1	4	7	5
minimal	0	0	0	1	0	0
mild	0	1	1	2	1	1
moderate	2	1	0	1	2	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

157

000544

Non-Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 8

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Uterus (continued)						
Cystic glands						
marked	0	3	0	0	4	3
Hydrometra	0	1	1	0	0	0
marked	0	1	1	0	0	0
Hyperplasia, endometrial	0	0	0	0	0	1
moderate	0	0	0	0	0	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

158

000545

Neoplastic Incidence for Males
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 9

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1	Group 5
	-----	-----
Skin	(0)	(1)
Keratoacanthoma	0	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm

() = Total Examined

Neoplastic Incidence for Females

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 10

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 -----	Group 5 -----
Mammary Gland	(15)	(13)
Fibroadenoma	0	2
Pituitary	(15)	(14)
Adenoma	1	0

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

() = Total Examined

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Neoplastic Incidence for Males

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 11

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Adrenal	(15)	(34)	(6)	(44)	(14)	(36)
Carcinoma, cortical	0	1	0	0	0	0
Ganglioneuroma	0	0	0	1	0	0
Pheochromocytoma, benign	1	1	0	4	0	4
Pheochromocytoma, malignant	0	0	0	0	0	1
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Bone Marrow	(15)	(32)	(5)	(42)	(0)	(0)
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Brain	(16)	(34)	(6)	(44)	(0)	(1)
Astrocytoma, benign	0	1	0	0	0	1
Oligodendroglioma, benign	1	0	0	0	0	0
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Eye	(12)	(33)	(6)	(44)	(2)	(3)
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Heart	(15)	(31)	(6)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Kidney	(16)	(34)	(5)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	1	0	1	0	1	0
Liver	(15)	(34)	(6)	(44)	(14)	(36)
Hepatocellular carcinoma	2	1	1	4	1	0
Hemolymphoreticular neoplasm present	2	1	1	1	1	0
Lung	(16)	(34)	(6)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	3	1	1	0	1	0
Lymph Node (abdominal)	(0)	(0)	(1)	(0)	(1)	(0)
Hemolymphoreticular neoplasm present	0	0	1	0	1	0
Lymph Node (mesenteric)	(12)	(33)	(6)	(44)	(0)	(1)
Hemangiosarcoma	0	0	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Pancreas	(13)	(33)	(6)	(43)	(12)	(34)
Adenocarcinoma	0	0	0	1	0	1
Islet cell adenoma	0	1	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Parathyroid	(6)	(15)	(5)	(31)	(7)	(25)
Adenoma	0	0	0	2	0	0
Pituitary	(15)	(33)	(5)	(41)	(13)	(34)
Adenoma	6	11	2	11	9	3
Salivary Gland	(12)	(32)	(5)	(41)	(10)	(34)
Carcinoma	0	0	1	0	0	0
Skin	(8)	(7)	(0)	(2)	(5)	(4)
Fibroma	1	0	0	0	0	0
Fibrosarcoma	1	0	0	0	2	1

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined

DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

161

Microscopic Incidence Page: 36

C00548

Neoplastic Incidence for Males (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 11

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Skin (continued)						
Keratoacanthoma	1	2	0	1	0	0
Liposarcoma	1	0	0	0	0	0
Papilloma	0	1	0	0	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Small Intestine	(1)	(3)	(5)	(44)	(1)	(0)
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Soft Tissues (abdomen)	(0)	(0)	(0)	(0)	(0)	(1)
Fibroma	0	0	0	0	0	1
Soft Tissues (thorax)	(0)	(0)	(0)	(1)	(0)	(0)
Histiocytoma, malignant	0	0	0	1	0	0
Spleen	(15)	(34)	(6)	(44)	(14)	(35)
Hemangiosarcoma	0	1	0	0	0	0
Hemolymphoreticular neoplasm present	1	1	1	0	1	0
Stomach	(15)	(33)	(6)	(44)	(14)	(36)
Adenocarcinoma	0	0	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Testis/Epididymis	(15)	(33)	(6)	(44)	(14)	(36)
Leydig cell adenoma	0	0	0	7	0	2
Thymus	(1)	(0)	(1)	(1)	(1)	(0)
Hemolymphoreticular neoplasm present	1	0	1	0	1	0
Thyroid	(12)	(31)	(5)	(42)	(12)	(35)
C cell adenoma	0	0	0	4	0	2
C cell carcinoma	0	2	0	0	0	0
Follicular adenoma	0	0	0	0	0	1
Urinary Bladder	(13)	(33)	(6)	(44)	(14)	(35)
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Hemolymphoreticular System [# affected]	[3]	[1]	[1]	[1]	[1]	[0]
Malignant lymphoma, lymphocytic	0	0	1	1	0	0
Malignant lymphoma, histiocytic	3	1	1	0	0	0
Leukemia, myeloid	0	0	0	0	1	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

162

Microscopic Incidence Page: 37

C00549

Neoplastic Incidence for Females
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 12

Project Number: 0291CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Adrenal	(25)	(25)	(20)	(29)	(25)	(24)
Adenoma, cortical	0	0	0	1	0	1
Carcinoma, cortical	0	0	0	0	1	0
Pheochromocytoma, benign	0	2	0	0	0	0
Pheochromocytoma, malignant	0	0	1	0	0	0
Hemolymphoreticular neoplasm present	2	0	0	0	0	0
Aorta	(21)	(23)	(19)	(27)	(0)	(0)
Hemolymphoreticular neoplasm present	2	0	0	0	0	0
Bone Marrow	(25)	(25)	(21)	(29)	(0)	(0)
Hemolymphoreticular neoplasm present	2	0	0	0	0	0
Brain	(25)	(25)	(21)	(29)	(0)	(0)
Oligodendroglioma, benign	0	1	0	0	0	0
Esophagus	(15)	(21)	(9)	(15)	(23)	(22)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Eye	(20)	(23)	(15)	(28)	(2)	(1)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Harderian Gland	(0)	(0)	(0)	(0)	(1)	(0)
Adenocarcinoma	0	0	0	0	1	0
Heart	(25)	(25)	(21)	(29)	(26)	(24)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Kidney	(25)	(25)	(21)	(29)	(26)	(24)
Hemolymphoreticular neoplasm present	3	0	0	0	0	0
Large Intestine	(24)	(23)	(17)	(29)	(0)	(0)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Liver	(25)	(25)	(21)	(29)	(25)	(24)
Hepatocellular carcinoma	0	0	0	1	0	0
Hemolymphoreticular neoplasm present	5	0	1	0	1	0
Lung	(25)	(25)	(21)	(29)	(26)	(24)
Hemolymphoreticular neoplasm present	5	0	1	0	1	0
Lymph Node (mesenteric)	(19)	(23)	(14)	(29)	(0)	(0)
Hemolymphoreticular neoplasm present	3	0	0	0	0	0
Lymph Node (thoracic)	(0)	(0)	(0)	(0)	(1)	(0)
Hemolymphoreticular neoplasm present	0	0	0	0	1	0
Mammary Gland	(23)	(23)	(17)	(27)	(23)	(22)
Adenocarcinoma	1	3	2	3	9	5
Adenoma	2	1	0	0	0	0
Carcinoma	0	1	0	0	0	0
Fibroadenoma	6	4	5	16	9	11
Lymphangiosarcoma	0	0	1	0	0	0
Hemolymphoreticular neoplasm present	2	0	0	0	0	0

Titles:

Group 1 CONTROL 0 ppm
Group 5 FC-143 300 ppm
Group 6 FC-143 30 ppm

() = Total Examined
DOS= Unscheduled Death(s)
SAC= Protocol Scheduled Sacrifice(s)

163

Microscopic Incidence Page: 39

000550

Neoplastic Incidence for Females (continued)
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 12

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Mesentery	(0)	(0)	(0)	(0)	(2)	(0)
Mesothelioma, malignant	0	0	0	0	1	0
Hemolymphoreticular neoplasm present	0	0	0	0	1	0
Ovary	(25)	(23)	(10)	(29)	(20)	(24)
Granulosa cell tumor, benign	0	0	0	0	0	1
Leiomyoma	1	0	0	0	0	0
Tubular adenoma	0	4	0	1	0	0
Hemolymphoreticular neoplasm present	2	0	0	0	1	0
Pancreas	(24)	(25)	(19)	(28)	(22)	(21)
Islet cell adenoma	0	1	0	1	1	0
Islet cell carcinoma	0	1	0	1	0	0
Hemolymphoreticular neoplasm present	2	0	0	0	1	0
Pituitary	(22)	(24)	(21)	(29)	(23)	(24)
Adenoma	16	17	14	22	20	19
Skin	(3)	(3)	(2)	(0)	(0)	(4)
Fibroma	1	2	1	0	4	1
Fibrosarcoma	0	0	0	0	1	1
Small Intestine	(24)	(25)	(18)	(29)	(1)	(1)
Leiomyosarcoma	0	0	0	0	0	1
Spinal Cord	(25)	(23)	(21)	(29)	(0)	(0)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Spleen	(25)	(25)	(21)	(29)	(24)	(23)
Hemolymphoreticular neoplasm present	3	0	0	0	1	0
Stomach	(25)	(25)	(20)	(29)	(25)	(24)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Thyroid	(25)	(25)	(15)	(25)	(23)	(22)
C cell adenoma	0	1	0	0	0	0
Hemolymphoreticular neoplasm present	2	0	0	0	0	0
Unidentified Tissue	(0)	(0)	(1)	(0)	(0)	(0)
Lipoma	0	0	1	0	0	0
Urinary Bladder	(25)	(25)	(16)	(26)	(25)	(22)
Hemolymphoreticular neoplasm present	1	0	1	0	1	0
Uterus	(25)	(25)	(19)	(29)	(26)	(23)
Adenoma	0	1	0	0	0	0
Hemangioma	0	0	0	0	1	0
Leiomyoma	0	0	0	0	0	1
Polyp	0	1	0	1	2	1
Hemolymphoreticular neoplasm present	2	0	0	0	0	0
Hemolymphoreticular System [# affected]	[5]	[0]	[1]	[0]	[1]	[0]
Malignant lymphoma, histiocytic	2	0	1	0	1	0
Malignant lymphoma, lymphocytic	3	0	0	0	0	0

Titles:

Group 1 CONTROL 0 ppm
 Group 5 FC-143 300 ppm
 Group 6 FC-143 30 ppm

() = Total Examined
 DOS= Unscheduled Death(s)
 SAC= Protocol Scheduled Sacrifice(s)

Summarized Single Tabulated Animal Report
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3516 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Lung

-Vascular mineralization, minimal

Lymph Node (mesenteric)

-Not examined, missing

Pancreas

-Acinar atrophy, mild

Parathyroid

-Not examined, missing

Small Intestine

-Within normal limits

Fewer than protocol number

Thyroid

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Mammary Gland, Pituitary, Adrenal, Trachea,
Esophagus, Salivary Gland, Eye.

Animal Number: 1R-3517 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Lung

-Vascular mineralization, mild

Parathyroid

-Not examined, missing

Thyroid

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Mammary Gland, Pituitary,
Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3520 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, bilateral,
moderate

Kidney

-Chronic progressive nephropathy, minimal

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 1

165

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Summarized Single Tabulated Animal Report (continued)

Individual Macroscopic and Microscopic Observations

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3520 Sex: Male Group: (1) CONTROL 0 ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Liver	-Hepatocyte alteration, vacuolated, focal, minimal
Lung	-Vascular mineralization, minimal
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3522 Sex: Male Group: (1) CONTROL 0 ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver -Light (pale) tan in color.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Mammary Gland, Pituitary, Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3527 Sex: Male Group: (1) CONTROL 0 ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Hemorrhage, multifocal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 2

166

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3527 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal,
Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3535 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mesentary

-Area of fat necrosis, 2 x 3 x 0.5 cm.

Microscopic Observations:

Lung

-Alveolar macrophages, multifocal, mild

✓ Atelectasis, focal, mild

Mesentary

-Necrosis, fat, marked

Steatitis, chronic, moderate

Parathyroid

-Not examined, missing

Thyroid

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Liver, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye, Spleen.

