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

(RIKER EXPERIMENT No. 0281CR0012)

Volume 1 of 4

CONDUCTED DURING

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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	-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

TABLE OF CONTENTS - Continued

					PAGE (s)
	TABLE	9	-	Mortality Data	. 44	1
	TABLE	10	-	Summary of Clinical Signs	. 46	5
	TABLE	11	-	Summary of Ophthalmologic Changes	. 48	3
	TABLE	12	-	Mean and Individual Hemogram Values - Males	. 50	נ
	TABLE	13	-	Mean and Individual Hemogram Values - Females	. 57	7
	TABLE	14	-	Mean and Individual Serum Chemistry Values - Males	. 64	1
	TABLE	15	· -	Mean and Individual Serum Chemistry Values - Females	. 71	L
	TABLE	16	-	Urinalysis Values	. 78	3
	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		
	TABLE	18	-	One Year	. 8	
	TABLE	10		Two Years	. 86	5
	IARLE	19	-	Summary of Major Microscopic Findings - Neoplastic Lesions	. 91	1
	TABLE	20	-	Summary of Major Microscopic Findings - Non-Neoplastic Lesions	. 92	2
REPOR	RT FIGU	JRES	3.	• • • • • • • • • • • • • • • • • • • •	. 93-9	96
	FIGUR	Ξ 1	-	Mean Body Weights - Males	. 93	3
	FIGUR	E 2	-	Mean Body Weights - Females	. 94	1
	FIGUR	Ξ 3	-	Mean Feed Consumption Per Kilogram Mean Body Weight - Males	. 9!	5
	FIGUR	E 4	-	Mean Feed Consumption Per Kilogram Mean Body Weight - Females	Q.	ร์

TABLE OF CONTENTS - Continued

	P	AGE(S)
APPENDIX		7-1223
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	
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
	- Chemical Analyses of FC-143 and Stability	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

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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 [Crl: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	Dosage Levels		Group Size & A Males	<u>nimal</u>	Numbers Females	
Groups	(ppm)	(An. Nos.)		(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 SGOT), 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 <u>in situ</u> 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
Adrenals (2)
Brain (3 Sections including

Liver (2 Sections)
Lung (2 Sections)
Lymph node (mesenteric)

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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 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-dese (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 intestines, lymph node(s), and spinal cord/bone marrow. 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.

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RESULTS

<u>In-Life Findings</u>: 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 ($p = \langle 0.05\rangle$) 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).

<u>Postmortem Findings</u>: 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. 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 ($p = \langle 0.05\rangle$) 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 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. 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. 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. 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. 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%.

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 extasia (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. 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.
- 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.
- 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. 0281CR0012 - TWO YEAR ORAL (DIET) TOXICITY/CARCINOGENICITY STUDY OF FLUOROCHEMICAL FC-143 IN RATS

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TWO YEAR ORAL (DIET) TOXICITY/CARCINOGENICITY STUDY OF FLUOROCHEMICAL 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)

	_	Dosage Le	evels (ppm)
Approximate Study Month	• · · · · · · · · · · · · · · · · · · ·	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	<u>b</u> -34.0%	- 6.7%
11	328	- 6.1%	
13	340	- 2.3%	+ 7.7%
6	366	+ 2.6%	+ 4.4%
19	38 4	+ 2.0%	+ 2.2%
:2	395	+ 3.0%	+ 3.3%
24	404	+ 9.4%	+10.0%
ean Deviati	on for the Study	<u>c</u> + 1.6%	+ 1.9%

 $[\]frac{a}{c}$ 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.

 $[\]frac{c}{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) $\underline{+}$ % Difference from Control

MALES

tudy	Control	300 ppm		30 ppm	
ek	Mean Wt.	Mean Wt.	% Diff.	Mean Wt.	% Diff.
0	165.3	162.1	- 1.9	167.0	
2	270.9	234.3	-13.5	271.0	+ 1.0
4	334.0	276.7	-17.2		+ 0.0
6	390.7	308.6	-21.0	328.5	- 1.6
8	429.2			369.4	- 5.4
10		353.2	-17.7	410.3	- 4.4
12	456.2	380.1	-16.7	441.5	- 3.2
4	475.5	398.0	-16.3	458.1	- 3.7
	493.2	412.8	-16.3	475.4	- 3.6
6	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
10	576.3	497.2	-13.7	558.6	- 3.1
12	580.6	505.7	-12.9	566.4	- 2.4
14	582.9	511.8	-12.2	571.3	- 2.0
66	591.0	514.2	-13.0	575.4	- 2.6
18	599.4		-12.4	584.0	- 2.6
.0	608.4	535.2	-12.0	592.5	- 2.6
12	612.9	540.9	-11.7	600.5	- 2.0
4	619.8	550.8	-11.1	610.4	- 1.5
.6	623.5	552.0	-11.5	612.1	- 1.8
8	626.1	558.5	-10.8	618.9	- 1.1
0	639.2	566.7	-11.3	627.1	- 1.9
2	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	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	Mean Wt.	% Diff.
54	6F.4. 2	E33 6	44 5		
5 4 56	654.3	577.6	-11.7	641.9	- 1.9
58	661.6	583.1	-11.9	646.4	- 2.3
	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) $\underline{+}$ % Difference from Control

FEMALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	Mean Wt.	% Diff.
0	138.2	138.1	+ 0.0	137.2	- 0.7
2	159.2	167.3	+ 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	+ 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	+ 0.0	406.2	+ 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	Control	300 ppm		30 ppm	
leek	Mean Wt.	Mean Wt.	% Diff.	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	
70	431.4	429.1	- 0.5	443.5	+ 4.2
72	435.2	432.8	- 0.6	443.5	+ 2.8
74	446.5	444.6	- 0.4	463.3	+ 3.1
76	455.2	447.4	- 1.7		+ 3.8
78		452.7	- 1.7	468.8	+ 3.0
80	474.9	457.0	- 2.6 - 3.8	471.3	+ 1.4
82	484.0	461.8	- 3.6 - 4.6	475.8	+ 0.2
84	484.8	457.6	- 4.6	485.7	+ 0.4
86		458.2	- 7.0	476.3	- 1.8
88	499.1	456.6	- 8.5	479.7 483.4	- 2.6
90		451.8	- 9.7		- 3.1
92	512.5	455.9	-11.0	485.2 486.3	- 3.1
94		451.0	-10.8	492.0	- 5.1
96	506.9	464.5	- 8.4		- 2.7
98		468.0	- 6.4 - 6.4	504.3	- 0.5
00		464.2	- 7.4	505.5	+ 1.1
02		462.8	- 7.4 - 8.1	505.6	+ 0.9
04	502.0	450.3	-10.3	503.3 501.8	- 0.1 + 0.0

Table 4

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

MALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.		% Diff.	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	+ 4.1
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	+ 2.3 - 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) + % Difference from Control

MALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	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

tudy	Control	300 ppm		30 ppm	
eek	Mean Wt.	Mean Wt.	% Diff.	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 Weigh (g of diet consumed per day) \pm % Difference from Control

FEMALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	Mean Wt.	% Diff.
54	48.1	47.1	- 2.1	477 2	4 7
56	51.5	48.4	- 6.0	47.3	- 1.7
58	46.3	47.6		47.1	- 8.5
60	49.6	47.6	+ 2.8	46.3	+ 0.0 - 3.8
62			- 0.8	47.7	
64	47.1	46.5	- 1.3	44.8	- 4.9
66	48.4	46.1	- 4.8	44.1	- 8.9
68	41.0	39.5	- 3.7	39.6	- 3.4
	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

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

MALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	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

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

MALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	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

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

FEMALES

Study	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	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	Control	300 ppm		30 ppm	
Week	Mean Wt.	Mean Wt.	% Diff.	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	+ 0.0	20.5	- 2.4
62	20.1	20.1	+ 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	- 7.8 - 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	- 4.6 - 5.5
78	20.5	19.9	- 2.9	20.6	
80	21.7	20.3	- 6.5	18.3	+ 0.5
82	21.3	19.4	- 8.9	19.0	-15.7
84	21.1	18.2	-1°3.7	18.2	-10.8
86	21.8	17.9	-17.9	18.1	-13.7
88	22.6	19.3	-14.6	18.0	-17.0
90	23.1	20.6	-10.8	18.7	-20.4
92	23.5	20.0	-14.9	19.4	-19. 1
94	23.7	21.4	- 9.7	21.0	-17.5
96	21.5	20.6	- 4.2	19.0	-11.4
98	23.4	20.7	-11.5		-11. 6
00	20.8	20.4	- 1.9	20.9 21.5	-10.7
02	21.4	21.4	+ 0.0		+ 3.4
04	20.9	22.9	+ 9.6	23.3 21.7	+ 8.9 + 3.8

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

Study	<u>300</u>	ppm	30	ppm
Week	Male	Female	Male	Female
1	29.6	29.0	3.1	2.9
2 4 6 8	29.0	30.5	2.6	3.1
4	25.2 20.3	24.5	2.3	2.5 2.5 2.2
8	20.3	24.3 22.5	1.8	2.5
10	18.9	21.8	1.9 1.7	2.2
12	17.5	21.1	1.5	2.2 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 22	16.4	18.4	1.5	2.0
24	15.6 15.6	18.3 17.4	1.4	1.9
26	14.8	16.9	1.4 1.4	1.8 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 38	12.8	16.3	1.2	1.7
40	13.8 13.2	15.8 15.5	1.3	1.6
42	13.2	16.1	1.3 1.2	1.5 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	300	ppm	30	ppm
Week 	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	$\overline{11.1}$	14.0	1.1	1.3
64	12.1	13.8	1.0	1.3
6.6	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	$\tilde{1}.\tilde{1}$	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

TWO YEAR URAL(DIET) TUXICITY-UNCOGENICITY STUDY OF FLUUHOCARBON FC-143 IN RATS MURTALITY DATA

							E E	WEEK OF	STUDY						
<u>nose group</u>	INITIAL NO.	1-1	1 Ed	12	13-	17-	21-	25-	29-	33-	37-	4 1 - 4 4 4	45-	52	53-
MALES															
CONTROL 0 PPM	9.0	•	0	0	0	œ	0	0	0		0	•	0	0	-
HIGH DOSE	50	0	0	0	0	-	•	-	0	0	0	•	0	•	0
LOW DOSE 30 PPM	20	0	0	0	0	Φ	0	0	0	0	-	•	0	0	0
FEMALES															
CONTROL 0 PPM	50	•	0	0	0	•	0	-	•	0	-	0	0	-	-
HIGH DOSE 300 PPM	5.0	e	0	0	0	æ	•	•	0	•.	0	0	0	-	-
LOW DOSE 30 PPM	50	0	•	Φ	0	€	0	0	0	0	0	-	-	-	0

TABLE 9

TAO YEAR ORAL(DIET) TOXICITY-UNCOGENICITY STUDY OF FLUDHUCARBON FC-143 IN RATS MURTALITY DATA

						.5	WEEK OF STUDY	F STU	υ¥							
<u> 20098_3200</u>	INITIAL NO.	57-	61-	-59 - 84	69-	73-	-77	81- 14-	85- 38	-68 -68	93-	100	101- 1	105- -108	1-109 MEEK TO NO. 3	MEEK TOTALS
MALES																
CONTRUC 0 PPM	20	0	-	0	0	-	0	7	4	-	7	-	2	-	16	32
300 PPM	50	0	0	0	~	0	0	•	0	-	0		•	0	ø	12
LOW DOSE 30 PPM	20	0	O	8	≈	0	0	0	~		4	7	~	0	14	28
FEMALES																
CONTROL 0 PPM	5.0	0	m	0	0	-	m)	Ni	~	4	m	r.	-	0	52	50
HIGH DUSE 300 PJM	5.0	-	~		0		~	1	m	يدر	4	~	e	0	21	2+
LOW DOSE	2.0	0	ē	0	-	-	0	G	~		•	~	-	0	56	52

CHI-SQUARE ITESTS FOR DUSE GROUP DIFFERENCES FRUM CONTROL

	MALES	ـــــــــــــــــــــــــــــــــــــ	FEMALES	LES
<u> </u>	CHI- SHUARE PHUH.	, 1010	CHI- SQUARE PROB.	PROB
300 PPM	* 4.72 0.02H	0.028	0.36	0.36 0.555
M94 05	9.05	0.05 0.11	00.00	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

	ပြ	Control	Ι.	3(300 ppm) N	30 ppm	
	Σ	Ŀ	5	X	F	5 8	Σ	F	S.
Initial number of rats	65	65	100.0	65	65	100.0	50	50	100.0
Survivors at end of study	34	22	45.4	44	29	56.2	36	24	0.09
Mass(es)— in various areas	6	38	43.8	10	40	38.5	7	41	48.0
(Mass[es] resolved prior to term)	=======================================	(7)	(13.9)	(8)	(7	(11.5)	. 4	(2)	(0.6)
Alopecia in various areas	9	14	15.4	6	16	19.2	9	16	22.0
Swollen throat	13	10	15.4	7	6	8.5	4	œ	12.0
Pale (blanched) eyes and/or appears thin (emaciated)	6	თ	13.9	ĸ	80	10.0	6	10	19.0
Excessive lacrimation	80	12	15.4	6	7	12.3	œ	S	13.0
Ataxia	4	7	4.6	7	15	13.1	ĸ	6	14.0
Convulsions (clonic)	რ	0	2.3	7	0	1.5	4	0	4.0
Occasional urinary incontinence and/or hematuria	្រហ	4	6.9	-	8	2.3	м	4	7.0
Raised ulcerated lesion on hind foot pad(s)	7	0	5.4	-	-	1.5	ιΩ	۰0	5.0
Occasional bloody nares	m	-	3.0	0	9	4.6	0	-	0.

 $\frac{a}{b}$ (Incidence in males + incidence in females) /total number of animals in the group x 100 $\frac{b}{c}$ To be detailed in the pathology report $\frac{c}{c}$ Indication of Sialodacryoadenitis (SDA) viral infection 46.

Table 10

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

Summary of Clinical Observations

	Control	300 ppm	Ppm F	30 ppm	mC.
Occasional bloody feces	7	7	•	-	0
Occasional episode of dyspnea	o 	-	0	0	0
Listing of the head	0	0	ស	-	7
Circular ulcerated area on skin	4	-	0	-	0
Swollen (distended) abdomen	0	7	0	0	7
Swelling in inguinal area	-	0	0	0	0
Swollen leg and/or foot	3	7	-	-	0
Swollen ears	0	0	***	0	-
Swollen penis	0	0	1	-	.1
Paresis of hind leg(s)/feet	0	-	0	71	0

Table 11

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

Summary of Clinical Ophthalmologic Findings

Observations	Eve(s)	Control M	Control - 0 ppm M F	30C	300 ppm F	30 M	30 ppm F
Obthicia Bulhi	Biaht	0	-	3	၈	-	ю
(Atrophy)	Left	0	-	0	0	0	0
Posterior Subcapsular	Right	М	0	-	0	0	0
Cateract(8)	Left	2	,	-	0	0	0
	Bilateral	-	0	0	0	0	0
Corneal (ocular) Opacity	Right	0	7	0	0	7	0
(Diffused: ulcerated; focal	Left	0	7	0	0	7	0
with iris staphyloma; with pannus; partially collapsed).	Bilateral	0	-	0	•	0	•
Chronic superficial	Right	0	,- -	7	0	0	0
Keratitis	Bilateral	-	0	7	0	0	0

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

Table 11

Summary of Clinical Ophthalmologic Findings

ty		Chronic uveitis (secondary to blood sampling) Diffused lens opacity and chronic iritis with microphthalmos	ulation	Chronic uveitis with anterior synechia in right eye Diffused lens opacity		ondary exophthalmia	Diffused lens opacity with pannus and microphthalmia
Description of Abnormality		Chronic uveitis (secondary to blood sampling) Diffused lens opacity and chronic iritis with	Posterior lens opacity Very pale choroidal circulation Dacryadenitis	Chronic uveitis with anterior synechial Diffused lens opacity	Theday 'toring' thou	Chronic uvaitis with secondary exophthalmia Dacryadenitis	Diffused lens opacity wi
Eye(s)		Right Right	Bilateral Bilateral Richt	Bilateral Bilateral		Left Right	Left
(N) Group	Males	(1) Control (1) Control	<pre>(1) Control (1) Control (1) High doge</pre>	(1) High dose (1) High dose	Females	<pre>(1) Control (1) Control</pre>	(1) Low dose

TABLE 17	

MONTH 3 MONTH 3 MONTH 3 MONTH 12 MONTH 12 MONTH 12 MONTH 18 MONTH 18	ERYTI (CELLS (CELLS 8.29 7.91 7.91 8.46 7.58 8.01 8.38 7.48 7.55 8.62	0.84L (D X 10**6 S.DEV* 0.322 0.475 0.475 0.354 0.354 0.354 0.354 0.354	2	XICITY-UNCOCYTE VA MGGLOBIN (G/DL) N S*DEV. 1 0.39 1 0.67 1 0.94 1 0.67 1 0.95 1 1.17 3 1.12 3 1.52	TOXICITY-ONCOGENICITY STUDY EHYTHROCYTE VALUES WITH STA HEMOGLOBIN HEMATOCRIT (6/DL) (% PACKED CELL (6/DL) (% PACKED CELL (6/DL) (% PACKED CELL 6/DL) (% PAC	TOXICITY-UNCOGENICITY STUDY OF FLUORGCARBON ERYTHROCYTE VALUES WITH STANDARD DEVIATIONS HEMOGLOBIN HEMATOCRIT MCV (6/DL) (% PACKED CELLS) (MICRONS**3 (6/DL) (MICRONS**3 (6/DL) (% PACKED CELLS) (MICRONS**3 (6/DL) (MICROS) (MICROS	MEAN S.DEV. MEAN S.DEV. MEAN S.DEV. MEAN S.DEV. 55 4.3 56 4.3 58 4.3 58 6.2 59 1.7 59 50 1.7 50 50 1.7 50 50 50 50 50 50 50 50 50 50 50 50 50 5		FC-143 IN RATS PEAN S-19.8 19.7 19.6 19.6 21.9 21.0	IN RATS MCH (PICUGRAMS) EAN S.DEV. EAN S.DEV. 1.55 0.83 0.64 1.34 1.41 1.41 1.55 0.84 1.64 1.05 1.07 1.093 1.44 1.093	MEAN (%) 33.9 8.6 34.0 34.8 34.8	S.DEV. S.DEV. 0.47 0.47 0.47 0.94 1.63
MONTH 24 0 PPM 15 300 PPM 15	7.84 7.92 7.95	1.083 0.670 0.869	14.5 14.6 14.7	1.59 1.42 1.23	® ® & & ⊗ ® & ® ® & ® ® &	5.34 5.72 4.22	សល្ល ÷ បេ÷	ωνα ••• •••	18.6 18.4 18.5	1.27 1.10 0.91	888 888 899 899	0.89 1.70 0.78

50.