Animal Number: 1R-3543 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, focal,
minimal

Lung

-Vascular mineralization, minimal

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3546 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Nodular hyperplasia, cortex, unilateral, moderate

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Hepatocyte alteration, vacuolated, multifocal, mild

Lung

-Perivascular mononuclear infiltrate, mild

Stomach

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3550 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Kidney

-Bilateral hydronephrosis

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative, focal, mild

Kidney

-Hydronephrosis, bilateral, moderate
Calculus, pelvic

Liver

-Portal mononuclear cell infiltrate, mild

Lung

-Vascular mineralization, mild

Pancreas

-Acinar atrophy, focal, moderate
Pancreatitis, chronic, focal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3551 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver -Pale tan

Microscopic Observations:

Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Lung -Pneumonia, interstitial, chronic, focal, mild
Hemorrhage, multifocal, mild
Hyperplasia, septal cell, focal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal,
Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3559 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney -Pyelitis, acute, bilateral, minimal
Nephritis, interstitial, chronic, focal,
unilateral, mild
Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Lung -Hemorrhage, multifocal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3568 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney -Chronic progressive nephropathy, mild
Pancreas -Pancreatitis, chronic, focal, mild
Acinar atrophy, focal, mild
Parathyroid -Not examined, not in plane of section

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3568 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal,
Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3570 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Cortical vacuolation, multifocal, mild

Lung

-Pneumonia, interstitial, chronic, focal,
minimal

Hemorrhage, multifocal, mild

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3575 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Soft Tissues (leg)

-Swollen left hind foot at the hock joint.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Lung

-Vascular mineralization, minimal

Alveolar macrophages, multifocal, mild

Hemorrhage, focal, mild

Pituitary

-Cyst, pars distalis

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid,
Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat
Project Number: 02B1CR0012

Summarized STAR Page: 6

170

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3580 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Kidney

-Dark cystic lesion, 0.4 cm dia., left.

Microscopic Observations:

Bone Marrow

-Not examined, missing

Kidney

-Chronic progressive nephropathy, mild
Cyst, cortical, unilateral

Lung

-Alveolar macrophages, multifocal, mild
Pneumonia, interstitial, chronic, multifocal,
mild

Pancreas

-Pancreatitis, chronic, focal, mild

Parathyroid

-Not examined, not in plane of section

Spinal Cord

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spleen, Liver, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta,
Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4578 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Pelvic mineralization, minimal

Lymph Node (mesenteric)

-Not examined, missing

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal,
Thyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4582 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mesentary

-Yellow nodular mass, 1 x 0.5 cm.

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative, focal,
minimal

Kidney

-Calculus, pelvic, unilateral

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4582 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Large Intestine	-Not examined, missing
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Hemorrhage, local areas, mild Perivascular mononuclear infiltrate, mild
Mesentary	-Necrosis, fat, nodular, moderate Steatitis, chronic, moderate
Parathyroid	-Not examined, not in plane of section
Urinary Bladder	-Not examined, missing
Uterus	-Hyperplasia, glandular epithelium, mild Metaplasia, squamous, glandular, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Stomach, Small Intestine, Aorta, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4585 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, focal, unilateral, mild
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4588 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Skin -Hair loss, neck.
Adrenal -Left enlarged

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, unilateral,
marked
Cortical degeneration, unilateral, mild
Kidney -Hyperplasia, pelvic epithelium, mild
Calculus, pelvic, unilateral
Cyst, medullary, mild
Liver -Hepatocyte vacuolation, multifocal, mild
Lung -Hemorrhage, diffuse, moderate
Spinal Cord -Not examined, missing
Spleen -Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta,
Uterus, Ovary, Mammary Gland, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye, Skin.

Animal Number: 1R-4589 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Pituitary -Slightly enlarged

Microscopic Observations:

Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Mammary Gland -Galactoceles
Parathyroid -Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Adrenal, Thyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)

Individual Macroscopic and Microscopic Observations

Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4590 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Lung

-Hemorrhage, local areas, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal,
Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4601 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Kidney

-Hydronephrosis, unilateral

Microscopic Observations:

Kidney

-Hydronephrosis, unilateral, moderate
Calculus, unilateral, mild

Liver

-Hepatocyte vacuolation, multifocal, minimal

Lung

-Hemorrhage, multifocal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4608 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Uterus

-Left horn cystic looking lesion, 1 x 0.6 cm.

Microscopic Observations:

Liver

-Hepatocyte vacuolation, multifocal, minimal

Lung

-Hemorrhage, multifocal, mild

Lymph Node (mesenteric)

-Not examined, missing

Uterus

-Cystic glands, focal, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid,
Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 10

174

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Table: 1

Metaplasia, squamous, glandular, mild

-Not examined, missing

-Cortical degeneration, focal, unilateral,
mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4629 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Aorta	-Not examined, missing
Large Intestine	-Nematodiasis
Liver	-Portal bile duct proliferation, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Lung, Stomach, Small Intestine, Urinary Bladder, Uterus, Ovary, Mammary Gland, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye, Skin.

Animal Number: 1R-4630 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver	-Possibly slightly pale in color.
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Microscopic Observations:

Kidney	-Calculus, pelvic, unilateral, moderate
Liver	-Hepatocyte alteration, vacuolated, multifocal, mild
Lung	-Hemorrhage, multifocal, mild
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4631 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Pelvic mineralization, minimal
Lung	-Hemorrhage, local areas, mild
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Small Intestine,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4631 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Trachea,
Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4632 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Pituitary	-Slightly enlarged with a dark red focus on surface.
Mammary Gland	-Small spherical mass, 1.2 cm dia., containing dark red fluid, left inguinal.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, focal, unilateral, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Galactoceles Chronic inflammation and hemorrhage in cysts.
Ovary	-Cyst, unilateral
Pituitary	-Adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4640 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Liver	-Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal,
Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3584 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver -Pale

Microscopic Observations:

Aorta -Not examined, missing
Kidney -Chronic progressive nephropathy, mild
Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Megalocytosis, moderate
Necrosis, focal, minimal
Lung -Vascular mineralization, mild
Alveolar macrophages, multifocal, mild
Parathyroid -Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3588 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney -Chronic progressive nephropathy, minimal
Liver -Portal mononuclear cell infiltrate, mild
Megalocytosis, mild
Necrosis, multifocal, mild
Lung -Vascular mineralization, mild
Spleen -Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3589 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta

-Not examined, missing

Liver

-Portal mononuclear cell infiltrate, mild
Megalocytosis, mild

Lung

-Vascular mineralization, mild

Parathyroid

-Not examined, missing

Thyroid

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Testis/Epididymis, Prostate, Pituitary, Adrenal, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3592 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Pituitary

-Small dark red mass, 0.3 cm dia.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, minimal
Hepatocyte vacuolation, multifocal, mild
Pigment, Kupfer cell, multifocal, brown, mild

Lung

-Vascular mineralization, mild

Parathyroid

Alveolar macrophages, multifocal, mild

Urinary Bladder

-Not examined, not in plane of section

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3598 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative,
multifocal, minimal

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3598 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal Necrosis, multifocal, minimal
Lung	-Alveolar macrophages, multifocal, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3604 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta	-Not examined, missing
Heart	-Myocardial fibrosis, focal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3613 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver	-Pale tan color.
Kidney	-Small depressed area, 0.2 cm dia., right kidney.

Microscopic Observations:

Eye	-Retinal atrophy, focal, minimal
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-3617 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Skin	-Ulcerated nodule in the dorsal area, 1.5 cm dia.
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Microscopic Observations:

Kidney	-Mineralization, multifocal, cortical Pyelitis, acute, unilateral, mild
Liver	-Megalocytosis, minimal
Lung	-Alveolar macrophages, multifocal, mild
Lymph Node (mesenteric)	-Hemorrhage, minimal
Skin	-Keratoacanthoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 17

181

000568

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3620 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta

-Not examined, missing

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild
Hepatocyte vacuolation, multifocal, minimal
Megalocytosis, minimal

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Lung, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3622 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Eye

-Ocular opacity, bilateral.

Testis

-Left testis small.

Microscopic Observations:

Eye

-Cataract, bilateral

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, minimal
Megalocytosis, minimal

Lung

Pigment, Kupfer cell, brown, minimal
-Vascular mineralization, minimal
Pneumonia, interstitial, chronic, multifocal,
mild

Lymph Node (mesenteric)

-Hemorrhage, mild

Parathyroid

-Not examined, not in plane of section

Prostate

-Not examined, missing

Testis/Epididymis

-Tubule atrophy, aspermatogenesis, unilateral,
marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Pancreas,
Salivary Gland.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3626 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild
Megalocytosis, minimal

Lung

-Alveolar macrophages, multifocal, mild

Parathyroid

-Not examined, not in plane of section

Pituitary

-Not examined, missing

Prostate

-Prostatitis, chronic, focal, interstitial,
minimal

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3627 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver

-Slightly pale tan in color.

Microscopic Observations:

Liver

-Portal mononuclear cell infiltrate, minimal

Lung

-Hemorrhage, local areas, mild

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal,
Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3638 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Liver

-Portal mononuclear cell infiltrate, minimal
Necrosis, multifocal, mild

Lung

-Hemorrhage, local areas, moderate

Lymph Node (mesenteric)

-Not examined, missing

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 19

183

000570

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3638 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Pituitary	-Not examined, missing
Prostate	-Not examined, missing
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Aorta, Testis/Epididymis, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3642 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Large Intestine	-Neematodiasis
Liver	-Megalocytosis, mild
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Lung, Stomach, Small Intestine, Urinary Bladder,
Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Trachea, Esophagus, Pancreas,
Salivary Gland, Eye.

Animal Number: 1R-3643 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart	-Myocardial fibrosis, focal, minimal Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, moderate Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Perivascular mononuclear infiltrate, mild

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 20

184

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-3643 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4642 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Eye

-Atrophy, right eye.

Uterus

-Both horns enlarged, filled with clear fluid.

Microscopic Observations:

Eye

-Panophthalmitis, unilateral, marked

Atrophy, unilateral, marked

Kidney

-Chronic progressive nephropathy, mild

Large Intestine

-Nematodiasis

Liver

-Hepatocyte vacuolation, multifocal, mild

Parathyroid

-Not examined, not in plane of section

Uterus

-Hydrometra, moderate

Endometritis, chronic, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Lung, Stomach, Small Intestine, Urinary Bladder,
Aorta, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4652 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Liver

-Hepatocyte vacuolation, multifocal, mild

Parathyroid

-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Lung, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 21

185

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M

FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4655 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta

-Not examined, missing

Liver

-Hepatocyte vacuolation, multifocal, mild

Lung

-Hemorrhage, local areas, mild

Pituitary

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Uterus, Ovary, Mammary Gland, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4656 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Mineralization, multifocal, cortical, mild

Liver

-Hepatocyte vacuolation, multifocal, mild

Lung

-Hemorrhage, multifocal, mild

Lymph Node (mesenteric)

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4664 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mammary Gland

-Subcutaneous mass, 3.5 cm dia., left inguinal
area.

Microscopic Observations:

Liver

-Hepatocyte vacuolation, multifocal, mild

Mammary Gland

-Fibroadenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Adrenal, Thyroid,

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 22

186

000573

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4664 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4666 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal,
Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4669 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Liver

-Hepatocyte vacuolation, multifocal, mild

Lung

-Hemorrhage, multifocal, mild

Mammary Gland

-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Adrenal, Thyroid,
Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4671 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mammary Gland

-Subcutaneous mass, 5 cm dia., behind left
shoulder.

Microscopic Observations:

Kidney

-Pelvic mineralization, mild
Calculus, pelvic, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4671 Sex: Female Group: (5) FC-143 300 ppm
Date: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Liver	-Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4674 Sex: Female Group: (5) FC-143 300 ppm
Date: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Large Intestine	-Not examined, missing
Lung	-Hemorrhage, multifocal, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Stomach, Small Intestine, Urinary Bladder, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Trachea, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4676 Sex: Female Group: (5) FC-143 300 ppm
Date: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mammary Gland	-Two subcutaneous masses in both inguinal areas, 1.5 and 2 cm dia. Left side milk cyst, right side cyst filled with rust colored fluid.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, focal, mild
Kidney	-Calculus, pelvic
Liver	-Hepatocyte vacuolation, multifocal, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4676 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Lung	-Alveolar macrophages, multifocal, mild
Mammary Gland	-Galactoceles Galactoceles One cyst involved with chronic inflammatory process with extensive hemorrhage into cyst.

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4687 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Urinary Bladder	-Distended with urine and containing greenish spherical calculi, 0.6 cm dia.
Ureter	-Bilateral dilatation of ureters; filled with calculi near the end of the bladder.
Kidney	-Bilateral marked hydronephrosis with numerous calculi in the pelvic area.

Microscopic Observations:

Esophagus	-No diagnosis, inadequate section
Kidney	-Hydronephrosis, bilateral, marked Pyelitis, chronic, moderate
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Ureter	-Calculus Inflammation, chronic, diffuse, moderate Dilatation, marked
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Cystitis, chronic, diffuse, moderate
Uterus	-Hydrometra

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Lung, Stomach, Small Intestine, Large Intestine, Aorta, Ovary, Pituitary, Adrenal, Thyroid, Trachea, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat
Project Number: 02B1CR0012

Summarized STAR Page: 25

189

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4689 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Eye -Right eye atrophied.
Liver -Pale tan in color.
Lymph Node (mesenteric) -Hemorrhagic

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, mild
Eye -Atrophy, unilateral, marked
Panophthalmitis, chronic, unilateral, marked
Liver -Hepatocyte vacuolation, multifocal, mild
Lung -Hemorrhage, local areas, mild
Lymph Node (mesenteric) -Hemorrhage, marked
Parathyroid -Not examined, not in plane of section
Thyroid -No diagnosis, inadequate section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea,
Esophagus, Pancreas, Salivary Gland.

Animal Number: 1R-4692 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Lung -Hemorrhage, local areas, moderate
Lymph Node (mesenteric) -Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal,
Thyroid, Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4699 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, mild
Large Intestine -Neumatodiasis
Liver -Hepatocyte vacuolation, multifocal, mild

Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 26

190

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 1

Animal Number: 1R-4699 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Lung -Hemorrhage, local areas, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4704 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal -Cortical degeneration, focal, unilateral,
mild
Liver -Portal mononuclear cell infiltrate, mild
Hepatocyte vacuolation, multifocal, mild
Lung -Vascular mineralization, mild
Hemorrhage, multifocal, mild
Thyroid -Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3518 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin -Raised inflamed lesion on right rear
footpad.

Microscopic Observations:

Adrenal -Cortical vacuolation, multifocal, mild
Medullary cell hyperplasia, multifocal, mild
Heart -Myocarditis, chronic nonsuppurative,
local areas, moderate
Kidney -Chronic progressive nephropathy, minimal
Pelvic mineralization, minimal
Liver -Portal mononuclear cell infiltrate, minimal
Portal bile duct proliferation, mild
Lung -Vascular mineralization, minimal
Pneumonia, interstitial, chronic, multifocal,
mild
Perivascular mononuclear infiltrate, moderate
Parathyroid -Not examined, missing
Pituitary -Adenoma
Skin -Pododermatitis, ulcerative, hindleg, marked
Thyroid -Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3519 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, multifocal, mild
Cortical vacuolation, multifocal, mild
Esophagus -Not examined, missing
Heart -Myocarditis, chronic nonsuppurative,
multifocal, mild
Kidney -Chronic progressive nephropathy, mild
Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Hepatocyte alteration, vacuolated, multifocal,
mild

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3519 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung

-Vascular mineralization, mild
Perivascular mononuclear infiltrate, moderate
Pneumonia, interstitial, chronic, multifocal,
moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3521 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 92) Sacrificed in extremis

Macroscopic Observations:

Skin

-Both hind footpads ulcerated.

Liver

-Pale

Spleen

-Enlarged

Microscopic Observations:

Adrenal

-Cortical vacuolation, local areas, mild
Medullary cell hyperplasia, multifocal, mild

Heart

-Myocardial fibrosis, multifocal, mild

Kidney

-Chronic progressive nephropathy, moderate

Liver

-Hepatocyte vacuolation, centrilobular,
moderate

Lung

-Vascular mineralization, mild
Pneumonia, interstitial, chronic, local areas,
mild
Edema, local areas, mild
Fibrosis, pleural, mild
Thrombus

Parathyroid

-Not examined, missing

Skin

-Pododermatitis, ulcerative, hindleg, marked

Spleen

-Hematopoiesis, extramedullary, increased,
moderate

Stomach

-Edema, submucosal, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Small Intestine, Large Intestine, Urinary Bladder, Aorta,
Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3523 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 95) Sacrificed in extremis

Macroscopic Observations:

Soft Tissues (thorax)

-Mass, 10 x 9 x 4 cm in left axilla involving muscle and rib, extending into left thoracic cavity, collapsing left lung. Mass soft and fatty.

Stomach

-Wall edematous with possible ulceration in cardia.

Microscopic Observations:

Adrenal

-Cortical vacuolation, multifocal, mild
Sinusoidal ectasia, cortex, diffuse, mild

Heart

-Myocardial fibrosis, multifocal, mild

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild
Hepatocyte alteration, vacuolated, mild

Lung

-Vascular mineralization, mild

Hemorrhage, focal, mild

Alveolar macrophages, mild

Prostate

-Prostatitis, acute, suppurative, marked

Skin

-Fibrosarcoma, thorax

Well differentiated, highly cellular with moderate collagen formation.

Stomach

-Ulcer, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3524 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary

-Small red lesion.

Microscopic Observations:

Adrenal

-Medullary cell hyperplasia, multifocal, mild

Kidney

-Chronic progressive nephropathy, moderate

Pelvic mineralization, mild

Large Intestine

-Neematodiasis, colon

Liver

-Hepatocyte alteration, vacuolated, moderate

Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3524 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Thyroid	-Follicular hyperplasia, cystic, unilateral, moderate Large cystic lesion occupying much of one thyroid lobe.

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3525 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Bone	-Joints of right forelimb and right hindlimb swollen.
Liver	-Raised pale circular lesion, 2 cm dia., in medial lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate
Bone	-Arthritis, synovitis; joints, foreleg, hindleg, marked
Heart	-Myocarditis, chronic nonsuppurative, local areas, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocellular carcinoma Large, poorly differentiated, anaplastic, infiltrative. Adenoid areas. Multiple tumor emboli in lung.
Lung	-Vascular mineralization, mild Metastatic neoplasm
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3525 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):

Aorta, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3526 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Cystoid degeneration, focal, mild

Hepatocyte alteration, vacuolated, mild

Lung

-Vascular mineralization, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3528 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney

-Hydronephrosis

Microscopic Observations:

Adrenal

-Cortical vacuolation, focal, mild

Kidney

-Chronic progressive nephropathy, moderate

Hydronephrosis, unilateral, moderate

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Hepatocyte vacuolation, multifocal, mild

Lung

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal, mild

Pituitary

-Hyperplasia, focal, pars distalis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3528 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3529 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Skin	-Areas of dermatitis with hair loss, some scabbed; back, side, abdomen.
Liver	-Raised pale mass, 1.2 cm dia. in left lateral lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocellular carcinoma Trabecular pattern, fairly well differentiated.
Lung	-Vascular mineralization, mild Edema, subpleural, moderate
Parathyroid	-Not examined, not in plane of section
Prostate	-Not examined, missing
Salivary Gland	-Not examined, missing
Skin	-Ulcer, back, abdomen, marked
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3530 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, moderate Hepatocyte alteration, vacuolated, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3530 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Peribronchial lymphoid hyperplasia, mild
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3531 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, local areas, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3532 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised red mass, 0.4 cm dia.
Kidney	-Fluid filled cyst, 1 cm dia., in right kidney

Microscopic Observations:

Eye	-Retinal atrophy, focal, mild
Heart	-Myocardial fibrosis, focal, mild
Kidney	-Chronic progressive nephropathy, moderate Cyst, cortical, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Hemorrhage, local areas, mild Perivascular mononuclear infiltrate, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3532 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lymph Node (mesenteric)	-Hemorrhage, mild
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland.

Animal Number: 1R-3533 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Spleen	-Pale circular depressed area, 0.4 cm dia.
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Microscopic Observations:

Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Perivascular mononuclear infiltrate, mild
Prostate	-Prostatitis, acute, suppurative, mild
Spleen	-Hemosiderosis, mild Fibrosis, local areas, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-3534 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations:

Thymus	-Enlarged
Pancreas	-Massive beige colored mass, 7.5 x 3 cm in area of pancreas completely surrounding spleen and adhering to posterior areas of right and left lateral

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3534 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations (continued):

Pancreas (continued)	-liver lobes.
Kidney	-Pale and pitted.
Testis/Epididymis	-Right testis small.
Liver	-Pale with yellowish circular lesion 0.3 cm diameter in right anterior lobe

Microscopic Observations:

Adrenal	-Cortical vacuolation, diffuse, moderate Medullary cell hyperplasia, local areas, moderate
Kidney	-Chronic progressive nephropathy, moderate Malignant lymphoma, histiocytic
Liver	-Hepatocyte vacuolation, diffuse, marked
Lung	-Hemorrhage, diffuse, marked Malignant lymphoma, histiocytic
Lymph Node (mesenteric)	-Hemorrhage, mild Malignant lymphoma, histiocytic
Pancreas	-Malignant lymphoma, histiocytic
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Small Intestine	-Malignant lymphoma, histiocytic
Spleen	-Malignant lymphoma, histiocytic
Stomach	-Malignant lymphoma, histiocytic
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
Thymus	-Malignant lymphoma, histiocytic Multiple sections of tumor from thymic and mediastinal areas.
Thyroid	-Not examined, missing
Urinary Bladder	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Trachea, Esophagus, Salivary Gland, Eye,
Large Intestine, Aorta, Prostate.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3536 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin

-Raised lesion, 1.5 cm dia., appears to be abscess.

Microscopic Observations:

Adrenal

-Cortical vacuolation, focal, mild
Sinusoidal ectasia, cortex, focal, moderate

Kidney

-Chronic progressive nephropathy, minimal

Large Intestine

-Nematodiasis, colon

Liver

-Portal bile duct proliferation, multifocal, mild

Portal mononuclear cell infiltrate, mild
Hepatocyte vacuolation, multifocal, minimal

Lung

-Vascular mineralization, mild
Perivascular mononuclear infiltrate, mild

Skin

-Keratoacanthoma

Raised lesion from back.

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Aorta,
Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye, Urinary Bladder.

Animal Number: 1R-3537 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Found Dead

Macroscopic Observations:

Liver

-Very pale

Lymph Node (abdominal)

-Renal lymph nodes enlarged.

Abdomen (internal)

-Multilobular, fleshy mass, 4 x 3.5 x 3.5
attached to omentum, left inguinal
area.

Pituitary

-Hemorrhagic mass, 0.7 cm dia.

Microscopic Observations:

Eye

-Not examined, missing

Heart

-Malignant lymphoma, histiocytic

Liver

-Hepatocyte vacuolation, diffuse, marked

Malignant lymphoma, histiocytic

Lung

-Malignant lymphoma, histiocytic

Hemorrhage, local areas, moderate

Lymph Node (mesenteric)

-Not examined, missing

Pancreas

-Not examined, missing

Parathyroid

-Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3537 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Found Dead

Microscopic Observations (continued):

Pituitary	-Adenoma
Skin	-Malignant lymphoma, histiocytic Mass from inguinal area was malignant lymphoma. There was extensive necrosis in tumor.
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Kidney, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-3538 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Small hemorrhagic area, 0.2 cm dia.
Liver	-Multiple pale foci, all lobes.
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Malignant lymphoma, histiocytic
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Malignant lymphoma, histiocytic Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Hemorrhage, minimal
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, marked
Spleen	-Malignant lymphoma, histiocytic
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Pituitary, Thyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3539 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Large Intestine

-Nematodiasis, colon

Liver

-Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, multifocal, mild

Lung

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal, mild

Perivascular mononuclear infiltrate, mild

Parathyroid

-Not examined, not in plane of section

Pituitary

-Cyst, pars distalis

Spleen

-Hemosiderosis, mild

Thyroid

-Ultimobranchial cyst

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3540 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Bone Marrow

-Not examined, missing

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

Prostate

-Not examined, missing

Spinal Cord

-Not examined, missing

Thyroid

-Ultimobranchial cyst

Urinary Bladder

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spleen, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3541 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin

-Raised lesion on left rear footpad.

Microscopic Observations:

Adrenal

-Cortical vacuolation, focal, mild
Sinusoidal ectasia, cortex, minimal

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild

Lung

-Vascular mineralization, mild
Pneumonia, interstitial, chronic, multifocal,
mild

Prostate

Hemorrhage, diffuse, marked
Perivascular mononuclear infiltrate, mild

Skin

-Not examined, missing

Testis/Epididymis

-Pododermatitis, ulcerative, hindleg, marked

Urinary Bladder

-Not examined, missing

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Aorta, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas,
Salivary Gland, Eye.

Animal Number: 1R-3542 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis

-Both testes small.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, moderate

Liver

-Hepatocyte vacuolation, multifocal, mild

Lung

-Vascular mineralization, minimal

Lymph Node (mesenteric)

-Hemorrhage, minimal

Pancreas

-Hyperplasia, islet cell, moderate

Testis/Epididymis

-Tubule atrophy, aspermatogenesis, bilateral,
marked

Thyroid

Polyarteritis, mild

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Salivary Gland, Eye,
Esophagus.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3544 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Hemorrhagic lesion, 0.7 cm dia.
Kidney	-Both enlarged, pale and pitted.
Testis/Epididymis	-Left testis small.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, moderate Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, marked
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Pancreas	-Acinar atrophy, mild Polyarteritis, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked Polyarteritis, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye, Heart.