<= .05, TWO TAILED DUNNETT T ON RAW DATA.</p>
<= .05, TWO TAILED DUNNETT T ON RANKED DATA.</p>

					TABLE 12	12					
	-	WO YEAR	URAL (DIE	T) TOXI	TWO YEAR URAL (DIET) TOXICITY-ONCOGENICITY MEAN LEUKOCYTE VALUES WITH	SENICITY LUES WITH	ET) TOXICITY-ONCOGENICITY STUDY OF FLUORUCARBO MEAN LEUKOCYTE VALUES WITH STANDARD DEVIATIONS	FLUORUCA DEVIAT	FLUORUCARBON FC-143 IN DEVIATIONS		RATS
		LEUK (CELLS	LEUKOCYTES LLS X 10*#3)	NEUTR (CELLS	NEUTROPHILS Ells x 10**3)	LYMPH	LYMPHOCYTES ELLS X \$0*43)	MONO (CELLS	MBNOCYTES LLS X 10*#3)	EBSINOP	EBSINOPHILS ELLS X 10*43)
	Z	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE											
MONTH 3											
Mdd 00 300 Mdd 00 30 Mdd 00	ស ម ស ម ស ម	12.73 14.93 15.22#	2.074 2.801 3.052	1.65 1.58 2.14	0.656 0.936 0.870	10.72 13.08* 12.83*	1:803 2:206 2:861	0.18 0.10 0.17	0.196 0.102 0.173	0.17	0.136 0.178 0.157
MONTH 6											
Mad 0 300 Mad 0 30 Mad 0 30 Mad 0	21 22 21 21 21	10.74 12.72 14.46	2.423 2.160 3.223	1.99	0.727 0.989 1.146	8.85 10.06 11.81*	25416 25316 25978	0.29 0.38 0.33	0.180 0.154 0.235	0.17	0.121 0.227 0.362
100 TH 10	4 6 7 7	7.94 8.14 10.38#	1.572 1.789 1.747	1.10 2.26 2.21	0.612 0.656 1.346	6.35 5.36 7.56	1\$256 1\$246 2\$151	0.0 0.0 0.0 0.0 0.0	0.216 0.247 0.233	0.10	0.107 0.105 0.117
MONTH 18	155 155	11.41 9.91 11.16	7.325 1.479 5.157	5.06 2.78 2.55#	6.402 1.657 3.353	5.61 6.30 8.20	13504 13070 23568	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.405 0.294 0.190	0.16 0.20 0.11	0.128 0.156 0.163
40 TH 24 0 PPH 300 PPH 30 PPH	15 15 15	10.79 9.09 10.44	7.529 2.351 3.464	3.72 3.24 3.24	5.666 1.488 2.032	6.56 6.34 6.72	2:140 1:619 2:171	\$ 9 5 M C	0.398 0.176 0.292	8 8 9 0 0 0 0 0 0	0.083 0.109 0.106

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

TABLE 12

TWO YEAR OHAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUDHOCAMHON FC-143 IN MALE RAIS INDIVIDUAL HEMOGRAM VALUES

---- MONTH=3

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	МСМ	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
	6	-	14.1	4	55,5556	19.8765	35.778	12.60	1.3860	10.9620	00000	0.252
2 0	2	17.0	- u	1 4	2	4,7	5.227	11.00	1.6500	\sim	•	.22
	9	•	1		,	18 9473	G. A69	10.00	1.0000	8.9000	000.0	=
	₽.	٠,	10.5	D :	F10 37	C 00 00	26.000		330	_	+26	0.133
	2	7	F • 0	t .	0 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	71.01	34 0000	, (486	H-8)40	00000	00.
	2	۲.	16.3	4 U	5655.45	20 771	2777906	•	475	6.4750	7	50
	8	٠.	16.7	46	57.2139	11// 07	n+00+60	•	777	١,٦	•	0
	2	۲.	16.8	47	54.0230	016	,	•	0 0 0 0 0 0	00000	, ,	
	2	٦.	16.5	47	57.0106	20.2452	201.0	00°61	0 4 0 4	0040.71	ָ	
	2	~	٠	94	56.0976	20.2439	6.0H7	14.00	000	000	9.0	9.0
	2	9	16.4	46	53,3024	19.0035	ū	11.50	c 0 35	021	000.0	
	-	۲.	15.6	45	51.5464	17.8694	34.6667	11.90	261	401	611.0	7 .
		٠,	16.6	2.4	56.1529	19.8.327	35,3191	12.60	.386	10.8360	0.252	0.126
		4	16.3	4	54.696B	19,3817	35.4348	9.58	۲.	819	000.0	9
		٠,		47	57.038A	20,3483	35.7447	ů	.790	.555	00000	0.155
		. 1		47	55.5556	19.6217	35,3191	17.00	Œ	15.4700	ď	. 17
	2 6	, (•	4	57.2988	20.4038	35,7143	14.20	1.1360	• 064	9	• 00
200	, ,	9 0		. 4 6	•	20.4342	36,3636	E,	1.7160	12.4410	•	• 1.4
1000	7 6	•	•	. 6	56.0626	9.687	35,1163	4	1.0720	11.9260	0.268	0.134
1000	26	•	1 0	7	42.00.00	10.4040	34.8837	£	.156	17.2480	0.000	• 19
200	,	•	•	7 -	67.3235	24.137	35,8537		0.5350	10.0580	0.107	0.000
1000	7 8	•	•	7 7	T. 05.75	10.8454	36.0465	0	~	12,3710	0.139	.13
300 total	7 (Çr	•	n n	54-0541	19.0476	35,2381		420	300	000.0	0.280
200	28	•	•	J 6	1000 A	20.1571	35.8140	15.20	128	•	00000	0.152
200	Y (* 0		ካ ሶ ተ ሩ	53.8173	10.1442	36.0465	21.70	689		•	.00
200	7 6	•		7 4	430.00	19-22-1	36,1364	17.90	969	15.3940	•	0.537
200	26	٠,	•	† <	57-1-50	20.7742	36.3636	14.40	.024	.088	•	0
Mdd 000	Y) [•		វ រ	10 T T T T T T T T T T T T T T T T T T T	17.7384	35.5556	13,50	350	610	•	• 40
200 DDK	יות צו	•	•	C <	77.00.67	10. 2865	35.4041	14.70	588	965	0.147	0.000
200 PPW	2 6		•	* (*	70,64	14.971	36.0465	12.20	732	* E	•	•
100 COE	4000	- <	10.0	7 d	47.5525	17.2669	36.222	14.30	.002	11,7260	0.143	• • 2
1100	9000	•	•) r	46.04	21.9718	16.2791	16.40	2.2960	13.9400	•	• 00
	4000KID	7.85	15.7	4	53.5032	20.0000	37,3410	10.40	0.5200	.880	000.0	• 00
	776		•	4	55,3411	20,3346	36.7442	~	.159	541	90	00.
300	446	•		4 در	57.1066	20,9391	36,6667	_	.352	.760	0.441	* .
	366	. "	17.0	46	55,3550	20,4573	36,9565	: (1	415	.740	0 • 345	00.
	P 367	٠.		4	53.2044	19,3470	36,3636	-	.567	•	0.151	00
	R367	. ~		42	57.5342	47+7	35.7143	_	400	.750	0.510	*
100	7467	8.58	•	46	53.6131	19.2 JOH	35,8696	14.50	.320	12.0350	000.0	0.145
	R36.7	4		94	54.6968	19.7384	36.0470	30	.288	515	.20	20
	RAGE	٩.		44	5A . 7484	21.0728	35,8696	7.5	.720	•480	•	00.
	R368		•	7 4	5454 P	21.0275	35.9184	5 • 7	.942	.601	5	9.
300	R 36.9	9		6 4	61.1664	22.0484	36.0405	14.40		13.0240	0.296	0.148
	H369	•	15.8	45	56.4620	20.000	35,1111	1.3	. 4 OB	892		00.
	R 469	٠,	•	7 7	45.625B	20.2276	36,3636	13.40	ď	.64 8	000.0	Š
	CIRAFOR	6.0		4.3	57,1809	20.7447	36.2791	12.40	1.1520	11.2640	0.256	~
	101 NT	•	•	?								

TABLE 12

TWO YEAR UMAL (DIET) TUXICITY-ONCUGENICITY STUDY OF FLUOMBCAKHON FC-143 IN MALE HATS INDIVIDUAL HEMOGKAM VALUES

-- MUNTH=6 --

00	SE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	MBC	PMNAB	LYMAB	MONOAB	EOSAB
9	Ĭ	1R35	•	ıń	46	30	18.2039	ò	۲.	60	.083	231	0.0770
0	PK	1835			42	49.3537	3.	34.2857	8.48	1.2572	7.6330	000000	0.0898
0	T T	1835	•	4	44	4.6	17,7400	33.1HIR	11.70	1.0530	10.4130	0.2340	.00
0	Œ	1R35	•	ň	đ.	2	16,9157	4.8	96.6	1.5936	896.	0	.298
œ.	ă.	1R35	•	ιń	47	7.8	ř	3.829	~	10	7.0378		*
G	PPM	A1R3541	8.42	15.9	46	Ð	H. H	ຮູ	.8	• 983		0.1966	.294
ī 0	Œ.	1835	٦.	÷	44	4.45		3.636	•	1.2600	12.0400	4	٦
<u>a</u>	Ĭ	1835		ŝ	4.5	÷	18.3771	3	7.71	•696	•626	6	٠
ā	Œ.	1835	`.		46		18.7952	6.		.597	6.6490	4	2
•	Σ	1835	•		37	•	14.5251	'n	4	1.7420	11.1220	0.2680	0.2680
<u>a</u>	Ī	1R35	٠.	ō	47	52.0487	17,9402	4.4	8.20	.574	7.0520		۳.
ā	Z Q	1835	٠,		45	447	•	2°8	۲.	1.1770	•	0.5350	.107
ā.	Œ	1835	۳.	ě	4.7	54.0852	-646	4.4	1.3	•33 6	10.7350	•	.226
ā. 0	I.	1835	٠.	ທີ	4.5	.724	_	33,3333	_	1.5820	004046	0.5650	0.1130
0	T.	1835	٦.	ĕ	41	44.5782	666.	å		1.6300	14.1810	0.4490	.000
00	Ī	1835	7	4	43	52.6961	•	34.4186	3.4	1.0720	10.7200	0.1340	.134
00	I	1835	Š	4	42	52.9634	•282·	34.5238	1.7	1.1700	10.0620	.46H	.000
6	ĭ	1R35	٠.	÷	43	50.3565	15.3342	27.2043	۲.	1.6510	10.5410	0.5080	•
0	Į.	1835	-	Ğ	6 4	55.7717	19.5850	35.1163	47.0	3.6038	5.8440	0.2922	
00	I.	1836	14		4	53.2044	1H.8634	35,4545	15,30	1.9890	13.1580	0.1530	0.000.0
0	T.	1836	٦.	÷	41	52,6316	•	33.6585	12.80	1.1520	.752	0.3840	•
00	I	1834	٠.	÷	£ 4	53.2178	18.3168	34.4]46	10.60	•2₽	• 784	4	0.1060
00	ĭ	1836	٠.	'n	\$	7.500	19.6250	34.1304	12.60	2.0160	10.2060	. 126	.252
00	X	IR36	-		4	* 5.	X.	34.0909	13.80	4.0020	.41B	.552	0.8280
00	Σ	R36	9	Š	4.5	*• T • •	21.5407	555	0.5	1.9950	• 085	.210	0.2100
00	ī	1R36	177	*	4	ۍ ۳	17,3077	727	2.1	.689	11,1760	.381	•254
00	¥	R36	9	4	6. 4	3.28	17.5960	3.023	18.70	•61	.334	.561	.187
0	ž	18363	٩.	•	6 4		1H.4309	34.4]46	11.50		005	0.4600	•
	X.	18363	٠.	•	39	52.5606	17.9245	4.10	12.60	٩,	•	.504	0.3780
<u>-</u> 0	Ŧ		ď	15.2	4	53,6585	18.4366	4	2 - 1	1.4520	164	4	000
	Į,	R364	4	٠	4 4	. 423	15.6524	33,4091	14.40		ď	.740	10
	I	R365	•	•	Մ	1.766	76°X	32,8484	5.3	454	•	•612	.153
	Z	R365	``	•	45	58.3658	0.3	34.8864	16.40	55	11.9990	60	0.5070
	3	18345	ç	•	42	5.263		4.9	•	٦.	5,3395	.181	.362
	ĭ	IR366	ຫຼ		45	5.404	r	ě	4.1	2.9610	10.7160	0.4230	000
	ΣA	1 R 366	J.	•	£ 43	7.257	.70	-3	13.40	2.5460	10.3180	0.1340	0.4020
	Σ	IR366	Σ.		4.1	44.	• 143	34.1463	11.20	Cυ	36	9	0.1120
	ĭ	R366	ō	•	45	Ť	• A69	33.777H	14.00	2.2400	.200	0.5600	000
	X	R36	ъ.	15.A	46	1.86]	14.4742	34.3478	20.50	1.6400	17.0150	00170	1.4350
	¥	R368	m.	•	4 1	•	19.1518	34.1463	14.00	1.8200	11.6200	0.2800	0.2800
	Ī	R368	σ		45	56.3204	14.1477	32,222	19.00	3.2300	15.5800	190	0.000.0
	ĭ	R368	œ.		5.0	493	21.00m3	3.400	~	0.0911	.745	000	0.3644
	Ĭ	R348	0		4 Z	54.5745	\circ	34.5714	13.10	0.7860	12.0520	0.1310	•
	Σ	R369	~		4ን	2042*45	19.6841	33.777H	3	1.0500	٠	0.5250	0.1750
	3	C1R3694	4	•	45	4516	18.2796	32,3810	15.00	1.2000		0.	• 6

TABLE 12

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

---- MONTH=12 ---

EOSAB	_	9	90.	.27	00.	.18	90	.08	00	.18	•	90	.0.		.32	2	• 05	.20		.08	00	N	. 09		0.0	.18	.37	3	. 10	00.		.30	•00	.08	.17	• 30	ď	0	.24	.20	2	00.	•0•	.10	66
MONGAB	0.632	• 15	•47	.46	.51	.81	.27	57	-22	.18		.24	0.070	59	.42		-22	.61		.32	5	0.485	00.	4	- 05	.18	.27	.13	.20	•56	0.575	•69	0.360	9	ě	=	.37	0.834	4.8	.20	S	.21	.37	.93	59
LYMA8	5.293	• 45	44.	• 72	• 06	• 00	• 79	.29	.07	.26	•	16	9	8	.91	33	.08	7	۳,	7	9	6.402	•	4	7	•	4	ď	•	۲.	8.510	4	6.390	6.400	4.730	5.100	10.416	8.896	6.882	5.202	• 06	0	•34	7.176	8.316
PMNAB	1.817	•	•	•	•	•		0.328	•	•	•	522	1.260	0.495	2.140	99.	23	.83	. 93	2.511	38	2.522	17	2	90	.63	.16	20	.36	.93	. 18	.23	.16	.12	35	4.692	• 36		58	59	23	• 8	48	. 18	8
MBC	7.9	ณ ช	6.8	9.5	7.4	9.1	6.9	8	5.7	9.5	•	8.0	7.0	6.6	10.7	7.6	5.6	6.8	6.9	8.1	α, α,	7.6	4.7	8	6		9.3	6.7	0	11.3	-				•	10.2	è	13.9	'n	•	-	0	•	•	6.6
MCHC	_	98P.	. 888	.893	.130	.666	.166	32.9091	156	.617		347	3	394	565	714	35.4545	341	69	147	3	36.0465	319	76	97	404	35.6818	9		981	5.2	33,4043	34.4186	33,1915	. 888	.5H]	.476	34.2553	000.	.761	428	.777	.260	.666	116
MCH	727	49.454	-492	8,362	.760	8.417	283	19,1130	.482		•	0.0	۲.	7.1	.776	.280	35	8.2B	•	9.27	28	19.2069	.79	.TC	1117	19.0652	.600	842	. 915	. 257	18,9032	18.0667	. 852	4	٦.	٦.	•	17.7118	18.8591	.318	٠,	.876	465	727.	. 954
MCV	57,6230	5.762	3,003	5.490	2,036	3.128	3,511	20	5.921	5.424		58,3756	469.9	2,269	7.213	3.984	4.590	6.0	1	3,3	4.726	53,2838	3.227	3,231	2.696		4.931	2+955	3.012	1.312	3.675		869	2.987	54.9451	3.416	2.500	÷	2.386	169.	3.2	5.555	.511	.021	-
HEMAT	4 8	45	4 0	14	46	6.5	4.8	52	51	47	•	46	47	38	46	24	44	4]	38	4 3	77	4	47	4	6.4	42	77	6 4	77	43	46	47	64	47	4 rc	43	42	47	45	42	42	.	46	45	64
HEMO	15.6	15.7	15.7	16.4	15.7	15.6	16.4	18.1	16.4	15.8	•	ŝ	è	12.5	ŝ	•	•		•		•	15.5			15.6	15.5				15.3		15.7	14.8	15.6	15.7			16.1	16.2		15.3		15.3		
ERYTH	8.33	•	٠	•	8	4	٠	74.6	7	8.48		8	N	7.27	8.04	7.78	8.06	8,15	6.60	7.68	H.04	8.07	8.83	7.89	8.16	8.13	8.01	8.12	8.30	8.38	8.57	8.69	8.29	8.87	8.19	8.05	8.00	9.02	8.59	7.97	7.89	8.10	8.76	8.33	8.41
ANIWAL	A1R3516	183	A1R3520	8	E	Ξ	5	3	£	R3	8	3	£3	R3	£	83	R358	H358	R359	Y	A360	~	R361	H362	H362	R362	H362	R363	H364	H364	T.	Œ	\boldsymbol{x}	Œ	Œ	T	I	C1R3676	Œ	H368	R368	T	4368	4369	1836
DOSE	đ		Mdd O					MQG C		Wad 0				MGG C			300 PPM		300 PPM				300 PPM			300 PPM			Q.	Œ		Œ		Q.		đ		9	30 PPM	đ		30 PPM	9	đ	30 pp.

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

-- MONTH=18 ----

(35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (35) (36) (36) <th>ቀጠ444444444 ቀጠ4 መጠጠጣ መጣ መጣ ቀጠ4444 ቀጠ448mm መጠጠ መጠጠጠ መጠጠ መመ መ © 40 m ∈ 20 m ∈</th> <th>20000000000000000000000000000000000000</th> <th>18.1710 29.0323 18.4478 20.0323 20.31474 20.1126</th> <th>34.7727 36.7327 36.7329 36.7329 37.5000 37.5000 37.5596 36.6667 37.6596 37.6596 37.6596 37.1111 36.774 36.3636 36.3636 37.66774 37.1111 36.3636 36.3636</th> <th>350 350 350 350 350 350 350 350 350 350</th> <th>2 4 4 4 5 5 5 6 8 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6</th> <th>7.000 7.0000 7.000 7.000 7.000 7.000 7.000 7.000 7.000 7.000 7.00000 7.0000 7.0000 7.0000 7.0000 7.0000 7.0000 7.0000 7.</th> <th>1.000 1.770 0.251 0.251 0.556 0.566 0.566 0.566 0.667 0.667 0.665 0.665</th> <th></th>	ቀጠ444444444 ቀጠ4 መጠጠጣ መጣ መጣ ቀጠ4444 ቀጠ448mm መጠጠ መጠጠጠ መጠጠ መመ መ © 40 m ∈ 20 m ∈	20000000000000000000000000000000000000	18.1710 29.0323 18.4478 20.0323 20.31474 20.1126	34.7727 36.7327 36.7329 36.7329 37.5000 37.5000 37.5596 36.6667 37.6596 37.6596 37.6596 37.1111 36.774 36.3636 36.3636 37.66774 37.1111 36.3636 36.3636	350 350 350 350 350 350 350 350 350 350	2 4 4 4 5 5 5 6 8 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	7.000 7.0000 7.000 7.000 7.000 7.000 7.000 7.000 7.000 7.000 7.00000 7.0000 7.0000 7.0000 7.0000 7.0000 7.0000 7.0000 7.	1.000 1.770 0.251 0.251 0.556 0.566 0.566 0.566 0.667 0.667 0.665 0.665	
2.00 4.00	ከሳትሳሳሳሳሳሳሳሳ ተጠሳ መጠጠ ጠ 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	00000000000000000000000000000000000000	29.0323 20.0323 20.0324 20.3146 20.3146 20.3146 20.3126 20.3126 20.3126 20.3144 20.31111 20.3244 20.324 20.324 20.334 20.334 20.334 20.334	4 WWWWWWWWWWWWWWWWWWWWWWWWWWWWWWWWWWWW	35 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	26. 44. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4	7.080 3.080 3.080 3.080 3.080 3.080 3.080 4.080 4.080 4.080 4.080 4.080 4.080 4.080	0.5740 0.5741 0.5741 0.57446 0.57446 0.57446 0.5746 0.5746 0.5746 0.6440 0.6465	· · · · · · · · · · · · · · · · · · ·
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8 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	ቅሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳሳ	50.00 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	20.20 20.30 20.30 20.1474 20.1474 20.50 20.3125 25.4426 19.4747 19.747 19.747 19.70		9 4 4 4 4 5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 6			0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566 0.566	· · · · · · · · · · · · · · · · · · ·
8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	ቀ ፋ ፋ ፋ ፋ ፋ ፋ ቁ ፋ ርሀ ፋ ጠ ጣ ጣ ፋ ሳ ጣ ፋ ፋ ሳ ፋ ፋ ሳ መ ጣ ካ ጣ ሳ ጣ ፋ ጣ ጣ ሳ ሳ ፋ ሳ ጣ ር ብ ር ብ ር ብ ር ብ ር ብ ር ብ ር ብ ር ብ ር ብ ር	55 55 55 55 55 55 55 55 55 55 55 55 55	14.31y6 20.1474 20.1636 20.5126 20.3125 19.4747 19.4260 25.4947 19.8364 20.841 19.0091 20.7092	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	160000000000000000000000000000000000000		0.4444 0.4444 0.4446 0.4446 0.4446 0.446 0.446 0.446 0.466	
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8	ተሳቀሳ ተጠሳ መጠጠጠ	14699 14699 14699 1474 1474 1474 1474 1665 1665 1665 1665 1665 1665 1665 166	19.1126 20.5630 20.3630 19.7425 19.7426 19.4260 19.3264 19.531 19.034 19.034 19.034		7	140000000000000000000000000000000000000	4.836 3.336 3.336 3.336 4.725 4.725 7.725 7.725 7.725 7.726 7.726 7.726 7.726 7.726 7.726 7.726 7.726 7.726 7.726 7.726 7.726	0.468 0.468 0.468 0.468 0.468 0.468 0.468 0.468 0.468	· · · · · · · · · · · · · · · · · · ·
8.37 9.47 9.49 9.40 9.70	ፋ ዓ ፋ ፋ ቁ ቁ ል ብ ፋ ብ ላ ቁ ል ል ል ል ል ል ል ል ል ል ል ል ል ል ል ል ል ል	15.00 to 15.	20.5630 19.3125 19.4247 19.4246 19.3247 19.3287 19.5641 19.6934 20.7092 20.7092	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	9 4 4 4 4 5 5 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 -	5.336 5.453 6.455 6.107 6.107 7.466 7.466 7.466 7.466 7.566 7.566 7.566 7.566 7.566 7.566 7.566 7.566 7.566 7.566	0.594 0.402 0.402 0.403 0.121 0.647 0.450 0.465 0.465	
8 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	ቅዱቱ ጣፋ መፋ ጣጣ ቀጣ ቀጣ ቀጣ ቀጣ ቀጣ ቀጣ ቀጣ ቀጣ ቀጣ መ መ መ መ መ	0865 4173 4173 7575 7575 8664 8664 8664 7376 7376 5837 5837	200.3125 190.4747 190.4747 190.4788 200.05447 190.4547 200.0544 190.454 190.459 190.459 190.459		7	1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	3.953 6.107 7.560 7.564 7.564 7.564 7.564 7.564 7.564 7.564	0.402 0.433 0.4435 0.0045 0.008 0.008 0.460 0.465 0.465	
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9.49 9.40 9.50	ቀጠ4 UU 4 UU 4 U 4 4 4 4 4 4 4 4 4 4 4 4 4	9801 7575 7575 7575 7575 7575 7575 7376 7376	19.44.44 19.44.44 19.44.44 19.44.41 19.41 19.61 19.61 19.61 19.61 19.61 19.61 19.61 19.61 19.61 19.61 19.61		7.00 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		4.850 6.107 6.107 7.59 7.584 7.584 7.584 7.584	0.485 0.183 0.183 0.183 0.480 0.480 0.460 0.465 0.665	
6. 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	ሠፋሪያ ቀጣጣ ቁጣጣ ቁጣጣ ቁጣጣ ችክመጠ ከጣጣ የመመ መ መ ቁ ቁጣ መ ብ መ መ መ መ መ መ መ መ መ መ ቁ ቁ ቁ ቁ መ መ መ መ	2653 2650 2664 2664 2666 2666 2660 2660 3653	25,8947 19,8788 24,7411 19,3247 19,5364 20,0541 19,64940 19,0496		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	4 E C C C - C - C - C	4.725 8.107 7.440 7.584 7.584 7.584 7.584 7.584 7.584	0.945 0.338 0.439 0.480 0.450 0.450 0.440 0.465	
8.25 8.25 6.54 7.28 7.28 7.77 7.78 7.79 7.79 7.79 7.79 7.79 7.7	ቀጠፋጠጠፋጠፋፋጠፋፋፋ ሕመኪክርያዊ ፍር ተርብረ	7576 1664 0664 0664 5358 5358 1976 1976 7376 5650 5837	19.8788 24.7411 19.3287 19.3287 19.0384 20.0581 19.0490 19.0490 20.7092	00000000000000000000000000000000000000	11. 12. 13. 14. 14. 14. 14. 14. 14. 14. 14		8.107 6.790 7.464 7.584 6.020 6.300 7.533	0.121 0.388 0.487 0.480 0.450 0.450 0.465 0.665	
0.50 0.50	U 4 M M 4 M 4 4 4 4 4 4 4 4 4 4 4 4 4 4	10000 10000	24,7411 19,8287 19,5364 20,0361 19,8981 19,093 20,7092	9 T T T T T T T T T T T T T T T T T T T	4 / 9 / 0 / 0 / 0 / 0 / 0 / 0 / 0 / 0 / 0		6.790 7.469 7.584 4.020 6.300 7.488	0.388 0.679 0.480 0.100 0.450 0.465 0.664 0.760	
8	4 ሠጠ 4 ጠ 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	5354 5354 5469 8469 1978 7376 7376 5660	19,3247 14,5364 20,0541 19,0934 20,7092		7 9 4 4 4 5 9 7 9 7 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	1.455 2.680 2.680 2.070 1.440 1.209	7,469 7,584 4,020 6,300 7,488 7,533	0.679 0.480 0.000 0.450 0.450 0.490 0.684 0.684	
6.00 6.00 7.00	mm 4 m 4 4 m 4 4 4 4 4 4 4 4 4 4 4 4 4	5358 5660 8469 1978 1376 2660 5837	14.5364 20.0541 19.0540 19.0934 20.7092		6.4444 6.4444 6.4444 6.4444	1.209			
7.00 A 4.00 A 4.	0 € € € € € € € € € € € € € € € € € € €	5660 5653 5653	20.0541 19.8980 19.0934 20.7092 20.4604		7.4 4.0 4.6 9.9 4.0 4.0	2.680 2.070 1.440 2.352			
7.88 7.288 7.288 7.500 7.111 7.500 8.030 8.030 8.030 8.030 1.000 7.000 1.000 7.0000 7.0000 7.00000 7.00000 7.00000 7.00000 7.0000 7.0000 7.0000 7.0000 7.00000 7.00000 7.00000	4 ጠ 4 4 ጠ 4 4 4 4 መ 80 ሮ ፋው ፡፡ ር ሃ ሀ	3469 1978 7376 2660 5837 5653	19.89H0 19.0934 20.7092 20.4604	36.38	2 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	2.070 2.352 1.209			
7.28 7.05 7.05 7.05 7.11 7.50 8.03 8.03 8.55 7.50 7.50 7.50 7.50 7.50 7.50 7.50 7	W 4 4 M 4 4 4 4 8 C 4 G M C V V	1978 7376 2660 5837 5653	19.0934 20.7092 20.4604	36.36	4.6 4.8 9.3 11.4	1.440 2.352 1.209		0.334 0.450 0.465 0.684 0.760	
7 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 -	4 4 W 4 4 4 4	7376 2660 5837 5653	20.7092	36.3	9.8 9.3 11.4	2.352	7.533	0.490 0.465 0.684 0.760	
7.887 7.77 7.79 7.79 7.79 7.79 7.79 7.79	4 W 4 4 4 4 4 D LL C W W	2660 5837 5653	20.4604	36.4 36.4	9.3	1.204	7.533	0.465 0.684 0.760	
7.71 7.71 7.00 8.00 8.00 8.00 8.00 8.00 9.00	W 4 4 4 4 B C . U V	5653	12.17	36	11.4	6 G P		0.684	
7.11 15. 9.59 114. 9.00 104. 9.00 104. 7.31 114. 7.31 14. 7.31 16.	4444 ~CVV	5653	0/1+·HI	77		2.100	4.788	0.760	0.4
7.59 8.03 8.03 8.51 8.4.7 7.31 8.31 8.31 8.31	4 4 4 C () ()		21.8003		9.6	1.805	6.935		ď
8.03 15. 8.16 14. 7.48 14. 7.31 15. 7.30 15.	4 U U	4007	19,3676	36	13.6	7.208	•	0.952	•
0.16 7.48 7.48 7.31 7.30 7.30	6,4	3039	14.4271	37.1	9.2	2.116	•	0.828	5
8.55 16. 7.48 14. 8.31 15. 7.36 14.		4100	18.2598	35	10.5	3,360	5.985	1.155	•
7.48 14. 8.31 15. 7.36 14.	4 U:	52.6316	19.4152		11.2	3.584	•	0.784	۳.
8.31 15. 7.36 14.	34	52,1390	19.1176	36.6667	6.3	2.046	.85	1.023	0.372
7.36 14.	4	52.9483	14.6522		10.0	2.700	•	0.500	7
6.20	*		19.4370	36.5000	6.6	1.980	7.227	0.495	. 13
	3.5	4.9	18.4710		21.9	11.826	9.1.6	0.657	~
8.70 16.	4.7	4.0	18./356		10.5	1.260	8.715	0.420	-0
R.19 15.	4 ቪ	54.945]	19.0476	£	9.5	0.570	8.740		•
8.98 15.	7.4	52,3385	17,7060		6.5	1.560	4.680		=
11.48 19.	53	46.1672	16.6376	7	21.5	7,955	12.900		00
9.21 16.	47	1.0	17.4810	255	6.3	1.953	6.975	0.372	•
9.26 16.	Œ †	.835	17.8146		8.7	609.0	7.830		00.
7.95 16.	54	67.9245	20.1547	30.5556	7.6	0.608	.91	• 0 7	00
8.79 16.	L+	53.4694	18.4300	34.408]	•	•	5,963	• 33	٠
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8.90 16.	4	9.	J.	35,8696		•	۲.	0.250	0.125
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8.74 15.	4	۲,	14,1922	34.5652		0	۳.	0.258	00000
8.37	4	4.454	7	643		0.426	6.319	0.264	0.071
× 1	. 4		2000	204.6	4	44	5.4.7	•	

INO YEAM OHAL (DIET) FOXICITY-ONCOGENICITY STUDY OF FLUOMOCAKHON FC-143 IN MALE HATS INDIVIDUAL HEMOGRAM VALUES

-- #0NTH=24 ---

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	ACH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
100	AIRAGIA	7.44	13.1	37	49.7312	17.6075	35.4054	13.2	3.036	9.108	0.924	0.132
100	18352	80.08		. E 4	3.217	17.8218	.48	6.8	•	4.760	0.340	0.068
100	AIDSEAR	A-70		. 4 . r.	51.7241	17.8161	34.4444	7.2	0.432	6.624	000.0	0.144
100	A183531	8.0		74	56.4226	19.2077	•	8.4	1.092	6.972	0.336	00000
300	•	7.96		46	57,7889	19.2211	33.2609	36.3	52.506	12.342	1.452	000.0
200	A1R3538	8. n. s		. 4 . 7	52,6932	17.6815	33.5556	7.2	1.584	5.256	0.288	0.072
10 D		9.86	16.0	94	1.418	. 05A	34.7826	7.1	0.710	0.248	0.071	0.071
T C	R 354	8.09	15.6	94	56.8603	19.2431	33,9130	8.5	1.445	6.885	0.170	000.0
T 0.		6.08		34	55.9211	19.4079	34.7059	4.4	0.264	4.136	000.0	000.0
I	A1R3557	9.47	•	ى 0	52.7483	17.6346	33.4000	B.0	1.840	6.000	0.00	0.080
T G	_	7.74		37	47.8036	17.0543	35.6757	12.6	5.922	6.300	0.378	00000
X C	R356	7.68		6.4	54.6875	18.7500	34.2857	12.4	4.712	6.820	0.620	0.248
M d	A1R3569	5.38		33	61.33R3	22.3048	36,3636	4.1	0.176	8.924	000.0	000.0
*44	A183573	8.52		24	55.1643	18.8967	34.2553	7.4	1,554	5.328	0.296	0.222
Mada	A1R3578	6.70	12.7	37	55.2239	18.9552	34.3243	12.7	8,255	4.191	0.127	0.127
₩ dd	H1H3581	8.42	15.5	46	54.6318	18.4086	33.0957	5.9	998.0	4.960	0.372	000.0
Mdd	B1R3585	7.94	14.8	6.	54.1562	18.0398	34.4186	10.5	2.100	8.085	0.210	0.105
¥ d d	B1R3591	7.98	16.0	74	60.1504	20.0501	33,3333	A.4	3.528	4.620	0.252	0.00
Idd	H1R3594	8.17	14.4	E 4	52,6316	17.0255	33.4884	5.7	0.741	4.845	0.114	0.00
I d	R1R3597	8.03	15,3	4	54.7945	19,0535	34.1727	8.7	2.697	5.655	•	0.087
MEG	R1R3601	6.21	12.0	35	56.3507	19.3237	34.2497	9.6	4.608	4.416	•	0.192
Mdd	B1R3605	8.02	15.8	53	66.0848	19.7007	29.8113	6.3	1.197	5.040	000.0	0.063
T d d	8143608	8.21	•	39	47,5030	16.5652	34.8718	9.6	1.862	7.142	0.196	0.00
E G	B1R3611	H.04	15.2	64	53.4426	18,9055	35,3488	11.0	1.540	8.910	•	0.220
PBH	R1R3618	8.58	٠	45	52.4476	17.4322	34.0000	8.2	1.722	6.232	0.246	0.00.0
¥ D D	B1R3623	8.00	15.6	5.5	65.0000	19.5000	0.000	9.5	1.805	7.410	0.190	0.095
P O G	B1R3630	8.59	16.3	£ \$	55.8789	18.9756	33.9583	7.5	1.050	6.300	0.075	0.075
Mad	B1R3633	6.51		33	50.6912	318	35,1515	14.2	4.544	4.514	0.142	000.0
E d d	B]R3636	8.15	13.4	38	525	16.4417	35.2632	12.6	5.544	5.425	0.756	0.378
Hdd.	H1R3641	7.92	13.н	0 4	50.5051	17.4242	34.5000	8.2	2.378	5.494	0.328	0.00
NO.	C1R3646	•	•	•	•	•	•	•	•	•	•	•
PDW.	R365	8.35	15.0	4 L	53.8922	17.7641	33,3333	6.3	5.208	3,613	•27	9
bor.	C1R3654	7.90	14.2	41	51.8987	17.9747	34.6341	13.1	3,537	6.40B	0.655	00000
Hdd	•	96.8	16.0	47	52.4554	17.4571	34.04≥6	2.0	1.400	3.450	0.100	٠
Had	-	A . 34	15.2	44	52.757H	18.2254	34.5455	8.7	2.349	88	0.435	0.087
Mad	C1R3667	7.34	15.2	6 4	58.543]	20.7044	34.3488	4.4	1.776	5.254	0.222	0.148
Wdd.	æ	7.21	13.7	36	54.0915	•	35,1282	2	4.096	7.808	0.768	0.12H
#dd.	C1R3672	8.87	15.4	44	51.8602	17,3619	33.4783	14.7	7.644	6.468	0.588	0.00
Mdd	H367	5.93	ď	31	52.2766	14.4870	36.1290	8	6.120	10.800	1.080	000.0
PPM	R367	9.14	15.7	46	50.32R2	17.1772	34.1304	12.5	2.375	9.750	0.125	0.250
₩dd 0	C1R3682	8.37	15.1	77	52.5687	18.0406	34.3182	ċ	4.590	5.202	0.306	0.102
MOG	C143684	7.73	14.7	C \$	54.3338	14.0168	35.0000	9.5	1.900	7.410	0.190	0.00
Had	C1H3689	8.14	15.2	45	55.2H26	14.6/32	33,7778	4.7	1.850	. 55		0.222
#ad I	C1R3691	6.97	13.4	36	54.5194	14.2253	35.2632	10.4	1.976	7.904		0.312
M dd	C1R3694	8.02	15.3	77	54.862H	19.0773	34.1727	7.2	0.576	6.552	0.072	0.00