Animal Number: 1R-3545 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 104) Found Dead

Macroscopic Observations:

Skin	-Circular lesions, 2.5 cm dia. on both hind footpads.
Liver	-Slightly pale

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate Cortical vacuolation, multifocal, moderate
Eye	-Not examined, missing
Heart	-Myocardial fibrosis, local areas, mild
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Pancreas	-Acinar atrophy, moderate
Pituitary	-Adenoma

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3545 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 104) Found Dead

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Microscopic Observations (continued):

Skin	-Pododermatitis, ulcerative, hindleg, bilateral, marked
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Liver, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland.

Animal Number: 1R-3547 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Mass, 0.4 cm dia.
Liver	-Pale

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Brain	-Oligodendroglioma, benign Large neoplasm composed of large, fairly uniform polyhedral cells in cerebral cortex.
Kidney	-Chronic progressive nephropathy, minimal Pyelonephritis, acute, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild
Pituitary	-Adenoma
Stomach	-Edema, submucosal, moderate

The following tissues were found to be within normal limits:

Spinal Cord, Bone Marrow, Spleen, Heart, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3548 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3548 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, mild Hepatocyte vacuolation limited to one area of liver.
Lung	-Vascular mineralization, mild Alveolar macrophages, minimal Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Thyroid	-C cell carcinoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3549 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 86) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1.4 x 0.8 cm.
Liver	-Slightly pale

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, minimal
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Kidney, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3552 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Spleen	-Circular raised lesion, 1.2 cm dia.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, local areas, moderate
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, mild
Spleen	-Hemangiosarcoma

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Salivary Gland, Eye.

Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Macroscopic Observations:	
Adrenal	-Left enlarged by a 1 cm dia. mass.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild Pheochromocytoma, benign, unilateral
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, moderate Hepatocyte vacuolation, multifocal, mild Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Microscopic Observations (continued):

Pancreas	-Not examined, missing
Pituitary	-Cyst, pars distalis
Salivary Gland	-Not examined, missing
Small Intestine	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3554 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Alveolar macrophages, multifocal, moderate Perivascular mononuclear infiltrate, moderate Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, moderate
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3555 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Sacrificed in extremis

Macroscopic Observations:

Kidney	-Pale, enlarged; mild hydronephrosis.
Urinary Bladder	-Enlarged, fluid filled, wall appears hemorrhagic.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate
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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3555 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Sacrificed in extremis

Microscopic Observations (continued):

Aorta	-Mineralization, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Nephrosis, tubular, moderate Papillary necrosis, moderate Hydronephrosis, mild Tubules dilated with low, basophilic epithelium, scattered mineralized tubules.
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, focal, mild
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, mild Edema, interstitial, moderate
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hemosiderosis, mild
Stomach	-Edema, submucosal, moderate
Urinary Bladder	-Hemorrhage, marked Epithelial hyperplasia, simple, diffuse, mild Cystitis, acute, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Large Intestine, Testis/Epididymis, Pituitary, Thyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3556 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Adrenal

-Right enlarged by mass, 2 x 1 cm.

Microscopic Observations:

Adrenal

-Carcinoma, cortical, unilateral
Large neoplasm, mostly necrotic. Cells
foamy, polyhedral arranged in cords and
sheets. High mitotic activity. Multiple
lung metastases.

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3556 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Pneumonia, interstitial, chronic, multifocal, mild Metastatic neoplasia Perivascular mononuclear infiltrate, mild Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3557 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild
Thyroid	-Hyperplasia, C cell, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3558 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 0.9 cm dia.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild Calculus, pelvic, minimal
Liver	-Cystoid degeneration, focal, minimal

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3558 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Lung, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3560 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 35) Sacrificed in extremis

Macroscopic Observations:

Brain	-Focal circumscribed dark area, dorsal surface, left cerebral hemisphere (0.2 cm dia.) and lateral surface of right cerebral hemisphere (0.2 cm dia.)
Lung	-Dark red diffuse mottling, all lobes; red frothy exudate at trachea.
Spleen	-Enlarged
Lymph Node (abdominal)	-Hepatic and renal nodes enlarged.
Liver	-Pale, appears enlarged.

Microscopic Observations:

Brain	-Abscess, mild Hemorrhage, multifocal, moderate
Liver	-Malignant lymphoma, histiocytic
Lung	-Malignant lymphoma, histiocytic Hemorrhage, diffuse, marked Necrosis, local areas, marked
Lymph Node (mesenteric)	-Hemorrhage, minimal
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hematopoiesis, extramedullary, increased, marked

The following tissues were found to be within normal limits:

Spinal Cord, Bone Marrow, Kidney, Heart, Stomach, Large Intestine, Urinary Bladder, Aorta,
Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3561 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Soft Tissues (leg)	-Right and left hindpaw and right forepaw swollen.
Kidney	-Right kidney polycystic.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, mild
Bone	-Arthritis, synovitis; joints, hindleg, foreleg, marked
Bone Marrow	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Cyst, cortical, unilateral, marked
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Perivascular mononuclear infiltrate, mild Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Hemorrhage, local areas, moderate
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, moderate Polyarteritis, marked
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Heart, Stomach, Small Intestine, Urinary Bladder, Aorta, Prostate, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3562 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Raised ulcerated inflamed lesion, right rear footpad.
Spleen	-Several pale foci.
Microscopic Observations:	
Adrenal	-Nodular hyperplasia, cortex, unilateral, moderate

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3562 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, mild Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Skin	-Pododermatitis, ulcerative, hindleg, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3563 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Thyroid	-One side enlarged, 1 x 0.8 cm.
Skin	-Mass, 1.7 x 1.4 cm, dorsal area.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Sinusoidal ectasia, cortex, minimal
Brain	-Astrocytoma, benign Poorly defined lesion in basal area of cerebrum. Tumor cells spindle.
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Hepatocyte alteration, basophilic, moderate Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, moderate Necrosis, focal areas, moderate
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pancreas	-Acinar atrophy, marked
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, moderate

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3563 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Skin	-Keratoacanthoma, back
Thyroid	-C cell carcinoma

The following tissues were found to be within normal limits:

Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3564 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Pale area in cortex of one kidney.
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Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, moderate
Bone Marrow	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Cyst, unilateral, moderate Area of multilocular cysts in cortex with lipid change in surrounding parenchyma.
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spinal Cord	-Not examined, missing
Testis/Epididymis	-Mineralization, focal, mild

The following tissues were found to be within normal limits:

Brain, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3565 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 84) Found Dead

Macroscopic Observations:

Skin

-Large mass, 7 x 7 cm, scrotal area.

Liver

-Pale

Microscopic Observations:

Adrenal

-Not examined, missing

Aorta

-Not examined, missing

Esophagus

-Not examined, missing

Eye

-No diagnosis, inadequate section

Kidney

-Chronic progressive nephropathy, mild

Large Intestine

-No diagnosis, inadequate section

Liver

-Hepatocyte vacuolation, multifocal, mild
Necrosis, multifocal, moderate

Lung

-Vascular mineralization, mild

Lymph Node (mesenteric)

-Not examined, missing

Pancreas

-Not examined, missing

Parathyroid

-Not examined, missing

Pituitary

-Not examined, missing

Prostate

-Not examined, missing

Salivary Gland

-Not examined, missing

Skin

-Liposarcoma

The scrotal mass was composed of large, vacuolated mononuclear cells. The degree of autolysis made diagnosis somewhat uncertain.

Small Intestine

-Not examined, missing

Spleen

-Hematopoiesis, extramedullary, increased, mild

Thyroid

-Not examined, missing

Trachea

-Not examined, missing

Urinary Bladder

-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Testis/Epididymis.

Animal Number: 1R-3566 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary

-Small dark lesion.

Microscopic Observations:

Adrenal

-Within normal limits

One of pair present

Kidney

-Chronic progressive nephropathy, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3566 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pancreas	-Polyarteritis, moderate
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Lymph Node (mesenteric), Salivary Gland, Stomach, Small Intestine, Heart, Eye, Esophagus.

Animal Number: 1R-3567 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin	-Raised papilloma type mass on back; raised inflamed lesion, right rear footpad.
Spleen	-Two pale foci.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Nodular hyperplasia, cortex, focal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, minimal Perivascular mononuclear infiltrate, minimal
Skin	-Papilloma, back Pododermatitis, ulcerative, hindleg, marked
Spleen	-Necrosis, local areas, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3569 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Kidney	-Bilaterally enlarged; pale, pitted.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, minimal Sinusoidal ectasia, cortex, mild Medullary cell hyperplasia, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pituitary	-Hyperplasia, focal, pars distalis, mild
Testis/Epididymis	-Polyarteritis, moderate

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3571 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Pale
Kidney	-Pale, pitted, enlarged.
Mesentery	-Mesenteric vessels thickened
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, minimal
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, minimal
Mesentery	-Polyarteritis, marked
Pancreas	-Polyarteritis, marked
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3571 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Small Intestine	-Polyarteritis, mesentery, marked
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Polyarteritis, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3572 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Pancreas	-Hyperplasia, islet cell, moderate
Parathyroid	-Not examined, not in plane of section
Stomach	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3573 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pancreas -Small circular pale mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
	Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Hepatocyte alteration, vacuolated, mild
	Hepatocyte alteration, basophilic, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
	Portal mononuclear cell infiltrate, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3573 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pancreas	-Acinar atrophy, moderate Islet cell adenoma
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Urinary Bladder,
Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Skin	-Ulcerated right and left hind footpads; circular white subcutaneous mass, 1.5 cm dia., in right inguinal area.
Thorax (internal)	-Filled with fluid.
Heart	-Slightly pale and flaccid.
Liver	-Slightly pale
Kidney	-Pale and pitted; 1.5 cm cyst in right kidney.
Testis/Epididymis	-Testes small

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
Aorta	-Necrosis, local areas, moderate Uniform intimal necrosis with reactive cellular infiltrate.
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked Cyst, unilateral, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Pneumonia, interstitial, chronic, diffuse, moderate Perivascular mononuclear infiltrate, mild Edema, local areas, marked
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Microscopic Observations (continued):

Pituitary	-Cyst, pars intermedia
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Not examined, missing
Skin	-Fibroma, subcutaneous, inguinal
	Pododermatitis, ulcerative, hindleg, marked
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Thyroid, Trachea, Esophagus, Eye.

Animal Number: 1R-3576 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 55) Sacrificed in extremis

Macroscopic Observations:

Skin	-Moist area around genital papilla.
Abdomen (internal)	-Large amount of gas in gastrointestinal tract; no food in stomach.

Microscopic Observations:

Kidney	-Pelvic mineralization, mild
Lung	-Hemorrhage, diffuse, marked
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Liver, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3577 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
	Cystoid degeneration, multifocal, mild
	Hepatocyte alteration, vacuolated, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3577 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
Mesentery	-Polyarteritis, marked
Pancreas	-Polyarteritis, marked
Small Intestine	-Polyarteritis, mesentery, moderate
Spleen	-Hemosiderosis, mild
Thyroid	-Cyst, colloid, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Large Intestine, Urinary Bladder, Aorta,
Testis/Epididymis, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3578 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.7 cm dia.
Skin	-Raised ulcerated inflamed lesion, 1.5 cm dia., left hind footpad.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild Hydronephrosis, unilateral, moderate Calculi present in ureter of hydronephrotic kidney.
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Sialadenitis, chronic, minimal Very minimal lesion, only one duct affected.
Skin	-Pododermatitis, ulcerative, hindleg, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3579 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 86) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Raised mass, 0.8 cm dia.
Liver	-Raised pale 2 cm dia. mass in right lateral lobe.
Skin	-Mass seen clinically on right side appears to be healed lesion.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal bile duct proliferation, mild Hepatocellular carcinoma Portal mononuclear cell infiltrate, mild
Lung	-Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Keratoacanthoma Skin lesion from right side.
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, mild Polyarteritis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Large Intestine, Urinary Bladder, Aorta, Prostate, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4576 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 25) Sacrificed in extremis

Macroscopic Observations:

Liver	-Enlarged; mottled yellow color.
Lymph Node (bronchial)	-Enlarged
Lung	-Pale
Spleen	-Enlarged
Stomach	-Red patchy areas on mucosa.
Lymph Node (mesenteric)	-Enlarged and reddened.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Bone Marrow	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic Mineralization, cortical, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4576 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 25) Sacrificed in extremis

Microscopic Observations (continued):

Liver	-Malignant lymphoma, lymphocytic
Lung	-Malignant lymphoma, lymphocytic Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Malignant lymphoma, lymphocytic
Pancreas	-Malignant lymphoma, lymphocytic
Salivary Gland	-Not examined, missing
Spinal Cord	-Malignant lymphoma, lymphocytic
Spleen	-Malignant lymphoma, lymphocytic
Stomach	-Ulcer
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Heart, Small Intestine, Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Thyroid, Parathyroid, Esophagus, Eye.