	Ĭ.	TWO YEAR G	BRAL (DIET)	4	TY-ONCO	GENICITY Alues Wit	TOXICITY-ONCOGENICITY STUDY OF FLUBROCARBON EHYTHROCYTE VALUES WITH STANDARD DEVIATIONS	FLUBROCARE DEVIATIO	30N FC-143	43 IN RAT	15		
		ERYTHRI	ROCYTES X 10**6)	HEMOGLOBIN (G/DL)	.081N)L.)	HEMAT	HEMATOCRIT Packed CELLS)	MCV (MIORONS**	(£**5	HCH (PICOGE	MCH (PICOGRAMS)	¥	MCHC (%)
	z	MEAN	S.DEV.	MEAN	Sedev.	MEAN	S.DEV.	MEAN S	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE													
MONTH 3 0 PPM 300 PPM 30 PPM	13 13 13 13 13 13 13 13 13 13 13 13 13 1	6.91 6.67 7.26 ⁴	0.319 0.266 0.505	15.8 15.4 16.0	0.48 0.56 0.70	# 0 * 0 # 0 * 0 * 0 * 0 * 0 * 0 * 0 * 0	4.11 1.85 1.75	6 6 6 6 6 6 6 1 6 6 6	8 8 8 8 8 8 8 8 8	22.9 23.0 22.1.	0.75 0.63 1.37	36.2 36.6 36.6	0 • 5 6 0 • 5 6 0 • 4 9
MONTH 6 0 PPH 300 PPM 30 PPM		7.32 7.37 6.92*	0.413 0.327 0.475	15.0 15.4 13.7	0 • 55 0 • 64 0 • 95	# K & B B B B B B B B B B B B B B B B B B	# # # • • • • • • • • • • • • • • • • •	ស ឃុ ស ១ ជ ១	ี 	20.6 21.0 19.9	0.95 0.93 1.93	88 86. 86. 88.	1.01 0.83 1.65
MONTH 12	សស ស កាតា កា	7.60 6.92* 7.29	0.300 1.193 1.212	15.6 14.6# 15.1	0.40 1.74 1.70	44.00.04.00.05.5.5.5.5.5.5.5.5.5.5.5.5.5	8.39 4.73 4.76	n • n ⊕ • •	6 6 6	20.6 21.5 21.6	3.19	35.0 35.5 35.5	0.48 0.62 4.63 4.63
MONTH 18	15 15 15	7.37 7.24 7.01	0.668 0.809 0.763	15.4 14.9 14.8	1.43 1.32	44. 9.114 9.114	# 8.13 8.86 3.85	ស ម	3.0 3.0 9.0	21.0 20.7 21.2	0.68 0.96 1.09	36.0 35.6 35.8	0 • 0 • 5 5 5 • 5 5 5 5
MONTH 24 0 PPM 300 PPM 30 PPM	11 15 15 15	7.06 7.14 7.06	1.129	8.44 4.4 6.4	1.80 1.26 2.03	4 4 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	© (€ © (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€) (€)	യെ <i>ത</i> ഗ സ് — സ	21.2 20.3* 20.47	1.45 0.74 0.91	35. 35. 35. 35.	0.87 0.99 0.81

57.

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

	Ē	WO YEAR	ORAL (DIE	T) TOXICEAN LEUM	SITY-ONCOG	ENICITY UES WITE	(DIET) TOXICITY-ONCOGENICITY STUDY OF FEUOROCARBON MEAN LEUKOCYTE VALUES WITH STANDARD DEVIATIONS	FEUGROCI DEVIAT	ARBON FC-143 Ions	2	RATS
		LEUP (CELLS	LEUKOCYTES (CELLS X 10*#3)	NEUTF (CELLS	NEUTROPHILS (CELLS X 10*#3)	LYMP)	LYMPHOCYTES (CELLS X ±0**3)	MONG	MONOCYTES LLS X 10*#3)	EOSIP	EBSINOPHILS (CELLS X 10**3)
	Z	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.BEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE											
MONTH 3	15	18.98	2.69R		1.406	15.73	2:970	0.37	0.217	0.31	292.0
300 PPM 30 PPM	15	18.51 18.06	3.778	3•24 3•33	1.728	14.78	21834 31105	0.28	0.312	0.22	0.258
MONTH 6											
Mdd 000 300 Mdd 000	15	7.52 8.60 7.18	2.559 1.953 1.723	1.55	1.586 0.705 1.023	5.87 6.73 5.06	22160 12784 12607	0.18	0.096 0.122 0.142	0.08 0.11 0.15	0.067 0.102 0.119
MONTH 12	15	5.73	2.120	1.27	1.562	4.13	12049	0.21	0.108	0.12	0.125
Mdd 000 Mdd 00	15	5.72	1.818	1.45	1.281	3.95 4.13	15061	0.22	0.165 0.098	0.00	0.094
MONTH 18		,			;			;	,	•	
Mdd 000 Mdd 000	មិត្ត	5.75 6.30 6.83	2.368 2.368 2.608	2.21 2.81 2.69*	1.631 1.950 2.240	9.68 9.58 8.51 8.51	02973 12305 15061	0.36 0.36 0.36	0.226 0.148	0.10*	6.057 0.108 0.074
MONTH 24 0 PPH 300 PPM 30 PPM	សក្សា	6.73 6.39 8.57	4.064 1.691 3.434	2.87 2.15 3.44	2.959 0.962 2.915	4	15329 15190 15641	0 + 11	0.151 0.062 0.241	0.0 0.0 0.0 0.0 0.0	0.074 0.057 0.094

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

TABLE 13

TWO YEAR OHAL (UIET) TOXICITY-ONCOGENICITY STUDY OF FLUGROCARBON FC-143 IN FEMALE RATS INDIVIDUAL HEMOGRAM VALUES

--- MONTH#3 ---

17.072 0.
715 14.555 0
.882 11.072 0
12.786 0.1 18.480 0.2
904
940
000
3.0
3636 21.
256 256 756
7 0 0 0 0 0 0 0 0 0 0 0
4 40 5 5
5 60 4
.73 15.0 42 62
4613 6.73 15.0 42 62
612 6.88 15.7 44 65 613 6.73 15.0 42 65

TABLE 13

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

-- MONTH=6 --

94.94.74.3 20.4914 3.48437 0.655 0.6054 0.1055 94.94.74.3 20.4914 3.48437 6.24 0.5160 5.6056 0.0006 94.948.7 20.2043 35.3446 6.24 1.925 6.5190 0.0006 97.803 21.2247 35.3446 6.24 1.925 6.5190 0.0006 97.803 21.2247 36.7201 6.63 0.9246 0.1000 0.1000 97.455 19.486 3.4717 6.619 0.0000 0.1000 57.1456 19.246 4.656 0.0010 0.1000 57.1457 19.247 3.4047 6.61 0.0010 0.0100 57.1467 19.2417 3.4047 6.61 0.9240 0.1000 0.0100 57.1476 21.0244 3.4047 6.61 0.4131 0.0240 0.0100 57.1476 3.4047 4.76 1.7451 0.0240 0.0100 57.1476 3.4047 4.761 4.760 0.0240 <th>ERYTH</th>	ERYTH
20.2643 35.3846 6.24 1.9344 4.0560 0.0624 2.0.2643 35.3846 6.254 1.9324 4.0560 0.0624 2.0.2664 35.9041 7.95 6.3155 6.3155 0.0016 35.9091 8.477 7.69 0.4170 6.3940 0.01286 19.9170 35.727 9.4727 5.98 0.5382 5.2219 0.0161 19.9170 35.222 9.4727 6.418 19.9170 9.220 0.0189 19.9170 35.229 19.920 0.4180 0.3810 0.01490	7,32 15,0 43
21,2796 35,5814 7,95 1,1925 65,190 0,2385 22,277 36,9924 7,43 0,9559 6,3155 0,000 22,273 36,9924 7,43 0,9559 6,3155 0,000 20,0008 35,9041 6,45 0,4170 6,3940 0,1386 19,8101 34,7727 5,98 0,5382 5,322 0,0598 19,8101 34,7727 5,98 0,4170 0,1394 0,1386 20,0187 35,1814 7,28 0,6184 35,924 0,0598 20,0187 35,1814 7,28 5,056 1,332 0,0598 20,0187 36,1824 36,066 1,3940 0,1490 0,1490 20,0187 36,1814 7,28 5,056 1,332 0,0598 20,0284 35,814 7,28 5,056 1,332 0,0661 20,0484 35,814 7,28 5,056 1,332 0,014 20,6284 36,814 7,78 2,158	13.8
20.6566 35.9524 7.43 0.9659 6.3155 0.0000 22.2727 35.9091 6.43 0.4614 5.727 0.1286 18.1818 33.1819 6.43 0.5787 5.727 0.1286 19.1818 33.1819 6.43 0.5787 5.727 0.1286 21.0294 34.0476 6.51 1.2559 5.2219 0.0661 11.0294 34.0476 6.61 1.2559 5.2219 0.0661 20.6284 34.0476 6.61 1.2559 5.2219 0.0661 20.6284 34.0476 6.61 1.2559 5.2219 0.0918 20.6284 37.000 11.00 1.2100 9.240 0.1340 20.6284 37.000 11.00 1.210 9.240 0.1340 20.6284 37.000 11.00 1.210 9.240 0.1340 20.6284 4.76 4.76 9.240 0.1340 0.1340 20.6284 4.76 6.61 1.210	15,3 4
20.0508 35.9091 6.43 0.5787 5.727 0.1286 0.600. 19.1816 33.1818 6.95 0.417 6.394 0.1390 0.1390 0.4170 6.394 0.41390 0.1390 0.6584 0.4170 6.394 0.41390 0.6588 0.4170 6.394 0.1390 0.1390 0.6584 0.4170 6.394 0.4131 4.0392 0.0918 0.0918 0.6584 0.4180 0.1390	15.1
18.1818 33.1818 6.95 0.4170 6.3940 0.1390 21.0294 34.0727 5.98 0.5882 5.2219 0.0698 22.0294 35.9524 14.90 4.760 9.8140 0.01490 20.6284 35.9524 14.90 1.0948 3.5224 0.0918 20.6284 35.9524 14.90 1.0948 3.5224 0.0918 20.6284 35.9524 14.90 1.0948 3.5224 0.0918 21.8440 35.8140 7.28 5.6056 1.332 0.01840 22.2222 38.6047 6.80 2.3120 9.2410 0.3310 22.2222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.281 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 9.2710 0.2841 22.6222 38.6047 6.80 2.3120 0.1872 22.6222 38.6047 6.80 0.2850 8.2650 0.2841 22.6222 38.6047 9.50 0.8850 8.2650 0.2841 22.6222 38.6047 9.50 0.8850 8.2650 0.2841 22.6222 38.6464 0.6550 0.8846 0.3394 23.6408 35.3446 0.8946 5.3037 0.1836 23.6408 35.3446 0.8946 5.3037 0.1836 23.6408 35.6467 9.99 0.8946 5.3037 0.1655 23.6407 35.3446 0.8980 3.5030 0.1655 23.6407 35.3446 0.8980 3.5030 0.1655 23.6407 35.3446 0.8980 3.5030 0.1655 23.6407 36.5448 5.65 1.8080 3.503 0.2449 24.871 35.556 7.23 1.3014 0.2044 24.871 35.647 0.83 1.2070 0.2849 25.6475 0.6658 0.6658 0.6440 0.0544 24.871 35.4248 0.406 0.6261 0.6244 24.871 36.5448 0.406 0.6261 0.6244 24.871 36.5448 0.406 0.6261 0.0622 25.6475 0.6658 0.6658 0.6440 0.0544 26.6475 0.6688 0.6688 0.6261 0.0644 26.6475 0.6688 0.6688 0.6698 0.6240 26.6476 0.6688 0.6688 0.6698 0.6240 26.6475	- 60 - 60 - 61
19,870 34,7727 5,98 0,5382 5,3222 0,0598 0,0294 35,0247 35,122 0,4131 2,4170 35,122 0,4131 0,4170 35,122 0,4131 0,4170 35,122 0,4131 0,4170 35,122 0,4131 0,4170 35,122 0,4131 0,4170 0,1390 0	14.6
21,0294 34,10476 0.61 1.2559 5.7219 0.0001	15,3
19, 17, 10 35, 9524 4, 99 4,769 9,840 0,1499 0,1091	14°3
20.7418 35.9524 1.0948 3.5224 0.0952 21.8440 35.9524 7.28 5.6056 1.3362 0.00952 21.8440 35.9524 7.28 5.6056 1.3363 0.2184 0.21844 0.21842 35.9524 7.28 5.6056 1.3363 0.2184 0.21842 35.9524 7.28 5.6056 1.3363 0.2184 0.21842 35.8222 38.6047 6.80 2.3120 4.1480 0.1360 0.2184 0.2262 21.82421 35.7143 7.86 1.8078 5.8950 0.1574 0.1754 21.8462 35.7003 8.77 1.4032 7.1914 0.1754 0.1754 21.5263 35.7143 7.29 2.3328 4.7785 0.1836 21.5246 35.9071 9.18 0.5508 8.3516 0.1836 21.5499 35.7143 9.18 0.5508 8.3916 0.1836 0.1836 21.5499 35.7143 9.18 0.5508 8.3916 0.1836 0.1836 21.5139 35.2174 5.55 0.7215 4.5510 0.1695 0.1862 21.5139 35.2174 5.55 0.7215 4.5510 0.1695 0.1695 0.187143 35.4286 5.16 0.8940 0.2160 0.187143 35.4286 5.16 0.8940 0.2160 0.187143 35.4286 5.16 0.8940 0.2161 0.187143 35.4286 5.16 0.18714 0.1	# ·
20.7418 35.9524 4.76 1.9948 3.5224 0.0952 0.218440 35.8144 7.28 2.6056 1.3832 0.21844 0.21.8440 35.8144 7.28 2.6056 1.3832 0.2184 0.22.2223 38.6044 35.8224 7.98 2.1546 5.7456 0.01360 0.22.2223 38.6047 12.70 2.9210 9.2710 0.3810 0.3810 1.4630 1.35.7143 1.2093 8.77 1.4032 7.1914 0.1754 0.1572 0.1872 1.5568 7.4921 0.3892 0.1572 1.5568 7.4921 0.3892 0.1872 1.5568 7.4921 0.3892 0.1872 1.5692 35.7143 7.29 2.3328 4.7385 0.2187 0.1882 1.5726 35.7143 7.29 2.3328 4.7385 0.2187 0.1882 1.5726 35.7143 7.29 2.3328 4.7385 0.2187 0.1882 1.0566 36.0465 6.39 0.6946 5.3037 0.1665 0.2167 0.2097 0	1.01
21.8440 35.8140 7.28 5.6056 1.3832 0.2184 21.822 35.9524 7.98 2.1546 5.7456 0.0000 22.222 38.6043 16.70 2.3120 4.1480 0.1360 20.628 36.8293 12.70 2.9210 9.510 0.3810 20.628 36.8293 11.30 11.4690 9.6050 0.2260 20.4272 35.5814 11.30 11.4032 7.1914 0.1572 21.6280 36.803 9.73 1.4032 7.1914 0.1572 21.7366 36.8046 9.73 1.4032 7.1914 0.1572 21.7366 36.8047 9.18 0.4558 0.2859 0.1842 21.7366 36.8047 9.18 0.4539 0.1836 0.1842 21.7366 36.8047 9.99 1.0480 5.2400 0.1846 21.7367 36.3446 10.80 1.0480 5.2400 0.1846 21.5139 36.4146 4.5510	15.1
21.8524 35.9524 7.98 2.1546 5.7456 0.0000 22.2222 38.6047 6.80 2.3120 4.1480 0.3360 20.4272 35.5814 11.30 1.4630 9.6050 0.2260 20.4272 35.5814 11.30 1.4630 9.6050 0.1572 20.4272 35.5814 11.30 1.4630 9.6050 0.1572 21.6802 37.2093 8.77 1.4032 7.1914 0.1754 21.5829 36.500 9.50 0.8550 8.2650 0.1572 21.5429 35.9091 9.18 0.5508 8.2550 0.1835 21.5366 35.9091 9.18 0.5508 8.3534 0.1835 21.5366 35.9091 9.18 0.5508 8.7752 0.1835 21.5369 35.9091 9.99 1.0840 8.3534 0.1835 21.5469 35.9091 0.9945 0.7215 0.1842 0.1836 21.5469 36.3415 6.55	15.4
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20.612H 34.4146 6.64 2.0584 4.3160 0.1992 0.06 19.4034 35.2508 7.07 0.7777 5.8681 0.2121 0.21 17.5892 34.8788 8.14 1.7094 6.2678 0.0814 0.08 20.2083 32.3418 7.48 2.3936 4.7872 0.1496 0.14	13.0
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TWO YEAR ORAL FDIET) TOXICITY-ONCOGENIGITY STUDY OF FLUOROCARBON FC-143 IN FEMALE RATS INDIVIBUAL HEMOGRAM VALUES

MONTH=12

EOSAB	~	70.0	, ,	? =	, ,		: -	٠,	, ,	9	•		0.00	4	0.208	0.070	0.153	0-106	0.243	0.374	0.092	0.044	860.0	840°0	00		4	2	-	0	=	12	9	.5		03	000.0	36	90	20	6	9	2	, 6	
MONOM	4		2		•	9		0.355	2		: 7		0.413			7	7	7	7	•	્	0.088	0.294	0.240	0.024	Ň	0.132	0.043	0.294	0.290	0.343	0.120	0.207	0.104	0.335	0.198	0.129	0.420	0.372	.33	.28	.27	0.180	26	19
LYMAB	•	1.865 1.865	•			4.48	3.54	N.	3.53	4 BB	5	4		2.891	•	ď	~	9	•							5.325			3.626		74	38	4.416	.52	•61	.93	Q.	5.	46	62	0 4 .	.76	. 0	00	100
PMNAB	0.840	0.621	1.0		3.264	0.648	0.598	0.710	0.152	0.156	6.171	1 - 365	1.239	1.666	0.728	0.560	1,530	1,378	2,187	2.349	5.428	0.660	1.421	0.960	0.024	1.562	0.440	0.688	0,833	1.740	1.666	1,380	2.277	0.416	2,613	0.132	0.258	1.680	1.302	1.541	1.440	1.700	1.170	1.170	1,364
WBC	e.	· [6	6.8			7.1	80.60	2.5	12.1	6.5	6.6	6.4	5.2	7.0	5.1	£,3				4.4	4.9	4.8	2.4	7.1	4.4	£.4	4.9	5.8	6.4	6.0	6.9	5.2	6.7	3,3	4.3	6.0	6.2	6.7	7.2	6.8	4 R	•	
ЭНЭЖ	35.6818	35.6818	35,3333	35.3488	_	2	35.3488	1	Ň	Ξ	Ň	35.4545	~	35.4948	0	35.5000	37.0000	37.3171	35.0000	35.7143	35.6410	35.5814	37.5000	36+3636	37.0000	32.6316	0	_	·	ċ	.0	35.5814	•	34 • 5455	•		'n	ŝ	ŝ	.363	ŝ	ŝ	6.585	0	.279
¥ CH	7967.02	9	N	21.0235	0	C	5	~	62	6	404	20.9677	572	583	369	19.6676	20.2462	21.9828	19.7183	160	144	368	582	20.2020	21.8935	18.9602	32.5088	P0.5369	22.2841	20.4694	ċ	w.	_	Ξ.	÷	_	•	20.1342	0.025	5.44	0.08	0.375	63	0.611	•
MCV	8	58.1242	7.93		4.1	7	59,9721	ø	57.3770	55.1282	5	_	8.5	60.9272	1.6	55.4017	54.7196	58.9080	w	~	.521	60.0559	57.5540	7)	59.1716	58.1040	E. B	۲.	~	57.3664	794	55.9168	139	281		54.4315		375	034	61.7111	Ų.	9	965.9	57.1809	56.8032
HEMAT	44	4	4 5	43	643	44	43	46	€	43	14	†	45	46	45	0 \$	0 4	- - -	4	42	36	64	0 4	44	0 4	38	25	4 3	44	4	7	e 4	n •	4 .	4	94	27	45	45	44	36	£43	4]	6 43	£.3
HEMO	15.7	15.7	15.9	15.2	15.1	15.8	15.2	16.3	15.1	15.3	16.0	15.6	15.8	16.3	15.6	14.2	14.8	15.3	15.4	15.0	13.9	15.3	15.0	16.0	D .	12.4	ر و و	15,3	16.0	15.7	15,5	15,3	15.6	21		19.1	о • о	15.0	15.8	16.0	0.4	15.2	15.0	15.5	15.6
ERYTH	7.55	7.57	7.84	7.23	7.94	7.44	7.17	8.26	7.32	7.80	7.84	7.44	7.68	7.55	7.30	7.22	7.31	96.9	7.81	7.11	06.9	7.16	6.95	7.92	9.79	40.0	2.H3	7.45	7.18	7.67	E .	69*/	* .	91.	90.	47.	3.15	7.45	7.89	7.13	26.9	7.46	7.27	7.52	7.57
ANIMAL	R457	45	R458	R458	R458	R459	8460	*	3461	3462	3462	3463	446	3463	5 992	404	* 465	\$4 65 10 10 10 10 10 10 10 10 10 10 10 10 10 1	465	466	466	466	967	1967	9	468	468	J '	3	•	3	4	* •	*	1 .	* •	4	4	4	4	4	4	P184749	4	4
DOSE	Mdd 0	Mdd 0													0	0	0	0	9	2	2	2 :	2 5	2 5	2 9	2 9	2 9	= 9		2 9										٥ ا			MOD OF		

TABLE 13

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

ANIMAL	ERYTH										
			HEMAT	#C<	¥CH	MCHC	MBC	PMNAB	LYMAB	MONOAB	EOSAB
R4581	6.16	12.3	34	55.1948	19.9675	36.1765	13.2	6.600	5.544	1.056	• 0 0
£83	7.52	15.6	- 4 4	-	\$	35.4545	5.2	0.208	. B3	15	0
K4586	7.08	14.5	41	• 90	20.4802	5,3	4.7	0.517	3.854	.18	• 14
Ç.	A.04	16.8	94	57,2139	20.8955	1521	6.5	1.690	9	0.130	00.
K4595	7.52	15.3	4	58,5106	20.345/	•	4•3	1.075	2.967	.12	.12
5.5	7.44	16.4	- 24	.483	43	44.0	5.0	0.200	•65	.15	.00
529	7.80	16.1	- 4	4.4	20.6410	6.590	4.8	0.384	• 12	*!	<u>+</u>
9	7.72	16.6	4 .5	58.2903	502	36.4889	6.5	0.195	.30	0	00.
9	7.97	16.4	- 24	. 471	77	4.89	6.4	0.441	.41	40	000
5	5.85	12.4	- 4 E	58.1197	96	6.470	5.1	1.632	• 06	4	000
3	7.07	15.5	41	57.9915	23	7.88	6.4	0.931	19.		00
5	6.95	14.7	4.1	566.	S	5.853	5.3	0.371			
5	R.27	16.5	7.4	.831	19.9516	•	7.0	0.840			0
	7,36	16.2	46	2,5	0 [5.217	5.0	0.050			0
5	7.76	16.4		7.5	21.1340	4	800	0.076			
.4	7.49	15.4	4	8.7	90	0	4 C	2.475			7
4	7.57	15.2	43		20.0793	4 3	4.5	1.215			
R4648	5.04	12.0	34	1.3	9	4	12.6	8.568			? -
35	7.60	15.3	43		Ε	8	5	1.378			
9	7.84	15.7	77	56.1224		8	3.7	1.184	2.109	0.370	ē
š	5.84	12.2	34	8.219	90	35.6824	10.1	Ξ.		0.808	00000
7	8.83	16.8	84	54.3601		00	7.8	55	•68	0.390	0.
~	7.31	14.4	4 1			35.1220	6.3	2.016	4.095		00
46A	4.57	14.3	C †	60.882B	65	ğ	6.3	Ξ	.70		0
46A	7.45	15.7	4 3	.402	73	•	7.1	Ξ	•61	•	1.4
•	7.21	15.3	42	.252	21.2205	6.43	4.5	4	1.806	=	90
469	7.97	15.4	64 3	955	22	5.H1	6.1	7	•	8	
40	7.30	16.4	46	(J)	65	35.6522	T.	36	•	32	0.5
9	6.95	14.4	0 \$. 554	20.7194	.00	5.3	=	•	3	.31
•	7.20	15.4	24	8.333	8	56	5,3	0.636	•	2	
41	4.67	13.5	38	56.9715	50.2399	35.5263	7.7	3.080	4.158	0.462	0.0
47	6.05	74.4	0 4	6-115	23.8017	000	3.7	4	•	ř	000.0
47]	7.46	15.3	4 3	.	20.5094	58	6.4	0.4.0	•	\$2.	40.
471	6.65	14.7	36	8.646	22.1053	695	•	_		•34	• 0 •
472	6.46	14.1	3.0	0.3	21.8266	. 15	•	Ū		.61	- 10
K4722	5.47	11.8	33	•	21.5722	757	9.2	5.428	3.312	0.460	0.000
472	7.54	16.8	4	3.6	22.2412	000	٠	Ξ	•	. 19	. 15
472	7.31	15.2	7 7	7.4	20.7434	190	5.1	ō		.30	00.
473	24.9	13.7	38	7	21,3396		10.8	=	•	.21	.21
H4733	HO.	15.7	4	4 • 455	19.4307	681	4•1	Ξ		.20	40
473	6.9]	15.2	£ 3	Š	21.9971	348	5.8	Ñ	•	• 34	0.174
474	7,32	14.7	75	.377	\boldsymbol{x}	ņ		₽	16	. 19	90
474	7.PA	16.2	4 .	7.106	Ω	00.9	A.2	_	ď	57	. 16
75	8.17	16.9	4.7	57.5275	20.6454	35.4574	ۍ.	~	4.012	4.	0
Ğ	F. B.	7 7 7	(7	205	3.0	9 6		• (•	3

TABLE 13

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

TABLE 14

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

		GLUCOSE (MG/DL)	OSE OL)	BLOOD URE,	BLOOD UREA NITROGEN (MG/DL)	15	ALT (10/L)	5	AST (TU/L)
	Z	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE									
MONTH 3									
¥ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2. r	120.6	_	16.3	1.84	21.4	2.67	6.53 €	7.26
30 DEW	111	134.6	6.00	17.1		84.5#	15.33	59.7	22.47
MONTH 6									
Wdd 0	15	119.0		17.5	1.36	24.1	3,75	49.7	14.98
300 PPM	15	123.7		20.74	1.40	54.8#	29.26	87.8	34.83
30 ppm	15	134.9*		15.9	1.44	63.3#	29.34	4 2.1#	45.60
HONTH 12									
#44 0	*	154.3	26.17	16.4		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 Pr	15	131-1#	8.10	16.2		47.6#	56.59	124.4	40.04
MONTH 18									
Mad 0	15	123.4	56.39	18.1	3,38	1.48	10.68	99.1	68.14
300 PPM	15	139.3	16.14	17.6	1.88	84.3#	55.95	123,3	65.98
30 PPM	15	120•6	27.62	16.5#	6.48	69.7#	33.41	116.4	57.99
MONTH 24									
Edd O	15	122.5	23.07	16.5	3.16	4.6	0.10	64.0	25.76
300 ppm	15	147.14	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	0.89	17.64

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

TABLE 14

MEAN S.DEV 1.10 0.80 CALCIUM (MG/DL) 0.30 0.24 0.29 0.43 TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUDRBCARBON FC-143 IN RATS BLOOD CHEMISTHY VALUES (TBILI, ALB, TPROT, ALKPHOS, CPK, GA) WITH STANDARD DEVIATIONS 11.5 11.1* 10.9 10.8 10.5* 10.8 10.5 10.6 10.6 11.1 10.8 10.4 CREATINE PHOSPHOKINASE (IU/L) 100.7 26.46 67.0# 24.24 60.5# 12.65 41.32 26.66 31.23 47.61 23.65 19.45 74.52 45.87 69.23 68.04 37.33 20.55 S.DEV 1111.1 88.3 71.1# 89.9 81.4 58.3* MEAN 79.7 68.3 67.6 79.9 82.5 106.5 26.22 91.86 93.14 #0.41 94.85 37.13 MEAN S.BEV #3.94 \$9.28 #1.75 93.76 73.37 92.61 ALKALINE PHOSPHATASE (IU/L) 25.58 22.84 26.20 91.1 153.5* 138.7* 97.1 147.3* 146.9* 105.8 166.5* 128.3 85.2 184.4* 112.5 70.1 113.5* 81.2 0.36 0.28 0.33 0.34 0.27 0.31 0.33 0.61 0.42 0.45 0.50 0.30 MEAN S.DEV TOTAL PROTEIN (GM/DL) 7.0 6.6* 6.7* 6.0 6.0 6.0 9.99 7.2 6.9 6.9 0.34 0.29 0.37 0.20 0.20 0.34 0.26 MEAN S.UEV 0.38 0.23 ALBUMIN (GM/DL) 4 N N. ₩. 4. 4 9. 6 8 8 8 8 8 8 8 8 2.8 3.1 TOTAL BILIRUBIN (MG/DL) 0.20 0.35 0.31 0.25 SADEV 0.25 MEAN 0.8 0.7 0.5 4.0 0.0 4.0 0.0 0.6 0.8 0.6 0.6 0.8 MEAN z 15 15 15 15 55 35 15 512 MONTH 17 0 PPM 300 PPM 30 PPM MONTH 18 0 PPH 300 PPM 30 PPM 0 PPM 300 PPM 30 PPM MONTH 24 MONTH 3 MONTH 6 0 PPM 300 PPM 30 PPM 0 PPM 300 PPM 30 PPM

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

N NUMBER IS 14 FOR THIS MEAN.

TABLE 14

TWO YEAR URAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUGHUCARBON FC-143 IN MALE RAIS INDIVIDUAL SERUM CHEMISTRY VALUES

CA	11.5	11.3	11.2	12.4	10.8	10.8	10.8	11.2	1:1	11.6	6.3	12.0	11.0	11.2	11.0	11.4	10.3	11.0	11.2	10.9	11.2	11.4		10.8	10.8	9.6	11.3	10.3	 	10.1	10.2	10.0	12.0	11.0	10.4	10.9	12.1	11:1	11.9	12.2	10.0	11.0	10.8	10.1	11.5
S P S	115	104	69	140	144	120	90	90	7.4	109	92	72	113	72	134	7	80	4 7	16	82	60	43	4	72	53	45	75	117	4	101	7.1	69	73	2	or G	67	16	0 \$	53	47	38	99	65	52	ņ
ALKPH0S	107	106	92	105	100	80	9	125	7.1	55	73	125	128	69	108	140	124	114	162	183	124	145	143	212	181	160	128	134	138	217	96	148	147	192	156	108	163	1.4.9	16	96	168	139	145	109	138
TPROT	6.8	9.9	7.1	7.8	9.9	6.5	6.7	6.5	6.8	9.9	6+5	9*9	8 • 9	6.5	7.0	6.3	6.	6+3	6.5	4.9	2.9	6.8	6.3	9.9	6.5	9•9	6.8	6.2	4.9	7.4	6.3	6.2	6.8	4.9	6•3	6.3	6.9	7.0	7.2	6.7	7•0	6.5	6.1	6.3	6.5
ALB	4.2	4.4	4.4	5.1	4.4	4 • 1	4.4	3.5	4.2	†• †	4.1	5.1	4.6	5.4	4.3	D	4.6	5.1	4.7	¥.	5.0	5.2	5.0	2.4	5.3	5.0	5•3	5.4	5.3	5 • 7	4.2	4.0	4.2	4.7	4.0	4.4	4.7	5.1	5.3	5.0	5.3	4.0	4.3	4	4.7
THILI	9•0	ភ ភ	o. c	0.0	0.8	0.5	0.7	្ច ទ	0.5	0.5	7. 0	P•0	5 . 0	9•0	7.0	0 • 5	c •0	o.5	٠.	0.5	7.0	0 0.5	1.0	9.0		1.0	7. 0	0.6	0.5	†• -	0.6	0.7	0.7	0.7	9.0	0.0	7.0	0.7	R • C	0.7	H.0	0.5	0.1	¥.0	9.0
AST	36	4	36	5.0	53	42	43	46	38	†	51	5.0	47	36	5.8	Ţ	15	37	84	20	\$ \$	42	45	14H	65	47	51	47	4	7.	4 3	29	20	55	120	19	82	45	37		Э Е .	. 82	7.	ņ	53
ALT	20	20	20	25	28	21	25	23	18	18	21	24	20	<u>5</u>	52	5 2	9₽	23	88 8	đ.	42	23	25	110	34	12	33	23	27	30	12	6 E	30	92	*	28	64 3	25	23	12	56	56	51	30	52
NOR	17	21	17	11	15	17	14	14	16	17	91	18	17	15	14	25	20	17	17	16	21	5.	16	<u>-</u>	17	2 4	18	25	16	61	16	50	16	16	16	17	18	16	15	H	۲,	1.5	16	18	17
6LU	112	140	138	112	129	102	111	5	141	108	130	125	129	114	120	135	128	139	128	121	131	1 + 1	145	124	120	136	115	124	128	127	120	152	130	136	134	119	139	135	142	144	132	138	125	138	131
ANIMAL	A183518	A183527	A183532	A1R3534	A1R3537	A1R3540	A1R3542	A1H3548	A1R3552	A1R3559	A1R3562	A1R3564	A1R3565	A1R3567	A1R3569	H1R3585	B1R3587	H1R3589	B1R3592	H1R3593	H1R3595	B1R3604	A1R3605	H1R3610	A1R3611	B1R3617	B1R3623	H1R3634	A1R3640	B1R3643	C1R3654	C1R3655	C1R3665	C1R3667	CIR366B	C1R3673	C1R3675	C1R3677	C1R3679	C1R3683	C1R3687	C1R3690	C1R3691	C183692	C1R3645
DOSE	M d d	Med d	10 d	Medical	Ndd 0	O PPM	NPP O	Mdd 0	Mdd 0	Mdd 0	M-PPM	N-d-d-O	Ndd 0	Ndd 0	Med 0		_			_		_				HOR DOE						30 PPM					_		_						30 pp

TWO YEAR UMAL (UIET) TUXICITY-ONCUGENIGITY STUDY OF FLUOMOGAHBON FC-143 IN MALE RATS INDIVIDUAL SEKUM CHEMISTRY VALUES

----- MONTH=6

S	10.	=	=	=	=	11.	12.	11.0	1	11.	11.	10.	11.	11.	11.	11.	11.6	11.	11	10.5	11.4	11.2	11.1	11.0	11.2	11.3	10.	10.9	11.0	11.1	11.0	10.6	10.6	10.9	10.6	10.9	11.2	10.8	11.4	11.3	1 . 0	11.5	10.7	10.4	10.7
CPK	7.0	2	51	119	204	28	29	57	57	119	85	61	85	144	7.7	11	16	08	106	75	46	6	142	52	58	110	63	65	115	26	<u>5</u> 0	61	49	42	64 3	28	0.4	4,	157	38	58	63	51	45	63
ALKPHOS	123	106	72	15	110	65	114	213	62	120	950	69	69	118	7.8	162	178	156	183	16	123	160	127	109	162	172	102	166	211	102	† 6	163	188	165	42	121	185	172	44	135	508	158	156	134	148
TPHOT	4.0	E• /	2.9	7.5	0°.	7.2	7.5	7.0	7.1	7.3	6.7	9.9		7.5	6.7	4.9	1.9	9.9	7.2	6•3	7.0	6.3	6.7	6.5	7.0	6.9	6.3	9.9	6.5	9.9	6.5	6.5	6.5	4.9	6.7	6.5	8·9	6.7	7.6	7.1	6.9	7.1	4.9	4.9	6.7
ALB	F. 4	4	4.7	3	4	3.4	3	4.7	4.0	4.7	4.5	4.7	4.0	5.0	4.4	5.7	5.1	5.3	6.0	5.1	5.4	5.3	5.5	2.0	5. 5.	30 10	4.0	5.5	5.5	5.7	5.0	4.0	8.4	4.7	6.4	4.5	ŷ. 4	5.0	5.8	5.6	4.4	5.3	5.2	4.4	5.1
THILE	9.0	A • 0	9.0	3]:]	1.0		9.0	0.7	1.1	6.0	9.0	9.0	1.0	1.0	0.7	1.2	5.0	8.0	1:1	0.5	7.0	3. 0	0.0	9.0	9.0	9•0	0 5	9•0	9•0	9.0	4.0	0.5	†• 0	4.0	7. 0	4.0	7. 0	9.0	9.0	4.0	٥.٠	4.0	0.3	0.5
AST	66	υ 4	52	1 •	58	35	28	64	53	47	5	55	64	74	19	57	112	47	122	47	96	80	68	174	73	95	4	7 0	130	99	64	83	212	65	64	118	148	12	11	. 77	139	74	34	105	59
ALT	18	7	20	28 1	2.2	61	62	25	56	22	21	28	23	5 6	25	58	#8	21	92	27	60	73	37	92	35	73	37	34	111	5	35	53	131	48	25	83	87	36	36	4	75	30	0.2	53	82 8
BON	61	7.	91	<u>5</u>	9	18	9	15	20	17	17	18	18	17	17	21	23	21	21	22	21	19	23	20	23	21	20	<u>*</u>	20	9	61	16	15	15	15	16	16	17	16	15	16	18	13	15	1.1
9°	133	139	130	124	109	124	115	128	66	109	100	133	129	102	111	119	152	119	121	110	144	117	123	112	122	120	122	117	129	128	146	151	149	137	138	138	133	133	144	130	122	112	128	134	129
ANIWAL	A1R3519	41R3524	A1R3529	A1R3533	A1R3537	A1R3541	A1R3547	A1R3550	A1R3553	A1R3557	A1R3559	A1R3562	A1R3567	A1R3573	A1R3575	B1R3583	H1R3584	B1R3596	R1R3598	91R3600	B1R3604	R1R3608	B1R3609	B1R3613	B1R3617	B1R3628	B1R3629	R1R3631	B1H3633	B1R3642	C1R3646	C1R3650	C1R3656	C1R3658	C1R3660	C1R3664	C1R3665	C1R3667	C1R3679	C1R3680	C1R3682	C1R3687	C1R3689	C1R3691	C1R3694
DOSE	MPG 0			0			N PPN		E POR	PPK	PPM	₩dd (Mad C	PP#	Mdd 0					ppw										Mdd			PPX			_									
		_	_		_	_	٠	_	9	_	_	٠	J	-	3	300	306	300	300	300	300	300	300	300	300	300	300	300	300	90E	30	30	30	36	30	30	30	30	30	. 30	30	30	30	30	30