Animal Number: 1R-4577 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.8 cm dia.
Mammary Gland	-Multilobular mass, 4.5 x 3.5 x 2 cm, in right axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pelvic mineralization, mild Nephrosis, tubular, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Lobular hyperplasia
Pituitary	-Hemorrhage, marked Necrosis, moderate
Spleen	-Hemosiderosis, mild
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Thyroid, Parathyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4579 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 84) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Raised mass, 0.5 cm dia.
Skin	-Raised thickened lesion with scab on right side.
Liver	-Slightly pale
Stomach	-Somewhat reddened
Kidney	-Fluid filled cyst in left kidney.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Aorta	-Mineralization, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, moderate
Kidney	-Nephrosis, tubular Pelvic mineralization, marked Cyst, cortical, moderate Hyperplasia, pelvic epithelium, diffuse, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Ulcer, marked Skin lesion from side.
Spleen	-Hemosiderosis, mild
Stomach	-Mineralization, mucosal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Small Intestine, Large Intestine, Urinary Bladder, Uterus, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4580 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 52) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged; dark red mass, 0.5 cm dia.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Galactoceles
Parathyroid	-Not examined, not in plane of section

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4580 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 52) Sacrificed in extremis

Microscopic Observations (continued):

Pituitary	-Adenoma
Spleen	-Hemosiderosis, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Liver, Kidney, Heart, Lung, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Uterus, Ovary, Trachea, Thyroid, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4581 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland	-Ulcerated mass, 6 x 6 x 3 cm behind right shoulder.
Liver	-Possibly slightly pale and swollen.
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, basophilic, mild Hematopoiesis, extramedullary, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Adenocarcinoma
Parathyroid	-Not examined, not in plane of section
Spleen	-Hematopoiesis, extramedullary, increased, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Kidney, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Trachea, Thyroid, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4583 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Extensive post bleeding inflammation of right eye.
Mammary Gland	-Firm nodular mass, 6 x 5 x 3 cm, left inguinal.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4583 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, marked
Eye	-Panophthalmitis, unilateral, marked
Kidney	-Pelvic mineralization, mild Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild Necrosis, focal, mild
Lung	-Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Fibroadenoma
Ovary	-Tubular adenoma, unilateral
Parathyroid	-Not examined, not in plane of section
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Pituitary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric),
Pancreas, Salivary Gland.

Animal Number: 1R-4584 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Slight atrophy with corneal opacity, right eye.
Pituitary	-Enlarged
Adrenal	-Left adrenal enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex
Eye	-Phthisis bulbi, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4584 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4586 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised dark mass, 0.3 cm dia.
Uterus	-Dark area, 0.5 x 0.5 cm, in left horn near cervix.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Perivascular mononuclear infiltrate, minimal
Ovary	-Not examined, missing
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4587 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Small nodular mass, 3 x 2 cm, axillary; large mass, 8 x 8 x 3 cm, throat area.
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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4587 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, marked
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, minimal
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Skin	-Fibroma, subcutaneous
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Pituitary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-4591 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Acinar atrophy, focal, minimal
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4592 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Macroscopic Observations:	
Pituitary	-Enlarged, 0.9 x 1 cm.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Lobular hyperplasia, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland,
Eye.

Animal Number: 1R-4593 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Liver	-Hepatocyte alteration, vacuolated, mild
	Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea,
Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4594 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 79) Found Dead

Macroscopic Observations:

Kidney

-Right kidney appears slightly enlarged;
filled with yellow milky fluid.

Urinary Bladder

-Enlarged, 4.5 x 2 cm; filled with large, hard
calculi.

Pituitary

-Hemorrhagic mass, 0.9 x 0.6 cm

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, moderate
One of pair present

Aorta

-Not examined, missing

Kidney

-Pyelonephritis, acute, bilateral, moderate
Hydronephrosis, bilateral, moderate
Nephrosis, tubular, bilateral, moderate

Liver

-Hepatocyte alteration, vacuolated, mild

Lung

-Vascular mineralization, mild

Lymph Node (mesenteric)

-Not examined, missing

Ovary

-Within normal limits

One of pair present

Pancreas

-Not examined, missing

Parathyroid

-Not examined, not in plane of section

Pituitary

-Adenoma

Small Intestine

-Not examined, missing

Spleen

-Hemosiderosis, moderate

Urinary Bladder

-Epithelial hyperplasia, papillary, diffuse,
marked
Calculus

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Large Intestine, Uterus, Mammary Gland,
Trachea, Thyroid, Esophagus, Salivary Gland, Eye.

Animal Number: 1R-4595 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary

-Hemorrhagic mass, 0.8 cm dia.

Mammary Gland

-Small lobular mass, 2.7 x 1.5 x 1.8 cm, left
axilla.

Pancreas

-Small lobular mass, 1 x 0.7 cm, in area of
pancreas.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, moderate

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4595 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

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Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Alveolar macrophages, mild
Mammary Gland	-Lobular hyperplasia
Pancreas	-Islet cell carcinoma Partially encapsulated with invasion of capsule. Well differentiated.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Adenoma Small circumscribed papillary lesion.

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye, Ovary.

Animal Number: 1R-4596 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 78) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Mass, 0.8 x 0.6 cm.
Mammary Gland	-Mass, 2.5 x 2 x 1.5 cm, in left axilla.
Liver	-Very pale
Kidney	-Bilaterally pale and pitted; slightly enlarged; 0.4 cm dia. cyst in right.
Adrenal	-Pale, bilaterally

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, moderate Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild Cortical degeneration, local areas, moderate
Aorta	-Mineralization, mild Mineralization also in media of an elastic artery in section of mesentery submitted for mesenteric lymph node.
Kidney	-Chronic progressive nephropathy, marked Cyst, cortical, moderate
Liver	-Hepatocyte vacuolation, diffuse, marked

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4596 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 78) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Alveolar macrophages, minimal
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, moderate
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Uterus,
Ovary, Trachea, Thyroid, Esophagus, Pancreas, Eye.

Animal Number: 1R-4597 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Adrenal	-Right adrenal enlarged.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Medullary cell hyperplasia, focal, mild
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-No diagnosis, inadequate section
Ovary	-Tubular adenoma, unilateral
Pancreas	-Cyst
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Mammary Gland, Pituitary, Trachea, Thyroid, Esophagus, Salivary Gland,
Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4598 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 0.7 cm dia.
Adrenal	-Left adrenal greatly enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Brain	-Oligodendroglioma, benign
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Ovary	-Tubular adenoma
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4599 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Found Dead

Macroscopic Observations:	
Mammary Gland	-Subcutaneous mass, 2.5 x 2 x 1 cm, in perineal area.
Liver	-Appears mottled
Stomach	-Areas of elongated ulceration.
Urinary Bladder	-Thickened walls; mass 1.5 x 1 cm, with adhesions to abdominal wall.
Eye	-No tissue taken due to postmortem changes
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Malignant lymphoma, histiocytic
Esophagus	-Malignant lymphoma, histiocytic
Eye	-Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4599 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Found Dead

Microscopic Observations (continued):

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Malignant lymphoma, histiocytic Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild Nephrosis, tubular, mild
Large Intestine	-Malignant lymphoma, histiocytic
Liver	-Malignant lymphoma, histiocytic Necrosis, local areas, marked
Lung	-Malignant lymphoma, histiocytic Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Malignant lymphoma, histiocytic
Mammary Gland	-Malignant lymphoma, histiocytic
Ovary	-Malignant lymphoma, histiocytic
Pancreas	-Malignant lymphoma, histiocytic
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Stomach	-Necrosis, mucosal, moderate
Thyroid	-Malignant lymphoma, histiocytic
Urinary Bladder	-Malignant lymphoma, histiocytic Epithelial hyperplasia, simple, diffuse, mild
Uterus	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Small Intestine, Trachea, Salivary Gland.

Animal Number: 1R-4600 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Mammary Gland	-Subcutaneous cystic mass, 4 x 3.5 x 2 cm, in region of throat; subcutaneous multilobular mass, 5 x 4 x 2 cm, in right axilla.
Liver	-Appears mottled

Microscopic Observations:

Adrenal	-Necrosis, unilateral, marked
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4600 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Nephrosis, tubular, moderate
Liver	-Portal mononuclear cell infiltrate, moderate Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, eosinophilic, moderate Telangiectasis, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Adenoma, papillary Lobular hyperplasia
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Uterus, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4602 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Cornea appears cloudy.
Pituitary	-Raised mass, 1 cm dia.
Adrenal	-Right adrenal enlarged.
Kidney	-Pale and pitted.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, diffuse, marked
Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked Pelvic mineralization, mild Cyst, cortical
Liver	-Hepatocyte alteration, basophilic, mild
Lung	-Hemorrhage, local areas, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4602 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4603 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Liver	-Circular raised lesion, 0.6 cm dia., left lateral lobe.
Skin	-Hair loss on forelimbs.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate Cortical degeneration, diffuse, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Perivascular mononuclear infiltrate, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Acanthosis, mild
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4604 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Adrenal	-Left adrenal enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Large Intestine	-Not examined, missing
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hyperplastic nodule
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Lung, Stomach, Small Intestine, Urinary Bladder, Mammary Gland, Pituitary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4605 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 77) Sacrificed in extremis

Macroscopic Observations:	
Kidney	-Slightly pitted
Lung	-Right apical lobe consolidated and somewhat enlarged; possibly tumor, mass, chronic pneumonia.
Microscopic Observations:	
Adrenal	-Necrosis, local areas, moderate Hematopoiesis, extramedullary, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, moderate Malignant lymphoma, lymphocytic
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, midzonal, moderate Malignant lymphoma, lymphocytic
Lung	-Vascular mineralization, mild Malignant lymphoma, lymphocytic Large circumscribed mass with extensive necrosis.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4605 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 77) Sacrificed in extremis

Microscopic Observations (continued):

Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-Malacia, local areas, moderate
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, moderate

The following tissues were found to be within normal limits:

Brain, Bone Marrow, Stomach, Small Intestine, Large Intestine, Aorta, Uterus, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4606 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Small mass, 1.4 cm dia., left lateral area.
Pituitary	-Enlarged; circular dark lesion, 0.4 cm dia.
Uterus	-Dark fluid filled lesion, 0.5 x 0.6 cm, right horn.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Cortical degeneration, bilateral, moderate Pheochromocytoma, benign, unilateral
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Pigment, moderate Scattered small foci of dark brown pigment-laden macrophages within alveoli.
Lymph Node (mesenteric)	-Hemorrhage, mild
Mammary Gland	-Adenocarcinoma
Ovary	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Hydrometra, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4606 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Urinary Bladder, Aorta, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4607 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 40) Sacrificed in extremis

Macroscopic Observations:

Soft Tissues (neck)	-Reddened gland like structures, possibly enlarged lymph nodes or salivary glands.
Lymph Node	-Enlarged axillary, hepatic, mesenteric and internal iliac lymph nodes.
Liver	-Possibly slightly pale.
Spleen	-Considerably enlarged.

Microscopic Observations:

Adrenal	-Malignant lymphoma, lymphocytic
Aorta	-Malignant lymphoma, lymphocytic
Bone Marrow	-Malignant lymphoma, lymphocytic
Esophagus	-No diagnosis, inadequate section
Eye	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic
Liver	-Malignant lymphoma, lymphocytic
Lung	-Malignant lymphoma, lymphocytic Hemorrhage, local areas, mild Abscess
Lymph Node (mesenteric)	-Hemorrhage, moderate Malignant lymphoma, lymphocytic Massive enlargement of node by mature appearing lymphocytes. All other nodes examined were similarly involved.
Mammary Gland	-Malignant lymphoma, lymphocytic
Ovary	-Malignant lymphoma, lymphocytic
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Spleen	-Malignant lymphoma, lymphocytic
Stomach	-Hemorrhage, submucosal, moderate Malignant lymphoma, lymphocytic
Thyroid	-Malignant lymphoma, lymphocytic
Uterus	-Malignant lymphoma, lymphocytic

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Heart, Small Intestine, Large Intestine, Urinary Bladder, Pituitary,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4607 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 40) Sacrificed in extremis

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Trachea, Pancreas.