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

----- MONTH=12 -----

CA	11.0	10.8	10.5	10.4	10.8	10.6	10.7	10.4	10.5	10.2	10.3	10.4	6	10.4	10.9	10.4	10.8	10.7	10.5	10.4	10.5	10.2	10.6	10,3	10.9	10.8	10.7	10.8	10.9	11.0	10.9	10.5	9°0	***	7 .	0 0	10.	11.3	10.6	10.6	10.7	10.7	10.5	10.	10.3
CPK	72	6 43	42	61	80	103	88	234	8	65	105	20	36	28	99	50	106	4 2	19	4.0	67	78	107	36	26	25	0 7	38	54	96	16	26	9 -	ų,	0 .	4 .	0 1 1	99	73	4	96	19	55	50	51
ALKPHOS	139	104	6#	108	102	113	115	107	225	56	88	84	72	7.0	152	202	145	153	118	212	208	103	235	117	190	158	101	105	139	309	68	168	177	20.0	C12	154	3	128	93.	145	124	19	159	131	109
TPROT	6.9	7.1	9.9	6.7	6.8	6.8	7.0	6.9	6.9	6.7	6.3	6.2	6.5	6.9	7.1	6•3	6.9	6.8	6.5	6.9	6.9	9. 4	7.2	6.5	7.3	7.0	7.1	9•9	7.1	7.1	7.0	7.1		6.0	5 .	æ :	9.	7.4	7.6	5.0	7.2	6.9	6.5	9. 0	6.5
ALB	3.6	9.6	3.8	3.7	3.9	3.8	3.9	÷	3.4	J. E.	3.5	3.3	3.6	3.5	3.9	3.7	1.4	4.7	4.1	£ • 4	9 ° E	Ď•€	4.4	4.5	4.7	4.3	4.2	4	4.7	4.7	4•1	4.3	3.7	ж М	1	Э. Г	£.	3.6	4.6	4.1	4•0	0.4	0•4	3.1	3.7
TBILE	5.0	. o	9.0	9.0	9•0	9.0	1.0	6.0	1.0	9.0	9•0	7.0	0.5	4.0	٥.٢	9.0	7.0	7. 0	5.0	0 • 5	9.0	7 • 0	1.0	†• 0	7.0	9•0	0.7	7.0	1.0	1.0	P • C	0.0	0.0	0.5	c :	10 f) • O	э• С	· c	9•0	1.4	1:1	7.0	0.7	0.7
AST	S.	0.4	64	123	29	56	85	118	47	96	212	43	54	63	59	164	66	116	35	171	202	137	236	100	126	53	99	75	92	326	42	66	75	103	430	127		4,0	*	. 193	121	. 65	73	126	62
AL.T	20	9	15	6.9	37	23	33	37	32	41	18	18	23	23	I E	133	35	105	30	162	185	40	208	105	76	50	4	4	34	261	36	40	5. 4.0	75	241	40,	105	37	52	159	62	ņ	53	e e	36 €0
BUN	ď	. <u>.</u>	16	12	18	17	17	17	18	20	19	*	•	16	17	17	17	18	16	17	15	18	16	19	22	1,	17	20	17	1.7	16	17	16	_	15	17	16	16	16	17	18	16	17	13	16
950	147	5.5	124	134	155	141	183	178	1.85	165	214	123	125	143	148	151	130	144	127	142	153	145	127	150	131	136	135	138	142	129	139	132	128	147	123	139	120	130	137	132	129	141	122	132	115
ANIMAL	1103614	A102517	025501A	4183522	A1R3527	A1R3535	A1R3543	A183546	A 1 12 25 50	A1R3551	A1R3554	A1R3568	A1R3570	A1R3575	A1R3580	B1R3584	B1R3588	B1R3589	B1R3592	B1R3598	B1R3604	B1R3613	R1R3617	H1R3620	B1R3622	B1R3626	H183627	R1R3638	B1R3642	H1R3643	C1R3649	C1R3650	C1R3652	C1R3663	C1R3668	C1R3670	C1R3672	C1R3676	C1R3679	C1R36R0	C1R3681	C1R3683	C1R3685	C1R3691	C1R3694
DOSE	700	. 0	300	Z di	¥ 0 0	E C	A C	10 C	30.00	¥ d d	Mdd U	D PP.	Mdd 0	Ndd D	M dd C																														30 PPM

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

-------- 81=HLNOW -------

₹	10.6	10.5	11.9	12.0	10.9	11.8	11.5	12.0	11.9	11.1	10.2	0.6	10.9	10.1	12.4	11.3	10.9	11.5	11.3	11.5	10.3	4.8	11.7	11.7	11.4	0.0	12.0	0.0	8	11.1	10.4	m .	10.	3 (14.5	10.8	x	10.6	11.0	•	10.5	٠	•	10.5	9.6
S A	37	6	36	4 0	96	38	64	7	69	108	56	7	11	47	334	9	4 2	29	ų,	83	57	49	52	212	104	152	23	25	109	7.1	£ :	4	9 : B	T.	327	991	7	4	115	80	110	69	108	56	100
ALKPHOS	128	164	57	56	113	85	41	55	9	124	06	18	99	82	99	148	214	113	142	213	172	177	202	168	129	106	233	156	413	180	105	138	26	134	100	69	133	124	186	105	99	82	56	156	101
TPROT	6.8	ស្វ	7.0	7.4	6.8	8•1	7.2	7.4	7.5	7.3	7.6	9•9	7.7	6.7	7.3	5.8	7.5	7.4	6•9	7.0	7.0	6.5	7.0	9.9	4.7	7.0	7.3	6•9	7.0	6.9	7.8	7.0	7.1	4.7	m • •0 ∣	7:	6•9	7.2	7.1	7.6	7.5	7.2	6.9	6.7	1.9
ALB	3.5	2.1	3.2	3.4	3,3	3.7	3.4	3.3	3.4	3.3	3.4	3.3	3.2	2.6	3.4	3.8	3.8	3.4	4.0	3.8	3.9	3.2	9.6	3.6	4.1	2.9	4.0	3.6	3.7	0. 7	Z.	9.	3.2	3,3	5.9	3•1	9. ¢	3.4	3.5	3.0			3.2		4 60
TBILT	7.0	0.2	9.0	1.0	7.0	6.0	1.1	1.1	5.0	1.1	5.0	5.0	o. 0	0.2	1.6	4.0	٠•0	1.0	7.0	9.0	9.0	†•0	7.0	9.0	9.0	5. 0	1:1	o. 0	1.5	7.0	0•3	9•0	H.O	9.0	0.1	0.7	0.8	9.0	7.0	1.1	1.0	7.0	8.0	7.0	6.0
AST	4	317	J.C	80	693	n 4	61	5.	4.	94	61	62	133	4	168	42	109	89	139	132	99	163	117	205	101	95	142	7.8	295	95	117	9	100	108	161	120	153	156	583	9	68	19	49	96	87
AL T	41	29	54	4	38	50	30	53	4	35	20	23	34	34	24	31	85	39	56	96	51	124	75	118	63	42	16	47	258	53	40	37	¢ 3	7	53	58	16	82	160	34	41	4	3 ¢	- 62	6
BON	<u>5</u>	50	5	. 00		9	18	2.7	17	17	17	15	17	17	17	19	17	19	16	1 t	20	14	6.	19	17	18	19	16	91	16	12	13	16	16	36	16	16	15	15	17	13	12	16	. Tu	4
eru G	151	125	148	F + 1	200	135	101	117	127	140	1.35	126	134	91	4	135	124	137	140	138	136	124	150	148	1117	118	168	145	173	136	116	142	134	156	31	121	125	134	128	110	123	136	113	126	114
ANIMAL	A183519	AIDSEST	ACREGIA	A 103531	SE SECTA	000014	A183542	A 10 35 57	A I D A F F A	A103654	195541V	A183565	A183567	A183574	719591A	RIBARRA	H1R3593	R1R3596	R1R3600	B1R3601	H1R3605	R1R3608	B183610	H1R3612	8183615	B1R3624	B1R3632	B1R3641	B1R3644	B1R3645	C1R3647	C1R3651	C1R3654	C1R3658	C1R3662	C1R3663	C1R3664	C1R3667	C1R3668	C1R3676	C183679	CIRSORI	CIRACAL PRACES	C183689	C1R3695
DOSE	NGG 0		0			000					0.0			. d.	1 d				300 PPM						300 PPW			300 PPM								30 PPM	30 PPM	30 PPM							30 PPM

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

-- #2#HINDW --

DOSE	ANIMAL.	0T9	BUN	ALT	AST	THILI	ALH	TPROT	ALKPHOS	CPK	CA
Mdd 0	A1R3518	130	14	56	5,5	5.0	2.6	9.9	118	1 н	10.5
Mdd 0	A1R3524	138	23	62	24	0.0	2.7	7.1	42	51	11.5
Med 0	A1R3528	141	15	28	47	0.2	3.0	6.8	36	63	10.8
Mdd 0	A1R3531	109	+	36	9	0•3	3.1	7.1	52	72	11.0
¥dd 0	A1R3534	67	20	21	142	F•0	2.7	5.9	61	140	11.1
MGG 0	A1R3538	147	12	38	7 0	0.2	2.8	4.9	99	69	10.5
Mad O	A1R3542	96	15	35	90	9.0	3.0	7.0	37	54	11.6
MGG 0	A1R3548	122	15	35	84	0. 4	2.9	7.0	47	108	10.9
M 1d 0	A1R3554	158	17	6 4	74	0.2	3•0	9•9	62	73	11.0
Mdd 0	A1R3557	117	91	4	66	0.6	3•0	7.3	109	06	11.2
Mad 0	A1R3562	134	17	33	53	0.1	2.4	6.9	68	16	10.1
MDG O	A183564	116	21	27	5.0	0.5	2.5	6.9	11	187	10.5
Nd O	A1R3569	143	25	58	74	1.0	2.1	7.4	58	568	10.3
MOD O	A1R3573	105	<u>*</u>	50	50	0 • 7	3.1	7.7	98	101	11,3
	A1R357B	115	15	53	26	0.4	Z•6	7.3	7.7	146	10.9
	B1R3581	120	15	4]	21	2.0	3.4	9•9	16	82	10.8
	B1R3585	155	17	111	133	0.5	3.2	6.8	122	57	10.5
	H1R3591	147	17	88	130	0.3	2.9	7.9	132	5	10.5
	B1R3594	159	16	75	109	0.3	3.4	7.1	162	176	10.8
	B1R3597	143	15	40	117	0.2	2.5	4.4	7.	95	10.6
	B1R3601	146	16	47	68	0.5	3.0	6.2	127	82	10.7
	B1R3605	157	14	4 3	55	0.1	3•3	7.4	66	83	10.5
	H1H360B	136	14	4]	75	0 . 2	2.8	6.5	108	96	10.7
	B1R3611	128	61	41	56	0•3	3.5	6.8	133	57	11.2
	H1R3618	169	17	82	152	7•0	3.1	6.9	105	54	10.8
	B1R3623	142	14	60	66	0.3	3.6	7.3	107	162	10.9
300 PPM	H1R3630	137	17	41	101	0.3	3.4	7.8	111	114	11.3
	H1R3633	163	34	62	110	0.2	2.7	6.7	121	15	11.0
	B1R3636	153	13	55	91	0.2	3.0	4.9	75	99	10.6
300 PPM	B1R3641	152	20	56	н3	0.3	3.0	6.0	129	57	11.0
	C1R3646	144	17	47	7.0	4.0	3.1	9.9	29	49	11.4
	C1R3650	147	14	35	51	0.3	2.H	7.1	100	71	10.4
Mdd 0E	C1H3654	133	13	40	5 X	£.	S. S.	6.7	102	74	10.2
	C1K3658	123	15	€	99	e.g	3,2	6.8	102	£ \$	10.8
	C1H3663	115	14	27	6 3	9.0	5.6	6.8	47	51	10.5
30 ppw	C1R3667	107	15	4 7	72	0 • 4	3.0	6.8	103	92	10.5
	C1R3670	110	۲۶	40	105	٥•٤	2.3	4.4	75	44	10.6
30 PPM	C1R3672	107	10	62	7 7	₹•0	2.6	7.7	50	47	10.1
	C1R3676	125	34	33	5.5	0.0	2.5	6.6	16	11	10.7
	C1R3679	122	16	4 1	54	4.0	5.9	7.1	49	24	10.5
	CIR3682	116	18	39	64	0.3	3.0	7.0	104	105	10.7
_	C1R3684	132	12	60	. 42	9. 0	3.1	6.5	7.7	90	10.4
30 PPW	C1 R3689	126	۲I	6 4	49	2 • 0	5.9	6.3	118	114	10.2
30 PPN	C1 R3 691	66	15	,	74	0•3	3.0	6.3	65	13	10.4
	C1R3694	113	15	a D	75	5 ° 0	3.1	7.3	88	90	10.6

MEAN S.DEV. 9.20 38.56 29.11 28.60 36.77 24.40 18.97 25.21 30.03 35.26 12.95 (IU/L) TWO YEAR ORAL (DIET) TOXICITY-UNCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS MEAN BLOOD CHEMISTRY VALUES WITM STANDARD DEVIATIONS \$8.0 51.6 69.7 69.2 69.9 66.2 72.6 70.1 63.5 63.5 67.8 67.0 17.20 20.46 14.55 4.87 6.72 3.18 15.17 21.59 12.94 11.60 6.36 14.31 MEAN S.DEV. 10.11 25.27 9.61 ALT (TUZL) 32.6 83.5 84.3 85.7 24.1 28.6 27.1 66.4 19.4 40.0 43.1 BLOOD UREA NITROGEN MEAN S.DEV. 3.22 2.96 2.96 1.62 3.91 2.07 2.14 5.21 2.83 2.49 3.37 4.10 3.76 3.35 (MG/DL) 19.7 24.5* 18.5 21.6 20.7 19.1* 19.8 21.2 19.9 18.1 18.7 20.1 17.9 16.2 15.3 MEAN S.DEV. 9.79 10.96 12.06 14.98 9.61 13.41 13.75 18.72 15.23 10.51 8.18 10.35 15.51 9.39 15.39 GLUCOSE (MG/DL) 154.8 133.6# 128.6# 138.9 132.9 132.1 134.9 135.3 135.4 123.5 120.0 122.2 122.2 115.3 119.4 z 15 15 15 15 55.5 15 15 MONTH 6 0 PPM 300 PPM 30 PPM 0 PPM 300 PPM 30 PPM M44 006 0 PPM 300 PPM 30 PPH HONTH 12 MONTH 24 MONTH 3

* : P < E .05. TWO TAILED DUNNETT I ON HAW DATA. # : P <= .05. TWO TAILED DUNNETT I ON RANKED DATA.

TABLE 15

MONTH 3 0 PPM 30 PPM	N 8115 115 115 115 115 115 115 115 115 11	MEAN 000 000 000 000 000 000 000 000 000 0	### TOTAL (MG/DL) AN S.DEV AN S.DEV 5 0.18 6 0.19 6 0.14 6 0.38 8 0.38 8 0.38 8 0.21	ጸ ጠ የሚኒ የሚያ 444 10 S WOO የታሪካ Wide EX	ALBUMIN (GM/DL) (AN S.DEV (AN S.DEV	TOTAL (GM/DL) MEAN S.DE 7.2 0.7.0 7.4 0.7.4 7.4 0.7.3 0.7.3 7.5 0.7.5	AAL DL) O.641 0.411 0.64 0.32 0.57 0.57 0.56	ALKALINE PHOSPHATASI (IU/L) MEAN \$.B 89.1 25. 69.9 25. 69.9 25. 82.1 22. 82.1 22. 82.1 22. 82.1 22. 82.1 22. 82.1 22.	11 N E	CREA PHOSPH (IU 87.7 86.7 86.7 86.7 86.7 86.1 18.7	CREATINE HUSPHOKINASE (IU/L) MEAN S.DEV 93.9 51.44 87.7 37.12 86.7 21.06 66.7 21.17 89.2 45.03 89.2 45.03 78.6 20.02 41.3 11.52	CAL (AG 110.0 110.5 110.7 110.7 110.7	CALCIUM (MG/DL) AN S.DEV 0 0.55 1 0.52 5* 0.69 7 0.43 8 0.45 1 0.33
MONTH 16 0 PPM 300 PPM 30 PPM 30 PPM MONTH 24 1 PPM 300 PPM	សិស្តិស សិស្តិ	000 000 000 040	0.26 0.23 0.24 0.31	क क क क क क क क क क क क क क क क क क क	0.23 0.23 0.26 0.26 0.28	PFB FF1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	300 300 310 400 400 400 400 400 400 400 400 400 4	900 130 130 130 140 190 190 190 190 190 190 190 190 190 19	37.3 335.1 27.6 68.4	9.61 9.64 19.18 32.23 27.06	111 10.0 4 11.0 4 11.0 5 6 8 11.0 5 11.0 5	00 00 00 00 00 00 00 00 00 00 00 00 00

72.