Animal Number: 1R-4609 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 1 cm dia.
Mammary Gland	-Mass, 5 x 4 cm, throat area; 3 cm dia., left axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	Pelvic mineralization, moderate
Liver	-Not examined, missing
	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Carcinoma
	Highly cellular very undifferentiated tumor.
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-C cell adenoma
Uterus	-Within normal limits
	Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4611 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Large lobular mass, 10 x 7.5 x 5 cm.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, local areas, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, eosinophilic, mild
Lung	-Hemorrhage, multifocal, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Thyroid, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.7 cm dia.
Mammary Gland	-Mass, 3 cm dia., left axilla; 4 cm dia., right axilla; 7 x 6 x 2 cm, right side.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Eye	-No diagnosis, inadequate section
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, diffuse, marked Alveolar macrophages, mild
Mammary Gland	-Galactocoele Fibroadenoma Fibroadenoma Two tumors present.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Thyroid, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4613 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 89) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Somewhat enlarged
Mammary Gland	-Mass, 10 x 8 x 5 cm, inguinal area; surface ulcerated.
Liver	-Appears pale

Microscopic Observations:

Adrenal	-Hematopoiesis, extramedullary, mild Sinusoidal ectasia, cortex, mild Cortical vacuolation, focal, mild
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild
Large Intestine	-Not examined, missing
Liver	-Hepatocyte vacuolation, periportal, mild Necrosis, multifocal, mild Hematopoiesis, extramedullary, mild
Lung	-Hemorrhage, multifocal, mild Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Aorta, Ovary, Trachea,
Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4614 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass in perineal area; possible milk cyst.
Uterus	-Large gelatinous cervical mass, 2 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pelvic mineralization, minimal Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Mammary Gland	-Adenocarcinoma
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-No diagnosis, inadequate section
Spleen	-Hemosiderosis, mild
Thyroid	-Ultimobranchial cyst
Uterus	-Polyp This was the mass at cervix noted at necropsy.

The following tissues were found to be within normal limits:
Brain, Bone Marrow, Heart, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Ovary, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4615 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild
Lung	-Pneumonia, interstitial, chronic, mild Alveolar macrophages, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4615 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Ovary, Pituitary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric),
Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4616 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Cortical degeneration, unilateral, marked

Heart

-Myocardial fibrosis, focal, mild

Myocarditis, chronic nonsuppurative,
multifocal, mild

Kidney

-Chronic progressive nephropathy, mild

Pelvic mineralization, minimal

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Hepatocyte vacuolation, multifocal, mild

Hepatocyte alteration, vacuolated, mild

Lung

-Perivascular mononuclear infiltrate, moderate

Vascular mineralization, mild

Alveolar macrophages, mild

Mammary Gland

-Not examined, missing

Ovary

-Cyst, unilateral

Parathyroid

-Not examined, not in plane of section

Spleen

-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Uterus, Pituitary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas,
Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4617 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Sacrificed in extremis

Macroscopic Observations:	
Ovary	-Hemorrhagic mass, 5 cm dia., left ovary.
Liver	-Pale; left lateral lobe dark red.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild One of pair present
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, diffuse, marked Massive necrosis of one lobe with compensatory increase in mitoses in another lobe.
Lung	-Vascular mineralization, mild
Mammary Gland	-Not examined, missing
Ovary	-Leiomyoma Large well differentiated neoplasia, mostly necrotic, probably arises from an oviduct.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,
Large Intestine, Urinary Bladder, Aorta, Uterus, Trachea, Thyroid, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4618 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 93) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 1.1 cm dia.
Mammary Gland	-Large ulcerated mass, 10 x 7 x 9 cm, right axillary area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4618 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 93) Sacrificed in extremis

Microscopic Observations (continued):

Skin	-Fibroma, subcutaneous Large neoplasm with extensive collagen formation, large portion necrotic. Described as mammary lesion but no mammary tissue present in section.
Thyroid	-Ultimobranchial cyst
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Ovary, Trachea, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye, Uterus.

Animal Number: 1R-4619 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Macroscopic Observations:

Spleen	-Slightly enlarged
Liver	-Pale with an irregular surface on all lobes.
Pituitary	-Enlarged with hemorrhagic foci.

Microscopic Observations:

Adrenal	-Necrosis, diffuse, marked Malignant lymphoma, histiocytic
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Kidney	-Nephrosis, tubular, marked
Liver	-Portal bile duct proliferation, marked Necrosis, local areas, moderate Malignant lymphoma, histiocytic
Lung	-Vascular mineralization, mild Malignant lymphoma, histiocytic
Lymph Node (mesenteric)	-Hemorrhage, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Malignant lymphoma, histiocytic Hematopoiesis, extramedullary, increased, moderate
Stomach	-Necrosis, mucosal, mild
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Small Intestine, Large Intestine, Aorta, Uterus, Ovary,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4619 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):
Trachea, Thyroid, Pancreas.

Animal Number: 1R-4621 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Slightly enlarged
Mammary Gland	-Subcutaneous ulcerated mass, 5 x 4 x 1.5 cm, in right axilla.
Liver	-Appears mottled.
Adrenal	-Slightly enlarged.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Nephrosis, tubular, moderate
Liver	-Portal mononuclear cell infiltrate, minimal Hepatocyte vacuolation, periportal, mild
Lung	-Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, mild
Mammary Gland	-Fibroadenoma Galactoceles
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Uterus, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4622 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 62) Found Dead

Macroscopic Observations:

Skin	-Small circular lesion on back; slight hair loss on left lateral side.
Mammary Gland	-Mass, 2 cm dia., right axillary area; 1.5 cm dia., left inguinal area.
Kidney	-Raised area, 0.3 cm dia., on surface of right kidney; appears fluid filled.
Pituitary	-Dark red gelatinous mass.
Lung	-Slightly mottled

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, moderate Hyperplasia, pelvic epithelium, local areas, mild
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Alveolar macrophages, mild
Mammary Gland	-Galactoceles
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Skin	-Ulcer, focal, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Uterus, Ovary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4623 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Eye	-Opacity, right eye.
Mammary Gland	-Multilobular mass, 11 x 12 x 3 cm, right axilla.
Adrenal	-Appear enlarged

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Eye	-Cataract, unilateral
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4623 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Sinusoidal ectasia, moderate
Mammary Gland	-Fibroadenoma
Pituitary	-Adenoma
Thyroid	-Follicular hyperplasia, cystic, unilateral, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Parathyroid, Pancreas, Salivary Gland.

Animal Number: 1R-4624 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.6 cm dia.
Mammary Gland	-Ulcerated, cystic mass, 4 x 4 x 3.5 cm, in left axilla-throat area; multilobular mass, 8.5 x 5.5 x 3 cm, in right inguinal area.
Lung	-Raised circular nodule, 0.6 cm dia., in left lobe.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Metastatic neoplasm Large metastasis of mammary adenocarcinoma.
Mammary Gland	-Fibroadenoma Adenocarcinoma
Ovary	-Cyst, unilateral

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4624 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4625 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged due to raised mass, 1.2 cm dia.
Mammary Gland	-Cystic mass, 2 cm dia., left axilla.
Adrenal	-Both appear enlarged.
Kidney	-Somewhat pitted

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, local areas, mild
Esophagus	-Not examined, missing
Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, local areas, moderate
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4626 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.9 cm dia.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta,
Uterus, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas,
Salivary Gland, Eye.

Animal Number: 1R-4627 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 1 x 0.6 cm.
Mammary Gland	-Firm mass, 5.5 x 4 x 3.5 cm, right lateral area; lobular mass, 7 x 6 x 5 cm, left axilla.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, moderate Hepatocyte alteration, basophilic, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Adenocarcinoma Neoplasm arises in several places in a fibroadenoma.
Ovary	-Tubular adenoma, unilateral Cyst, bilateral

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4627 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Pancreas	-Islet cell adenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Fibroma, subcutaneous
Uterus	-Cystic glands, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland,
Eye.

Animal Number: 1R-4628 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 1.2 cm dia.
Mammary Gland	-Small nodule, 1.5 cm dia., right axilla; possible milk cyst.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Galactoceles Adenoma, papillary Small highly cellular neoplasm lying adjacent to several large galactocoels.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas,
Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4633 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 63) Sacrificed in extremis

Macroscopic Observations:

Liver	-Very pale
Spleen	-Slightly enlarged
Mammary Gland	-Large subcutaneous mass, 6 x 10 x 2.5 cm, with necrotic areas, containing dark brown fluid, ventral abdomen.

Microscopic Observations:

Adrenal	-Hematopoiesis, extramedullary, cortical, mild Sinusoidal ectasia, cortex, mild
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal Vacuolation, conv. tub. epithelium, moderate
Liver	-Hepatocyte vacuolation, centrilobular, marked
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Mammary Gland	-Adenocarcinoma Well differentiated, ductular pattern, areas of moderate mitotic activity, large areas of necrosis.
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Uterus, Ovary, Pituitary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas,
Eye.

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.7 cm dia.
Mammary Gland	-Lobular mass, 8 x 6 x 4 cm, right axilla; lobular mass, 9 x 7 x 3.5 cm, left inguinal.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, moderate Hepatocyte alteration, eosinophilic, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma Fibroadenoma Both masses were fibroadenomas. Areas of necrosis and cystic areas in tumors.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Uterus, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4635 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 94) Found Dead

Macroscopic Observations:

Small Intestine	-Jejunum appears inflamed with reddish fluid; ileum appears inflamed near cecum.
Mammary Gland	-Mass, 7 x 7.5 x 2 cm, multilobular and ulcerated, right inguinal; mass, light beige in color, spherical, 2 cm dia., in left axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Hematopoiesis, extramedullary, cortical, moderate
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4635 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 94) Found Dead

Microscopic Observations (continued):

Liver	-Hepatocyte vacuolation, diffuse, mild Hematopoiesis, extramedullary, mild Mitotic activity, increased, moderate
Lung	-Vascular mineralization, mild Metastatic neoplasm
Mammary Gland	-Adenoma Adenocarcinoma Extensive necrosis.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, marked
Thyroid	-Ultimobranchial cyst

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Lymph Node (mesenteric), Pancreas.

Animal Number: 1R-4636 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Mass in right axilla appears to be milk cyst.
Liver	-Slightly raised dark mass, 0.6 cm dia., left lateral lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, mild
Heart	-Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Neumatodiasis, colon
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Mammary Gland	-Lobular hyperplasia
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4636 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Spleen -Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Urinary Bladder, Aorta, Uterus,
Ovary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4637 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 82) Sacrificed in extremis

Macroscopic Observations:

Pituitary -Reddened mass, 1 cm dia.
Lung -Focal areas of consolidation in anterior part
of right and left lung.
Liver -Possibly pale

Microscopic Observations:

Eye -Keratitis, acute, marked
Kidney -Pelvic mineralization, mild
Mineralization, cortical, mild
Chronic progressive nephropathy, mild
Liver -Hepatocyte vacuolation, periportal, moderate
Lung -Pneumonia, acute exudative, local areas,
moderate
Hemorrhage, multifocal, mild
Mammary Gland -Galactoceles
Pituitary -Adenoma
Spleen -Hemosiderosis, moderate
Uterus -Cystic glands, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Ovary, Trachea, Adrenal, Thyroid, Parathyroid, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary -Mass, 0.5 cm dia.

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, mild
Esophagus -Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, moderate
Lung	-Vascular mineralization, mild
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-No diagnosis, inadequate section
Spleen	-Hemosiderosis, mild
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland,
Eye, Ovary.

Animal Number: 1R-4639 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 56) Sacrificed in extremis

Macroscopic Observations:

Skin	-Midsternal subcutaneous mass, 8 x 8 x 3 cm.
Liver	-Slightly pale

Microscopic Observations:

Kidney	-Pelvic mineralization, mild Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Urinary Bladder, Aorta, Ovary,
Pituitary, Trachea, Adrenal, Thyroid, Parathyroid, Esophagus, Lymph Node (mesenteric), Pancreas,
Eye.

Summarized Single Tabulated Animal Report
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3581 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, moderate
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-C cell adenoma

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3582 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Ulcerated mass, 2.8 cm dia., dorsal.
Pituitary	-Hemorrhagic lesion, 0.2 cm dia.
Kidney	-Pale
Adrenal	-Left adrenal enlarged, 0.7 cm dia. mass.
Testis/Epididymis	-Testes small, bilateral.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Eye	-Retinal atrophy, diffuse, marked
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Skin	-Keratoacanthoma, back

Species: Rat
Project Number: 02B1CR0012

Summarized STAR Page: 95

259
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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3582 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, mild
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas.