: 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-ONCOGENIGITY STUDY OF FLUUROCARBON FC-143 IN FEMALE RATS INDIVIDUAL SERUM CHEMISTRY VALUES

--- WONTHES ---

8	DOSE	ANIWAL	0.19	BUN	ALT	AST	14161	ALB	TPROT	ALKPHOS	CP.	∀
	700	N194574	143	6	ć	4.7	0	8.4	5. B	120	11	10.1
	E 3	0104014	150	י ני) n	0 1	10 10 10 10		7.0	61	95	10.7
	L	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		1 6		i ii	9	3	4.7	15.2	150	11.7
	Ę	Noce XIX	167	0 0	- 0	<u> </u>		9	7.1		. 10	10.6
		5004X1N	130	9	0 1	1 4	9 6	a d		c.	234	11.2
		60570IN	134		, í	2	9.0	5.5	7.0	128	168	11.3
	2 2	NIBARIO	4 4		1 (2)	57	7.0	0.5	7.8	6,8	9	12.2
	M	NIRAGIZ	147	50	16	36	0.5	8.4	6.6	68	58	10.8
	Į.	NIRAGIA	129	61	19	4.1	S • 0	4.0	7.0	61	20	10.6
	E d	N1R4619	139	19	25	51	1.0	5.3	6.9	65	す	11.2
	FPR	N1R4621	131	51	23	64	S • 0	6.4	7.1	19	80	10.7
0	Mede	N184626	163	20	28	4	4.0	5.3	7.1	120	58	10.6
	Mdd	N1R4627	133	19	16	64	0.5	5.7	7.0	4 0	99	10.9
	Ā	N1R4633	134	22	25	32	B•0	J	8°0	70	6	11.4
	Ā	N1R4640	133	21	27	0.4	ъ. С	D. Q	7.6	58	16	11.7
	Ā	0184645	126	82	68	37	4.0	4.7	5.9	5	72	10.1
	Ā	0184654	129	5 1	35	47		5.3	7.2	65	63	10.8
	ă.	0184660	119	58	32	45	0.5	3•6	5.2	73	57	10.5
	ğ	0184664	122	92	25	56	4.0	5.1	7.1	125	06	10.9
	ď.	0184668	130	20	32	7.0	9.0	Տ	7.3	ų,	136	11.2
	ğ	0184669	138	27	20	36	5.0	5.1	7.0	98	48	10.6
	D D X	01R4672	136	61	21	0 4	č.0	5.3	7.1	118	40	11.3
	Œ.	0184673	129	5	38	11	0.3	5•0	6.6	106	123	
	g E	0184674	124	52	31	72	4.0	5.0	7.1	111	186	11.9
	Ā	01R4679	154	23	56	40	0.3	5.0	7.0	A2	٥ ٢	11.5
	Ā	0184680	139	52	15	33	†• 0	4. B	6.8	52	26	9.1
	Ā	01R4693	145	28	13	5 4	0.6	5.1	6.8	95	100	0.0
	ğ.	0184698	130	31	20	26	0.5	0.5	2.9	124	6 1	11.8
	Ā	01R4700	152	20	21	43	1.0	6.1	7.4	66	21	11.6
	¥	01R4701	120	21	56	58	9.0	4.7	6.1	66	H8	4.
	Ā	P1R4708	148	20	19	4 4	9.0	5.3	9•9	75	* !	11.8
	Ť	P1R4710	121	6	16	32	0 0	.	7.0	104	65	£ .
	Œ	P1R4720	135	91	26	50	0.7	5.1	7.5	4 (0)	φ.	9.6
	Ī	P184721	142	18	22.52	4.7	9.0	6. 4	7.0	26	3 ·	10.
	Ž.	P1R4730	140	16	18	36	9.0	S•1	7.3	53	63	6.01
	Į.	P1R4731	145	21	22	0 4	0.7	4.4	2.9	66	Ť Đ	10.8
	Ā	P1R4734	137	Ŧ	21	50	1.0	5.5	7.4	-	114	11.5
	Ā	P1R4735	117	12	14	€ *	0.6	•	7.0	41	109	11:1
	A C	P1R4736	106	25	20	53	0.0	5•3	7.1	33	111	11.0
	Ā	P184737	125	91	15	.50	9.0	4.6	6.9	33	69	6
	Ĭ	P184738	141	16	17	45	ŋ•p	4.6	1.9	55	н3	6.6
	Ğ.	P184744	118	18	23	446	9.0	5.4	7.3	66	£ .	10.6
	T O	P1H4749	133	2.1	16	38	9.0	\$. 4	6.6	58	28	G 1
	Ā	P1R4752	140	18	20	44	9°0	5.5	7.4	91	121	10.7
30 P	Š	P1R4753	133	16	16	51	0.4	4•3	4.4	86	63	ъ.

TWO YEAR CHAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUCHOCARHON FC-143 IN FEMALE MATS INDIVIDUAL SERUM CHEMISTRY VALUES

		1			4-HINOM	= 9=				ò	Š
			į	F 4	AST	THILI	ALB	TPHOT	ALKPHOS	ž	5
005	ANIMAL	9 F0	Z C C	į	i I		•		137	7.1	12.9
ı			10	2	37	6.0	. ·	. 0	125	55	11.2
	N1R4582	2.1	12	i it	118	9.0	0 i		9.5	41	12.2
Mdd 0	N1R4584	221	33	. T	183	0 5	ر ب		101	69	11.8
	N1R4586	159	9 6	9 6	1949	0.0	o.	, r	ั้งก	33	11.6
	N1R4590	E 6) c	200	48	9.0	n. C	u u	36	85	11.6
	N1R4598	141	> (2 0	7.1	4.0	6.1	n «	7	40	11.4
	N1R4603	161	7,0	ا ار در	96	ស.	ស្វ	•	r.	52	11.0
M d	N184607	147	, i	ט נ זיי	99	4.0		D 1		99	11.8
	N1R4616	150	D :	7	5.7	0.6	6.0	Z•7	. 5	73	12.2
	N1R4619	140	9 ;	e 4	. 4	7.0	6.9	9.1	40.	90	11.0
	N1R4621	154	20	9 4	6.2	J.	5.6	7.5	200	in T	11.4
T d	N184622	160	2 2	† °	. I	4.0	4.5	ر دور	9 5	35	11.3
	N1R4629	130	0 7	0 0	, ur	4.0	5.5	9. (2	65	12.3
	N1R4631	137	2.2	27	30	7.0	4.0	0 ·	9 O	57	11.8
- d	N1R4632	154	e i		4	9.0	4.9	9.7	ים הים	25	12,3
200	N1 R4639	156	31	0.5	122	9.0	2.9	4.4		63	11.7
10000	0184650	133	£ (0 6		0.0	6.2	9.7	111	0.9	11.5
000	0184653	128	<u>د</u>	00	9	5.0	5.2	7.5	0 0	106	11.4
100	0184657	123		٠ د د		9•0	5.1	7.3	0 0	44	11.0
1000	0184660	136	52	V .		4.0	0.4	7.0	6	, c	12.3
300	0184663	125	17	9 ;	7 6	9•0	0.9	7.9	t dr (9 4	11.9
2000		151	10	†	9 6	4	5.7	7.5	- ·	1	11.9
000		125	54	99	007		4.0	7.5	ec i	7.7	12.1
E 100 C		125	21	34	9		T.	7.7	26	10	9,6
300		118	25	56	† (•		7.4	5.7	ก	
1000		142	25	23	4	•		7.0	16	* 0	
MAD 000		137	54	23	4 6	•		6.8	73	9	4.
3000	3 6	144	11	23	£ (•		7.3	100	0 0	
3000	01044010	138	5	52	193	9	, (f	7.0	116	201	100
300 000	2 0	147	18	27	Մ.	•	4	8.0	101		7 - 1
300 PPM			20	31	40	- 11 - 0	9 4	6.7	110	# T	7 - 7
300 PPN			61	52	40	0 4	9	9.1	140	ų.	11.8
30 phi			25	4 1	97	0.0		7.8	95	7	12.1
# 0E			11	32	£) 4			7.7	78	- 1	12.3
200			50	4 (60		6.3	8.0	٠ د د ا	7	11.1
300			18	10.0	10%	. UT	4	6.3	100	47	12.3
1 20			5	2	+ r		5.7	7.3	20 t	- 1-	11.3
200	P1R4732		50	ę c	S 4	7.0	5.0	9.9	ñ	4	11.9
200	P184733		18	V ;	9 9	, ,	5,3	7.4	* :	i d	12.0
200			18	72	÷ 4		4.6	7.0	<u>ن</u>	40.	11.6
101			21	28	CC.	9	4.4	7.1	7	100	8
200			61	27	4		9	1.9	50	202	
30.00			14	23	2	1	7.4	7.9	18	-01	
30 00			2	58	102	01		1.1	19	0.80	110
30 06			21	38	4	0.	, d	7.65	99	2	2 • 1 1
30 PPM			0	19	140	• 0	0				
30 PPH	P1R4750	?									

TABLE 15

TWO YEAR ORAL (DIET) TOXICITY-ONCUGENICITY STUDY UF FLUOROCARBON FC-143 IN FEMALE MATS INDIVIDUAL SERUM CHEMISTRY VALUES

----- WONIH=12 -----

∀	11.7	12.5	11.5	10.6	 	11	10.€	11.1	10.	10.5	10.5	10.5	10.6	12.4	11.1	1:1	11.7	11.5	11.4	11.2	10.7	10.9	11.5	10.7	5.01	10.5	1:1	11.2	11.8	1.0	12.1	11.3	6.0	10.5	20.	1:1	10.4	11.0	11.2	10.9	10.8	11.5	11.1	11.2	11.2
CPA	29	85	42	56	20	38	4 1	9	104	52	4 0	37	58	92	47	31	42	36	4 1	0 4	51	37	19	58	4 0	4 1	16	4 4	38	38	52	38	271	32	42	248	4 2	56	48	39	59	94	1	145	44
ALKPHOS	n	134	₩	4	104	4	127	36	72	7.	80	54	6 6	6.4	42	39	115	137	46	66	;	101	99	155	132	124	96	36	142	1 +	121	4 5	96	102	131	122	102	108	45	76	87	22	53	84	104
TPROT	7•3	9•6	7.6	7.0	7.7	7.3	7•3	7.2	7.1	7.0	6.7	9•9	7.4	8.2	7.2	7.7	7.8	7.5	7.4	7.0	9•9	7.0	7.1	6.7	7.0	9•9	6•9	7.2	7.8	6•3	8.1	8.3	7.2	6.9	7.7	7.9	6.9	7.7	7.4	7.3	6.9	H.2	7.5	7.5	7.6
AL8	4.1	4.7	4 .0	4.4	4.6	4.5	4.1	4.2	4.1	4.1	3.9	3.8	4.4	4.3	4.4	ų. 1	4.6	4.6	4.6	4•3	3.7	4. 3	4.3	0.4	ۥ	3.5	4.2	4.2	\$.4	4.1	4.7	4.7	4.1	4.0	4.7	4.7	1.4	4.1	4.4	6. 3	0.4	4.5	4.6	4.4	4.4
TBILI	1.2	1.5	P • 0	0 • S	7.0	0.0	9•0	1.1	1.0	9•0	† • C	¢.	6.5	j.	5.0	0.5	9•0	1.0	9.0	9.0	†• 0	9.0	0 . I	†• 0	5°C	0 43	4. 0	9.0	5. 0	9 • 0	1.2	9•6	P•0	9•0	0 • A	1.0	4 • C	0.5	1.0	7.0	Ð.0	1.0	J.	Đ • O	T.0
AST	48	42	9	47	183	46	57	51	62	51	119	19	76	33	14	51	163	51	56	54	57	84	59	62	65	55	55	20	53	103	29	57	69	ኒ ረ	51	72	4	4	58	5.4	55	194	83	47	43
ALT	27	22	33	23	19	24	40	24	25	31	67	42	4 3	<u>.</u>	5 6	92	112	28	32	58	56	E C3	33 E)	0 4	4 1	26	35	32	34	51	38	53	4	36	31	36	92	33	37	36	30	56	45	36	18
BUN	24	18	24	20	6 .	19	20	18	21	19	18	25	20	18	17	16	20	54	22	25	15	23	18	22	17	37	22	18	19	18	17	17	19	6	22	19	19	19	18	19	52	21	27	¥.	19
GF.U	146	124	132	137	132	136	143	131	127	146	136	157	128	113	135	137	128	132	136	127	125	129	139	125	134	132	148	146	149	143	141	121	142	128	134	124	159	149	131	135	135	125	146	130	131
ANIMAL	N1R4578	N1R4582	N1R4585	N184588	N184589	N1R4590	N184601	N184608	N184610	N184620	N1R4629	N1R4630	N1R4631	N1R4632	N1R4640	0184642	01R4652	0184655	0184656	0184664	0184566	0184669	01R4671	0184674	0184676	0184687	0184689	0184692	0184699	0184704	P184711	P184714	P1R4715	P184716	P184717	P184721	P1R4725	P184727	P184729	P1R4734	P1R4742	P1R4743	P1R4749	P1R4750	P1R4755
DOSE	PPM	PPM	PPH	₽ M	₽₽	P M	E E	T d d	7 0	P P	1 0 0	P P	E E	¥dd															M d	_	_	_		_								_	_	Z d d	_
_	0	0	0	0	0	0	0	•	•	0	0	0	0	•	0	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	30	30	ŝ	30	30	30	30	30	30	30	30	30	30	30	30

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENIOITY STUDY OF FLUGHOCARHON FC-143 IN FEMALE MATS INDIVIDUAL SEHUM CHEMISTRY VALUES

---- MONTH=18 ----

۲ ک	11.8	11.7	11.3	11.7	11.5	11.7	11.3	12.1	11.0	11.6	11.3	11.2	10.0	12.2	11.0	11.0	0.0	10.6	11.3	11.3	10.9	10.9	11.3	11.2	11.5	11.4	11.6	11.0	11.5	11.3	15.1	8.8	11:1		70.5	11.5	11.0	9.0	10.5	8.6	11.1	11,3	11.6	9.3	11.6
CP.	33	36	27	42	37	35	47	37	27	27	33	36	99	4	35	31	Š	18	37	56	E.	4	92	32	92	53	38	Q	64	42	30	9	5	80	7	37	52	11	16	25	18	17	68	35	15
ALKPHOS	88	51	152	16	63	04	53	52	62	88	56	17	9	27	19	36	68	59	105	1.	149	18	65	63	06	4	16	65	30	68	53	53	23	30	64	31	4	42	0 \$	7	57	21	13	4	55
TPROT	4.9	4.60	7.8	4.8	9.6	7.8	7.7	8.2	7.4	7.8	9.6	7.5	7.9	7.8	8.3	7.2	8°9	9.9	7.4	8.2	7.6	8.2	8.1	8.1	7.9	7.9	7.8	9•0	7.7	7.9	7.7	8.7	4.6	6.8	.	6.7	7.6	8.8	8.0	9.6	8.0	8.0	0.6	6.3	0.8
ALB	6.0	6.6	3.7	4.2	0.4	0.4	4.0	0.4	3.8	3•B	4.2	4•0	3.8	3.7	0.4	3.7	* ·1	3.4	0.4	6.4	3.4	3.6	3•B	0.4	0.4	4	4.2	0.4	3.8	3.9	3.9	3.6	3.5	3.0	3.6	3•3	3.6	3.8	3•B	4.2	3.6	3.6	4	9.6	0 •
THILE	0.3	D •0	О	0-0	7.0	0.5	0.5	B.0	0 • 2	0.7	1.0	0.0	1.2	9•0	7.0	0.5	1.2	0•3	0.5	0.7	€*0	R• O	9.0	0.0	n.	. O	0.5	9•0	e.0	S • 0	7.0	7.0	1.0	o •	9•0	0•3	0.3	Ð.0	9•0	1.0	0 • B	0	9.0	1.2	S • 0
AST	50	¢	66	53	132	62	106	58	4	79	65	64	64	65	69	65	64	61	48	57	112	Ξ	52	47	69	99	66	47	51	25	62	60	45	51	56	65	51	4.8	59	76	6.0	¥ 7	148	20	4.
ALT	37	4	, it	35	7.1	13.	69	64	38	58	₩	04	45	42	7	50	56	51	33	3	40	52	42	4	. 4 .0	4	44	4	37	4	18	51	36	45	28	54	21	25	39	9	48	24	4	; ;	37
8 0 0	22	17	6	23	18	11	10	21	14	18	15	19	18	16	18	21	19	21	20	13	19	24	16	5	8	<u> </u>	20	15	212	23	02	22	20	24	20	16	14	27	19	21	23	13	19	, 2	25
GLU	128	200	9	107	116	123	133	103	150	126	110	143	138	116	141	119	117	121	130	134	121	116	118	601	128	124	118	134	112	66	102	118	123	122	96	126	148	127	120	143	136	45	116	127	133
ANIMAL	NICAGRI	L SCHOOL N	SOUTH N	NIRAGO	N184595	N184598	N1R4599	N1R4602	N1R4604	N184606	N184609	N184611	N184612	N1R4627	N1R4638	01R4645	0184647	0184648	0184651	0184663	0184667	0184675	0184679	0184684	0184688	0184690	0184693	0184694	0184696	0184698	P1R4707	P1R4709	P1R4714	P1R4718	P1R4720	P1R4722	P1R4725	P1R4729	P1R4732	P1R4733	P184737	P104748	P184749	0184752	P1R4754
DOSE	200	200		100	A C	A d d	12 dd 0	Mdd 0	Hdd 0	MPP 0	Mdd 0	Tada o	Wdd 0	Mdd 0	Mdd 0							300 PPM				Mad Cor							30 PPM					30 PPH							30 PPM