Animal Number: 1R-3583 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Pale raised masses, 1.3 cm dia., right lateral lobe; 0.6 cm dia., left lateral lobe.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocellular carcinoma Megalocytosis, mild Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral Vascular mineralization, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3585 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Lung	-Raised pale lesion, 0.5 cm dia., left lobe.
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Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
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Summarized Single Tabulated Animal Report (continued)
 Individual Macroscopic and Microscopic Observations
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3585 Sex: Male Group: (5) FC-143 300 ppm
 Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Malignant lymphoma, lymphocytic Hepatocyte alteration, basophilic, moderate Megalocytosis, minimal
Lung	-Vascular mineralization, mild Fibrosis, pleural, moderate
Pancreas	-Acinar atrophy, mild Hyperplasia, acinar cell, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
 Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid,
 Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3586 Sex: Male Group: (5) FC-143 300 ppm
 Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Possible pale foci on one lobe.
Testis/Epididymis	-Pale mass, 1 cm dia.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, moderate Megalocytosis, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, moderate
Salivary Gland	-Sialadenitis, chronic, moderate
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, moderate Mineralization, tubular, mild Leydig cell adenoma, bilateral

The following tissues were found to be within normal limits:

Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Pituitary,
 Brain, Spinal Cord, Bone Marrow, Thyroid, Parathyroid, Trachea, Esophagus,
 Lymph Node (mesenteric), Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3587 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Eye	-Hypopyon, right eye.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, minimal
Eye	-Phthisis bulbi, unilateral, marked Lesion characterized by retinal atrophy, cataract, and corneal vascularization with collapse of the globe.
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Hepatocyte alteration, basophilic, minimal Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, minimal
Pancreas	-Hyperplasia, islet cell, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Salivary Gland	-Sialadenitis, chronic, moderate Moderate reactive hyperplasia of included lymph node.
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric).

Animal Number: 1R-3590 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 19) Sacrificed in extremis

Macroscopic Observations:	
Thymus	-Enlarged, 1.5 x 1.5 x 0.3 cm, dark red.
Liver	-Enlarged, brown/yellow mottling.
Spleen	-Markedly enlarged, 8 x 2 x 1 cm.
Lymph Node (mesenteric)	-Enlarged
Lymph Node (abdominal)	-Hepatic lymph nodes enlarged.
Small Intestine	-Peyer's patches enlarged and reddened.
Large Intestine	-Peyer's patches enlarged and reddened.
Kidney	-Slight dilatation of renal pelvis, bilateral.
Urinary Bladder	-Distended with urine.
Penis	-Swollen

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3590 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 19) Sacrificed in extremis

Microscopic Observations (continued):

Adrenal	-Malignant lymphoma, lymphocytic
Bone Marrow	-Malignant lymphoma, lymphocytic
Brain	-Malignant lymphoma, lymphocytic
Eye	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic
Liver	-Malignant lymphoma, lymphocytic Parenchyma almost completely replaced by diffuse neoplastic cell infiltrate.
Lung	-Malignant lymphoma, lymphocytic Hemorrhage, local areas, moderate
Lymph Node (abdominal)	-Malignant lymphoma, histiocytic Extensive neoplastic involvement of hepatic node.
Lymph Node (mesenteric)	-Malignant lymphoma, lymphocytic
Parathyroid	-Not examined, missing
Pituitary	-No diagnosis, inadequate section
Small Intestine	-Malignant lymphoma, lymphocytic
Spleen	-Malignant lymphoma, lymphocytic
Thymus	-Malignant lymphoma, histiocytic
Thyroid	-Not examined, missing
Urinary Bladder	-Malignant lymphoma, lymphocytic Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:

Heart, Stomach, Large Intestine, Aorta, Testis/Epididymis, Prostate, Trachea, Esophagus,
Pancreas, Salivary Gland, Spinal Cord.

Animal Number: 1R-3591 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-No diagnosis, inadequate section
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, moderate Hepatocyte alteration, basophilic, moderate Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate

Species: Rat
Project Number: 0291CR0012

Summarized STAR Page: 99

263

000650

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3591 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary -Adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3593 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver -Raised pale lesion, 0.6 cm dia., inferior
caudate lobe.

Microscopic Observations:

Kidney -Chronic progressive nephropathy, mild
Liver -Megalocytosis, minimal
Portal mononuclear cell infiltrate, mild
Cystoid degeneration, multifocal, mild
Hepatocellular carcinoma
Well differentiated, trabecular pattern,
moderate mitotic activity, vascular invasion.
Lung -Vascular mineralization, mild
Alveolar macrophages, mild
Parathyroid -Not examined, not in plane of section
Thyroid -C cell adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3594 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver -Pale foci throughout.

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, moderate
Heart -Myocarditis, chronic nonsuppurative,
multifocal, minimal
Kidney -Chronic progressive nephropathy, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3594 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Hepatocyte vacuolation, diffuse, moderate Cystoid degeneration, mild Hepatocyte alteration, vacuolated, moderate Megalocytosis, moderate Centrilobular cells enlarged with finely granular, eosinophilic, "ground glass" appearing cytoplasm.
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Testis/Epididymis	-Vascular mineralization, moderate
Thyroid	-Hyperplasia, C cell, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3595 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Firm mass, 3 x 2 x 1.5 cm, right axilla.
Pituitary	-Hemorrhagic mass, 0.5 x 0.7 cm.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Bone Marrow	-Not examined, missing
Kidney	-Pelvic mineralization, mild Pyelonephritis, acute, mild Hyperplasia, pelvic epithelium, diffuse, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, acute, moderate Mass described at necropsy as mammary gland was apparently the enlarged, inflamed salivary gland. No mammary tissue was present on any slide.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3595 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta,
Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Pancreas, Eye.

Animal Number: 1R-3596 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Pale, enlarged and pitted, bilateral.
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Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, minimal Medullary cell hyperplasia, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked Cyst, cortical, moderate
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, marked
Pituitary	-Adenoma
Testis/Epididymis	-Polyarteritis, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3597 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
-------	---

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3597 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, mild
Prostate	-Prostatitis, acute, suppurative, minimal

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3599 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Hydronephrosis, right kidney.
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Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Hyperplasia, pelvic epithelium, multifocal, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3600 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Mottled
Microscopic Observations:	
Adrenal	-Cortical vacuolation, mild
Bone Marrow	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild Megalocytosis, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Hemorrhage, minimal
Pituitary	-Not examined, missing
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Vascular mineralization, mild

The following tissues were found to be within normal limits:
Brain, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3601 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Mottled; yellow raised lesions, 0.7 and 0.9 cm dia., posterior caudate lobes.
Lymph Node (mesenteric)	-Enlarged
Stomach	-Enlarged gastric rugae
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, moderate Hepatocyte alteration, vacuolated, mild Megalocytosis, moderate Hepatocyte alteration, basophilic, moderate

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3601 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Hemorrhage, local areas, marked
Lymph Node (mesenteric)	-Hemorrhage, mild Hemangiosarcoma
Pancreas	-Acinar atrophy, moderate
Pituitary	-Cyst, pars distalis
Stomach	-Adenocarcinoma Extensive infiltration into submucosa and muscularis. Well differentiated, high mitotic index. Probably parietal cell origin. Tumor cells in lymphatics.

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland,
Eye.

Animal Number: 1R-3602 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, focal, mild Medullary cell hyperplasia, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Pancreas	-Islet cell adenoma
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Vascular mineralization, mild
Thyroid	-C cell adenoma

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Prostate, Pituitary, Parathyroid, Trachea, Esophagus, Salivary Gland, Eye.

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3603 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal
Kidney
Liver

-Sinusoidal ectasia, cortex, minimal
-Chronic progressive nephropathy, mild
-Portal mononuclear cell infiltrate, mild
Cystoid degeneration, focal, mild
Megalocytosis, minimal
Hepatocyte alteration, basophilic, mild
-Vascular mineralization, mild
-Not examined, not in plane of section

Lung
Parathyroid

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3605 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Pale, mottled

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative,
multifocal, minimal

Kidney
Liver

-Chronic progressive nephropathy, mild
-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Hepatocyte vacuolation, multifocal, mild
Cystoid degeneration, multifocal, mild
Megalocytosis, minimal

Lung

-Vascular mineralization, mild
Pneumonia, interstitial, chronic, multifocal,
mild

Salivary Gland
Spleen

Alveolar macrophages, moderate
Perivascular mononuclear infiltrate, moderate
-Sialadenitis, chronic, moderate
-Hematopoiesis, extramedullary, increased,
mild

Testis/Epididymis

Hemosiderosis, mild
-Tubule atrophy, aspermatogenesis, unilateral,
marked
Vascular mineralization, mild

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3605 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3606 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Nodular hyperplasia, cortex, focal, mild

Kidney

-Chronic progressive nephropathy, minimal
Pyelonephritis, acute, mild

Liver

-Portal mononuclear cell infiltrate, mild
Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Parathyroid

-Not examined, not in plane of section

Spleen

-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3607 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary

-Hemorrhagic mass, 1 x 0.7 cm.

Microscopic Observations:

Adrenal

-Cortical vacuolation, multifocal, moderate
Pheochromocytoma, benign, unilateral

Kidney

-Chronic progressive nephropathy, mild
Pyelonephritis, acute, moderate

Liver

Hyperplasia, pelvic epithelium, diffuse, mild

Lung

-Portal mononuclear cell infiltrate, mild

Lung

-Vascular mineralization, mild

Pancreas

Alveolar macrophages, mild

-Acinar atrophy, mild

Hyperplasia, islet cell, moderate

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3607 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid	-Adenoma
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, marked
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild
Thyroid	-Ultimobranchial cyst
Urinary Bladder	-Epithelial hyperplasia, simple, local areas, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3608 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin	-Raised inflamed lesion, left hind footpad.
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Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Nodular hyperplasia, cortex, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Skin	-Pododermatitis, ulcerative, hindleg, marked
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, moderate
Thyroid	-Ultimobranchial cyst

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Pituitary, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3609 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Nodular hyperplasia, cortex, focal, mild

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Megalocytosis, mild

Lung

-Vascular mineralization, mild

Hemorrhage, local areas, moderate

Lymph Node (mesenteric)

-Sinusoidal ectasia, mild

Pancreas

-Acinar atrophy, moderate

Polyarteritis, moderate

Parathyroid

-Not examined, not in plane of section

Testis/Epididymis

-Leydig cell hyperplasia, focal, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Salivary Gland, Eye.

Animal Number: 1R-3610 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Few pale foci.

Testis/Epididymis

-Testes appear somewhat small.

Microscopic Observations:

Adrenal

-Pheochromocytoma, benign, unilateral

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, multifocal, mild

Cystoid degeneration, multifocal, mild

Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,
mild

Perivascular mononuclear infiltrate, minimal

Hemorrhage, local areas, moderate

Pancreas

-Acinar atrophy, mild

Testis/Epididymis

-Mineralization, tubular, mild

Tubule atrophy, aspermatogenesis, bilateral,
marked

Summarized Single Tabulated Animal Report (continued)
 Individual Macroscopic and Microscopic Observations
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3610 Sex: Male Group: (5) FC-143 300 pps
 Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Thyroid

-C-cell adenoma
 Follicular hyperplasia, cystic, unilateral,
 moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
 Urinary Bladder, Aorta, Prostate, Pituitary, Parathyroid, Trachea, Esophagus,
 Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3611 Sex: Male Group: (5) FC-143 300 pps
 Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Few pale foci; raised pale lesion, 0.7 cm
 dia., in median lobe.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, mild
 Cortical vacuolation, focal, minimal

Esophagus

-Not examined, missing

Heart

-Myocarditis, chronic nonsuppurative,
 multifocal, mild

Kidney

-Chronic progressive nephropathy, mild
 Pelvic mineralization, minimal

Liver

-Portal mononuclear cell infiltrate, mild
 Hepatocyte vacuolation, multifocal, mild
 Cystoid degeneration, multifocal, mild
 Hepatocyte alteration, vacuolated, mild
 Megalocytosis, minimal
 Hyperplastic nodule
 Cells in cords of single cell thickness. Many
 cells vacuolated. Large central blood filled
 space.

Lung

-Vascular mineralization, mild
 Hemorrhage, local areas, moderate

Pancreas

-Acinar atrophy, mild

Parathyroid

-Not examined, missing

Salivary Gland

-Sialadenitis, chronic, marked
 Extensive squamous metaplasia of duct
 epithelium with some ducts occluded by
 hyperplastic, metaplastic epithelium.

Thyroid

-Not examined, missing

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3611 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Trachea

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3612 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Liver

-Multilobular mass, 4.5 x 4 x 3 cm in area of
right lateral lobe, attached to
caudate lobe.

Microscopic Observations:

Adrenal

-Cortical vacuolation, focal, minimal

Kidney

-Chronic progressive nephropathy, marked

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Hepatocellular carcinoma

Well differentiated, trabecular pattern,
large areas of necrosis within tumor.

Lung

-Vascular mineralization, mild

Alveolar macrophages, marked

Medial hypertrophy, arteries, moderate

Pancreas

-Hyperplasia, islet cell, moderate

Thyroid

-Cyst, colloid, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Parathyroid, Trachea, Esophagus,
Salivary Gland, Eye, Lymph Node (mesenteric).

Animal Number: 1R-3614 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis

-Pale masses of various sizes in both testes.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Cystoid degeneration, focal, minimal

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3614 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Prostate	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, moderate Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3615 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.8 cm dia.
Testis/Epididymis	-Right testis small.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, marked Extensive hyperplasia and metaplasia of duct epithelium.
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Pancreas, Eye.

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3616 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 72) Found Dead

Macroscopic Observations:

Pituitary

-Enlarged, 0.9 cm dia.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, multifocal, minimal

Cystoid degeneration, multifocal, mild

Necrosis, multifocal, moderate

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

Hemorrhage, diffuse, marked

Pancreas

-Hyperplasia, acinar cell, moderate

Pituitary

-Adenoma

Salivary Gland

-Not examined, missing

Spleen

-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3616 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Appears pale; pale raised mass, 1 cm dia.,
caudate lobe.

Microscopic Observations:

Adrenal

-Cortical vacuolation, multifocal, mild

Sinusoidal ectasia, cortex, mild

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, multifocal, minimal

Necrosis, focal, minimal

Megalocytosis, minimal

Hepatocellular carcinoma

Trabecular pattern, many tumor cells
vacuolated, moderate mitotic activity.

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3618 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):

Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3619 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Raised lesions, 2 x 1.5 cm, median lobes.
Kidney	-Hydronephrosis, left kidney.
Urinary Bladder	-Distended into abdomen, filled with dark colored fluid.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Nodular hyperplasia, cortex, focal, moderate
Kidney	-Chronic progressive nephropathy, minimal Hydronephrosis, bilateral, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, mild Hepatocellular carcinoma Poorly differentiated, adenoid and trabecular patterns, moderate mitotic activity.
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Salivary Gland	-Not examined, missing
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Hemorrhage, focal, minimal

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3621 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
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Species: Rat
Project Number: 0281CR0012

Summarized STAR Page: 114

278

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3621 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3623 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, mild Necrosis, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Pituitary	-Not examined, missing
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Sialadenitis, chronic, marked
Testis/Epididymis	-Vascular mineralization, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Thyroid, Parathyroid, Trachea, Esophagus, Eye, Pancreas.

Summarized Single Tabulated Animal Report (continued)
 Individual Macroscopic and Microscopic Observations
 Riker Laboratories, Inc. 3M
 FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3624 Sex: Male Group: (5) FC-143 300 ppm
 Fate: (Week= 90) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1 x 0.5 cm.
Liver	-Possibly pale
Kidney	-Slightly enlarged and pitted.
Testis/Epididymis	-Both testes appear somewhat small.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, multifocal, mild
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, marked
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
 Urinary Bladder, Aorta, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric),
 Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3625 Sex: Male Group: (5) FC-143 300 ppm
 Fate: (Week= 27) Sacrificed in extremis

Macroscopic Observations:

Soft Tissues (neck)	-Large multinodular mass, 9 x 8 x 6 cm, in left neck and throat region. Possibly of mammary gland or salivary gland origin. Mass contained several cystic areas that were filled with dark fluid.
Spleen	-Possibly slightly enlarged.

Microscopic Observations:

Liver	-Portal mononuclear cell infiltrate, mild Necrosis, focal, mild Megalocytosis, minimal
Lung	-Metastatic neoplasia Thrombus Large thrombus containing tumor cells from salivary gland tumor. Multiple small metastases of salivary tumor throughout lung.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3625 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 27) Sacrificed in extremis

Microscopic Observations (continued):

Salivary Gland

-Carcinoma

Highly cellular, anaplastic tumor. Appears to have arisen in parotid gland duct. Small rim of salivary gland tissue around mass.

Spleen

-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3628 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Cortical vacuolation, focal, moderate

Kidney

-Chronic progressive nephropathy, moderate

Liver

-Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild
Cystoid degeneration, multifocal, mild
Megalocytosis, minimal

Lung

-Vascular mineralization, moderate

Alveolar macrophages, mild

Hemorrhage, local areas, moderate

Parathyroid

-Not examined, not in plane of section

Spleen

-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3629 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative,
multifocal, mild

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild
Megalocytosis, mild

Lung

-Vascular mineralization, mild
Alveolar macrophages, mild
Hemorrhage, local areas, moderate

Salivary Gland

-Sialadenitis, chronic, marked

Thyroid

-Ultimobranchial cyst

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3630 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, mild

Heart

-Myocardial fibrosis, local areas, mild
Myocarditis, chronic nonsuppurative,
local areas, mild

Liver

-Portal mononuclear cell infiltrate, mild
Cystoid degeneration, multifocal, mild
Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Pituitary

-Not examined, missing

Testis/Epididymis

-Vascular mineralization, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3631 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Nodular hyperplasia, cortex, focal, mild
Medullary cell hyperplasia, focal, minimal

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Hepatocyte vacuolation, local areas, mild
Megalocytosis, minimal

Lung

-Vascular mineralization, moderate

Alveolar macrophages, mild

Hemorrhage, local areas, moderate

Salivary Gland

-Sialadenitis, chronic, marked

There were two sections of gland on the
slide, only one was involved.

Spleen

-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3632 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Few pale foci.

Testis/Epididymis

-Pale mass, 1.5 cm dia.

Microscopic Observations:

Kidney

-Chronic progressive nephropathy, moderate

Liver

-Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, multifocal, mild

Megalocytosis, mild

Hepatocyte alteration, basophilic, mild

Single subcapsular area of basophilic
alteration. About one half of the cells have
multiple cytoplasmic vacuoles.

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

Hemorrhage, focal, mild

Pancreas

-Hyperplasia, islet cell, moderate

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3632 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):
Testis/Epididymis

-Tubule atrophy, aspermatogenesis, unilateral,
marked
Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3633 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Eye -Opacity, right eye.
Kidney -Bilaterally pale and pitted.

Microscopic Observations:

Adrenal -Sinusoidal ectasia, cortex, mild
Ganglioneuroma
Large, well differentiated tumor arising in
medulla of one gland. Composed of nerve
fibers and large ganglion cells.
Eye -Keratitis, chronic, moderate
Heart -Myocarditis, chronic nonsuppurative,
local areas, mild
Kidney -Chronic progressive nephropathy, marked
One of pair present
Liver -Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Cystoid degeneration, multifocal, mild
Hepatocyte alteration, vacuolated, mild
Megalocytosis, moderate
Lung -Vascular mineralization, mild
Alveolar macrophages, mild
Perivascular mononuclear infiltrate, minimal
Hemorrhage, local areas, mild
Thyroid -Cyst, colloid

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland.

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3634 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis

-Pale masses, 1 cm dia., in each testis.

Mesentery

-Mass, 3 x 1.5 cm in area of pancreas.

Microscopic Observations:

Liver

-Portal mononuclear cell infiltrate, mild
Cystoid degeneration, multifocal, mild
Hepatocyte alteration, vacuolated, moderate
Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

Pancreas

-Adenocarcinoma

Large, highly cellular, well differentiated
neoplasm with high mitotic index. Lymphatic
invasion.

Parathyroid

-Not examined, not in plane of section

Spleen

-Hemosiderosis, mild

Testis/Epididymis

-Tubule atrophy, aspermatogenesis, bilateral,
marked

Leydig cell adenoma, bilateral

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Kidney, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3635 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary

-Hemorrhagic area, 0.5 x 0.2 cm.

Microscopic Observations:

Adrenal

-Medullary cell hyperplasia, focal, minimal

Kidney

-Chronic progressive nephropathy, mild

Liver

-Portal mononuclear cell infiltrate, mild

Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Alveolar macrophages, mild

Perivascular mononuclear infiltrate, minimal

Pituitary

-Adenoma

Salivary Gland

-Sialadenitis, chronic, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,

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Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FD-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3635 Sex: Male Group: (5) FD-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits (continued):

Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3636 Sex: Male Group: (5) FD-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Bone

-Swollen metatarsal joints, bilateral hind
limbs.

Testis/Epididymis

-Both testes appear small.

Microscopic Observations:

Bone

-Arthritis, synovitis; joints, hindleg,
moderate

Heart

-Myocarditis, chronic nonsuppurative, focal,
minimal

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Cystoid degeneration, focal, minimal
Megalocytosis, minimal

Lung

-Vascular mineralization, mild
Alveolar macrophages, mild

Lymph Node (mesenteric)

-Granuloma, multifocal, moderate

Pancreas

-Polyarteritis, moderate

Testis/Epididymis

-Tubule atrophy, aspermatogenesis, bilateral,
marked
Polyarteritis, moderate
Vascular mineralization, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,
Salivary Gland, Eye.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3637 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Thyroid	-Possibly slightly enlarged.
Pituitary	-Mass, 0.5 cm dia.
Thymus	-Slightly enlarged and hemorrhagic.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Necrosis, multifocal, moderate
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Pancreas	-Acinar atrophy, minimal
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Thymus	-Hemorrhage, marked

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3639 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised dark mass, 0.7 cm dia.
Adrenal	-Enlarged, right adrenal

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, marked Medullary cell hyperplasia, focal, mild
Kidney	-Mineralization, cortical, mild
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, moderate Granuloma Fragment of unidentified foreign material in granuloma.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Uncarcinogenicity Study in Rats

Table: 2

Animal Number: 1R-3639 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3640 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 72) Sacrificed in extremis

Macroscopic Observations:

Spleen	-Possibly smaller than normal.
Abdomen (internal)	-Gastrointestinal tract from stomach to cecum distended with gas.
Eye	-Right eye slightly atrophied

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, focal, minimal
Eye	-Keratitis, acute, marked Lesion in right eye. Extensive corneal ulceration.
Kidney	-Calculus, pelvic, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Spleen	-Hemosiderosis, mild Atrophy, moderate
Stomach	-Gastritis, acute, diffuse, mild

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Salivary Gland.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3641 Sex: Male Group: (5) FC-143 300 ppm
Date: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Yellowish foci, 0.3 cm dia., median lobe.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, local areas, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, minimal Hyperplastic nodule Circumscribed, expansive lesion with preservation of normal architecture. Portal areas present. Cells in nodule more basophilic, vacuolated.
Lung	-Vascular mineralization, mild Hemorrhage, focal, mild
Pancreas	-Acinar atrophy, moderate
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aorta, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Salivary Gland, Eye.

Animal Number: 1R-3644 Sex: Male Group: (5) FC-143 300 ppm
Date: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Appears mottled; small pale area in median lobe.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild Nodular hyperplasia, cortex, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Megalocytosis, minimal Hyperplastic nodule Cells of nodule have slightly more basophilic cytoplasm; many are vacuolated.

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3644 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Salivary Gland	-Sialadenitis, chronic, marked
Testis/Epididymis	-Vascular mineralization, moderate

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3645 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis	-Pale mass, 1.3 cm dia., in left testis.
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Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, multifocal, mild
Aorta	-Metastatic neoplasia
Esophagus	-Metastatic neoplasia
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, minimal Portal bile duct proliferation, minimal Megalocytosis, minimal
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, mild Hemorrhage, focal, mild
Pancreas	-Acinar atrophy, mild
Parathyroid	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Soft Tissues (thorax)	-Histiocytoma, malignant Diffuse infiltrate of histiocytic cells in mediastinal tissues. Moderate number of multinucleate giant cells. Infiltrate extends into muscle around bone.
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral
Trachea	-Metastatic neoplasia
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, minimal

Summarized Single Tabulated Animal Report (continued)
Individual Macroscopic and Microscopic Observations
Riker Laboratories, Inc. 3M
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Table: 2

Animal Number: 1R-3645 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Prostate,
Pituitary, Thyroid, Lymph Node (mesenteric), Eye.

Animal Number: 1R-4641 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 73) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland

-Large multilobular subcutaneous mass, left
inguinal and perineal area,
10 x 7 x 3.5 cm. Mass ulcerated on the dorsal
surface; inside cystic with milky
fluid present.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, marked

Esophagus

-Not examined, missing

Kidney

-Chronic progressive nephropathy, minimal

Liver

-Portal bile duct proliferation, mild
Hepatocyte alteration, vacuolated, focal,
minimal

Lung

-Hemorrhage, local areas, mild
Alveolar macrophages, multifocal, mild

Mammary Gland

-Fibroadenoma

Ovary

-Not examined, missing

Salivary Gland

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Uterus, Pituitary, Trachea, Thyroid, Parathyroid,
Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-4643 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 78) Sacrificed in extremis

Macroscopic Observations:

Pituitary

-Hemorrhagic mass, 0.8 cm dia.

Microscopic Observations:

Esophagus

-Not examined, missing

Kidney

-Pelvic mineralization, mild

Liver

-Hepatocyte vacuolation, diffuse, mild