TABLE 15

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

---- #SONTH=24 ----

DOSE	ANIHAL	GLU	BUN	ALT	AST	THIL!	ALB	TPROT	ALKPHOS	СРК	V
Mag	NIUAGRA	136	1.	9	Ċ,	0.1	(T)	8-1	6*	16	12.4
. a	NIDAGRA	121) (L	1 60	. m	4.6	7	140	4	11.2
. 0	1037017	1 .		1 0	or L		. r.	7-B	127	109	12.
200	NIDAGOG	. c	11	1 4			9	. c	į	57	12.0
M C	8054GIN	1 0) E	55	4.0	4.6	2.7	38	*	11.5
¥0.0	N184603	138	56	9 E	56	4.0	3.4	7.2	35	59	11.0
Ndd 0	N1R4606	120	17	36	52	0.7	3.3	7.9	18	119	11.4
Ndd 0	N1R4611	148	21	45	81	0.5	3.2	6.5	10	20	11.3
NGG 0	N1R4614	115	17	37	42	9.0	3.7	7.6	76	36	11.3
Mdd 0	N1R4616	118	16	42	73	4.0	3.3	7.5	9*	80	11.0
NGG 0	N1R4626	112	10	27	52	2.0	3.7	8.6	36	25	1:1
M PPK	N184628	107	15	ဗိ	4	4.0	3.8	7.5	96	75	11.0
NG O	N184634	6	56	54	86	o • 2	ر د د د	6.1	87	<u>г</u>	50.
E C	N1R4636	130	15	53	4	9.0	9. 6	7.5	9	90	11.6
	N1R4638	111	17	52	99	. .	3.5	J.	94	141	2.6
	0184644	154	6.	30	4 J	* · C	3.4	7.0	11	4	
	0184646	113	15	4.	15	0.5	3 • 5	7.0	63	18	7.5
	01R4649	100	1.7	9 7	50	0.2	2•8	6.5	47	96	10.3
	01R4657	117	15	33	52	4.0	3.4	7.2	51	59	6.01
	0184659	108	13	32	5.8	0.3	3.0	6.7	60	110	10.8
	0184661	148	56	37	54	0.4	3.4	7.2	91	62	10.9
	0184663	121	12	36	7	8°0	3.H	7.5	73	98	11.5
	0184672	100		58	55	†• 0	3.5	7.2	29	38	11.5
	0184679	114	6.	37	26	9.0	3.2	7.8	4 6	117	11.9
	0184683	105	14	46	100	9.0	3.2	8.8	27	111	1:1
	0184688	109	13	131	183	5.0	3.4	7.4	40	25	10.9
	0184693	129	16	36	61	0.7	3.7	7.9	75	7.	11.7
300 PPM	0184695	8	18	33	53	0.3	Э•н	6.9	30	42	12.0
	0184697	104	17	45	83	0.3	3.6	7.5	72	53	11.0
	01R4701	127	15	53	5 5	0.5	3.6	7.0	*	4 5	11.6
	P1R4708	108	17	33	. 05	0.5	3•3	6. 4	56	35	11.2
	P1R4711	106	- -	37	26	1• 0	3.4	7.8	76	83	11.3
	P1R4714	114	15	27	41	4.0	3.5	7.7	93	37	11.5
30 PPM	P1R4716	117	17	34	63	0.2	3°3	6. 8	70	37	10.
	P1R4720	115	4	40	53	9. 0	3.2	8. 1	65	7.0	1:1
	P1R4723	141	17	36	80	0.3	3•3	7.2	35	45	11.3
	P1R4726	103	16	58	86	0.6	3.3	7.5	72	58	11.4
	P]R4729	119	14	Эн	54	9.0	3.2	6.9	63	63	11.5
	P1R4733	127	15	61	7.8	0.6	3.8	4.9	57	101	11.7
	P1R4736	137	12	38	. 62	4.0	3.6	7.4	56	75	11.4
	P1R4739	101	15	32	7.1	0.2	2.2	5.5	104	54	11.5
30 PPM	P1R4745	121	10	30	. 55	0.3	3.1	9.9	40	66	10.4
	P1R4747	116	13	31	29	0.3	3.0	2•9	36	171	10.7
	P1R4752	110	15	36	5#	0.6	3.7	θ.0	99	64	12.0
	P1R4754	156	2.4	4	5	4.0	3.6	7.3	64	46	11.6

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	Hď	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
3 Mo. Male Control	1.025-1.062	7-9	Y T-N	N N	Z 1 2	N A+	2
300 PPM	1.030-1.046	7-9	N-1+	N-N	N N	Z Z	N N
30 PPM		7-8	N-Tr	NIN	N-N	N-3+	N-N
3 Mo. Female Control	1.011-1.052	7-8	N-1+	N.N	Z	N-N	N N
300 PPM	1.015-1.052	7=9	N-N	N-N	N-N	NIN	N-N
30 PPM	1.016-1.056	7-8	N-N	N-N	Z I Z	N-N	NIN
6 Mo. Male							
Control	1.021-1.066	6-8	N-3+	N-N	N-N	N-3+	N-N
300 PPM	1.022-1.054	78	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+	NIN
6 Mo. Female		į		;			
Control	1.028-1.072	6-7	N-3+	Z Z	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	ıtive	1+ - slight	u	3+	- moderate marked	ked	
Tr - trace	ce	2+ - sligh	slight to moderate		- 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	НД	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
12 Mo. Male Control	1.040-1.093	7.0-8.5	N-4+	N.	Z I Z	+ ₩ +	H-N
300 PPM	1.015-1.054	7.0-8.5	N-3+	NIN	NIN	N-Tr	N-T-N
30 PPM	1.029-1.063	7.5-8.5	N-4+	N-N	N.I.N	N-3+	N-N
12 Mo. Female 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
18 Mo. Male							
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	NIN	N-N	N-N
30 PPM	1.022-1.066	6.5-8.0	N-4+	N-N	N-N	N-3+	N-N
18 Mo. Female							
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 Tr - trace	1+ - slight 2+ - slight	to moderate	3+ -	moderate to m marked	to 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	Hď	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
24 Mo. Male Control	1.018-1.054	6.5-8.5	N-4+	N-N	N-N	N-4+	N-N
300 PPM 30 PPM	1.023-1.043 1.018-1.056	6.5-8.5 6.0-8.0	N-4+ N-4+	N-N N-N	N N N	N-N N-4+	N-N N-N
24 Mo. Female Control	1.012-1.034	7.0-8.5	N-2+	N-N	N N N	N-N	N I N
300 PPM	1.009-1.037	5.0-8.0	N-2+	N-N	N-N	N-N	N-N
30 РРМ	1.014-1.030	7.0-8.0	N-1+	N-N	N-N	N-4+	N-N
Code:	N - negative Tr - trace	1+ - slight 2+ - slight	slight slight to moderate	3+	moderate to markedmarked	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)

			300 111	!
MALE	N = 15	ļ.	N = 15	
ORGAN	WI	SD	WT	SO
	25.5+-6	905	80.8+-5	- 4
EART	.629+- 0	15	452+-	.05
KIDNEYS	000	20.5	4.047+-0	4.5
EST	.553+	4	459+-	32
14 11 12 13 14 15 15 15 15 15 15 15 15 15 15 15 15 15	0205+-	-8	.064+- 0115+-	88
FEMALE	N = 15		Z = 15	
ORGAN	TW	SO	T.W	SO
	01.1+-7	1 ~ 0	03.1+-6	7.02.
ART	117+-	300	- 4980	225
IONE	.533+-	38	. 599+-	. 28
DRE TER	0761+-	-4	0796+-	. 22
RAINITO	963	128 006	970	0.119

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 (%)

	O PPM	300 PPM
ALE	15	"
ō		34
LIVER HEARE SPLEEN KIDNEYS ADRENALS TESTES BRAIN PITUITARY	3.053+-0.318 0.262+-0.021 0.144+-0.025 0.617+-0.057 0.011+-0.002 0.570+-0.057 0.340+-0.057	

FENALE	S = X	S = X
ORG/	8	SD ×
LIVER	.090+-0.29	.239+-0.4
HEART	0-	274+
PLE	168+-0.03	.158+-0.048
NO	.642 + -0.09	.649+-0.1
~	020+-0.00	020+-0.0
TER	.2014-0.07	. 181+-0.0
7	.507+-0.10	.499+-0.0
110	.006+-0.00	0.0-+500

P <= .05, TWO TAILED DUNNETT I ON RAW DATA. P <= .05, TWO TAILED DUNNETT I ON RANKED DATA. 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

(GRAMS)
WEIGHT
BRAIN
WE I GHT
ORGAN

	Mdd 0	300 PPM
MALE	N = 15	N = 15
ORGAN	T10	
LIVER	.049+-1.3	339+-1.1
SPLEEN	424+-0.0	389+-0.0
KIDNEYS ADRENALS	1.821+-0.192 0.032+-0.006	1.964+-0.227 0.027+-0.004*
TESTES	678+-0.1	.675+-0.1
FILILIAR	0.0140.0.	
FEMALE	N 15	N = 15
ORGAN	T10	RATIO SD
LIVER	273+-	50+-0.82 52+-0.06
SPLEEN	337+-0.0	312+-0.06
ADRENALS	.039+-0.0	.041+-0.01
١.	.397+-0.1	.356+-0.11
PITUITARY	.012+-0.0	. 010+-0.00

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

TWO YEAR ORAL (DIET) TOXICITY-ONCOGENICITY STUDY OF FLUOROCAKHON FC-143 IN MALF HATS ONE YEAR INTERIM INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	RODY	LIVER	HEART	SPLEFN	KIDNEYS	APHENALS-	TESTES	HHAIN	PITUTAKY ^a
100	A18-3516	720	23.AB	1.786	1.079	3.970	*	3.727	2.330	7
Idd	A1R-3517	651	21.74	1.565	0.674	4.043	46	4.147	2.111	<u>.</u>
H d d	A1R-3520	655	20.R7	1.719	0.172	4.352	42	3,467	2.204	5.
	A1R-3522	627	16.18	1.675	9.776	4.24]	19	3.744	2.227	5-0
Ndd 0	A1R-3527	634	16.71	1.517	0.65A	3,356	5.7	3.316	2.0HB	33
T dd	A1R-3535	594	18.12	1.654	0.895	3.474	18	3.238	1.453	77
T C C	A1R-3543	747	24.96	1.783	*06*0	4.365	54	3,704	.2.194	4
A O	A1R-3546	656	17.61	2.018	906*0	3.958	7.7	3.460	2.079	5 4
Wood C	A1R-3550	566	15.19	1.476	0.704	3.656		3.411	2.150	<u>.</u>
E G	A1R-3551	*5*	13.96	1,361	0.751	2.657	59	2.581	1.920	ž.
E C	A1R-3559	627	19.53	1.536	0.672	3.548	7.8	3.331	2.074	23
E G	A1R-3568	688	22.31	1,629	1.001	4.574	40	3.870	2.207	Ξ
400	A1R-3570	575	16.55	1.526	0.491	3.525	\$	3,503	2.114	ሂ
NGG O	A1R-3575	551	19.88	1.636	1.113	3.7H]	41	5.944	1.471	ī
E d d	A1R-3580	598	19.77	1.556	1.028	4.170	76	3.805	2.071	
	81R-3584	547	18.56	1.487	0.603	3.845	6.9	3.226	1.081	£
300 PPM	B1R-358R	564	25.31	1.516	0.593	4.5A4	63	3.945	2.147	<u>.</u>
300 PPM	R18-3589	555	24.34	1.506	10.794	3.852	55	3.700	2.076	=
	B1R-3592	657	18.67	1.402	0.820	3.694	65	3.R39	2.165	50
	B1R-3598	565	22.98	1.448	0.742	4.396	61	3.264	2.014	=
	R18-3604	554	21.43	1.503	0.854	4.87£	62	3.224	1.547	- -
	B1R-3613	999	18.07	1.368	0.963	3,593	70	3,376	2.046	7
300 PPM	B1R-3617	552	20.50	1.445	0.475	3.915	Z ¢	3.604	2.033	<u>-</u>
	B1R-3620	641	22.41	1.444	0.850	4.096	56	3.484	2.109	-
	B1R-3622	487	17.88	1.357	0.780	3.442	6 1	2.700	555°I	÷
300 PPM	B1R-3626	603	25.32	1.395	0.813	245.4	47	3.205	2.066	12
	B1R-3627	545	20.94	1.481	0.715	3.7A3	47	3,381	2.124	=
300 PPM	B1R-3638	559	20.30	1.412	0.746	3,793	4.7	3.822	2.124	ع
300 PPM	B1R-3642	543	20.35	1.439	0.887	3.886	54	3.649	2.101	<u>*</u>
300 PPM	å	209	22.38	1.449	0.958	4.446	4 3	3.41A	1.434	

NOTES: Body weights and organ weights in grams. a indicates organ weights in mg.

TABLE 17

TWO YEAR OHAL (DIET) FUXICITY-ONCOGENICITY STUDY OF FLUCHOCARHON FC-143 IN FEMALE HATS ONE YEAR INTERIM INDIVIDIAL ORGAN WEIGHTS

DOSE	ANTHAL	AODY	LIVER	HEART	SPLEFN	R INNEYS	ADMENALS A	UTERUS	HHAIN	PITUTARY
Nad 0	N1R-4578	540	15.34	1.390	0.751	3.279	90	0.696	2.044	~~
D D I	N1R-4582	385	12.26	1.185	0.418	2.405	H.	0.470	1.674	. ~
D PDM	N1R-4585	353	12.90	1.035	0.626	2.223	35	0.674	1.912	· •
100	N1R-4588	386	11.99	1.117	0.679	2.535	19	43.4	2.073	<u> </u>
	N1R-4589	375	13.19	1.095	0.651	3.106	78	1.032	1.05	ં ર્
0 PP4	N1R-4590	373	10.52	1.037	0.571	P. 308	7.8	0.433	1.875	1.1
D D	N18-4601	470	13,39	1.164	0.868	3.115	24	0.407	1.928	. K
7 0 0	N1R-4608	459	13.00	1.021	0.64A	2.356	9.5	0.963	2.124	<u> </u>
0	N B-4610	345	11.31	0.9HZ	0.68]	2.435	87	1.371	1.000	0.5
NG O	N1R-4620	320	11.45	1.176	0.789	2.470	89	0. A46	2.1.35	<u>*</u>
Hdd O	NIR-4629	401	11,33	1.084	0.663	2.176	65	0.523	1.967	2
Ndd O	N1R-4630	466	13,63	1.240	0.725	2.616	90	0.570	2.154	
T C C	NIR-4631	248	7.37	0.830	414.0	1.844	5.2	0.520	E E H	. =
T Q Q	N18-4632	531	14.70	1.128	0.723	2.520	59	0.400	- F45	
	NIR-4640	395	11.69	1.234	0.731	2.512	92	0.833	W 7 4 .	: {
	01R-4642	323	10.85	0.920	0.732	2.479	*	1.150	1.445	, 2
	01R-4652	383	13.12	> = - C	0.40	2.072	*	0.756	2.265	χ.
	018-4655	372	12.16	1.045	0.603	2.577	7.1	0.543	1.740	· •
	078-4656	447	13.49	1.160	0.405	3.020	7.	2. H.H.	2.011	.
	018-4664	366	14.26	1.156	0.685	2.384	75	1.557	1.048	
	018-4666	339	12.28	1.066	0.61A	2.7AA	104	6.44.0	7.064	ć.
	018-4669	385	12.10	0.952	0.4.70	2,396	ō.	0.756	1.856	· •
300 PPM	018-4671	101	17.67	1.161	0.663	2.H52	* :	0.435	2.000	_
	018-4674	355	13.59	0.927	1.594	2.240	₹9	0.448	5.009	χ.
	01R-4676	519	14.36	1.206	0.630	2.8AR	Ę,	0.704	7.048	30
	01R-4587	329	12.56	1.108	0.437	o I	£.	0.924	2.0.7	-
	01R-45RG	363	11.72	1.312	0.799	2.647	115	0.558	1.437	. 7
	01R-4692	531	13.54	1.210	0.468	2.4RR	40	0.355	1.941	22
MCIG DO	01R-4699	395	11.59	0.942	0.561	2.384	7.0	0.70H	1.430	. 5
	, , ,									

NOTES: Body weights and organ weights in grams.

 $rac{a}{b}$ Indicates organ weights in mg. - Kidney weights not recorded due to marked hydronephrosis.

TABLE 18

TWO YEAR ORAL (DIET) TOXICITY+ONCOGENICITY STUDY OF FEUOROCARHON FC-143 IN RATS Absolute and Relative Mean Drgan Weights

ABSOLUTE ORGAN WEIGHT (GRAMS)

	wdd 0		
MALE	N = 15	Z = 15	N 15.
ORGAN	OS LA)	WT SD
RODY	966	632,6+-91.947	648.2+110K.9K
LIVER	18.15+- 3.074	· ·	A. 81+-
HEART	.720+-	1.665+- 0.295	ļ
SPLEEN	1		1+105+1 0.206
KIDNEYS	4.404+- 0.5746	0	5-185+- 1.782
ADRENALS	.0801+- 04018	.0866+- 0.018	7/0-0 -+0060-
EST	3-478+- 06702	0	
BRAIN	2.105+- 0.133	•	0 -
FEMALE	N # 15	Z = 15	N 15
ORGAN		WT \$0	MT SD
RODY	51744487,585	451794140-184	1 .
LIVER	15.11+- 3:752	14.05+- 2.7354	17.06+# 3.867
HEART		ŧ	
SPLEEN	0.797+- 0:140	e t	c
KIDNEYS		3+195+- 0+465	
ADRENALS	1	·1:126+- 0.039	0
DIEMUS	.814+- 0.29	0.849+- 0.391	0
2 4 4 1	2.034+- 0:102	2.049+- 0.111	2.030 0.131

: 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 STUBY OF FLUOROCARBON FC-143 IN RATS ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS

	0	300 PPM	о О
انط	N = 15	N = 15	N 15
ORGAN	1	;	QS %
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	0.666+-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
RRAIN	0.322+-0.049	0 4353+-0.054	0.347+-0.056
FEMALE	N 15	51 # Z	N = 15
i	8 6	OS *	88
LIVER	2.94]++0.465	3.125+=0.414A	3-196+-0-550
HEART	0.269+-0.036	0.296+-0.056	0.283+-0.046
SPLEEN	04158++0.033	0.187+-0.046	0.210+-0.078*
KIDNEYS	0.621++0.040	0.709+-0.120*	0.6620.102
ADRENALS	0.030+-0.008A	0.025+-0.010	0.026+-0.007
UTERUS	04161+-0+055	0.183+-0.076	0.163+-0.092
BRAIN	0.408+-0.077	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) FOXICTTY-ONCOGENICITY STUDY OF FLUOROCARBON FC-143 IN RATS ABSOLUTE AND RELATIVE MEAN ORGAN WEIGHTS

(GRAMS)
WEIGHY
GHT/BRAIN
AN WEIGHT
ORGAN

		•	
MALE			N = 15
ORGAN		RATIO SD	
LIVER	8.648+-1.587	8.756+-1.42#	8.544+-1.485
HEART	0.819++0.103	0.7600.119	0.821+-0.141
SPLEEN	0.578+-0.155	0.531+-0.149	0.501+-0.086
KIDNEYS	2.099+-0.377	2.101+-0.232	2.360+-0.827
ADRENALS	0.038++0.010	0.040+-0.00B	0.041+-0.013
TESTES	1.658+-0.336	1.699+-0.287	1.675+-0.297
FEMALE 14	N 15	N = 15	N = 15
ORGAN		RATIO	ATIO
LIVER	7.456+-1.918	6.883+-1.508A	8.460+-2.162
HEART	0.673++0.100	160-0-+249-0	0.7380.117
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 MAW DATA\$
: P <= .05, TWO TAILED DUNNETT T ON MANKED DATA.
A : N = 14 ANIMALS.

TWO YEAR OHAL (DIET) TOAICITY-ONCOGENICITY STUDY OF FLUORUCARBON FC-143 IN MALE RATS TWO YEAR INDIVIDUAL ONGAN WEIGHTS

									•
00SE	ANIMAL	400B	LIVER	MEANT	SPLEEN	K JONEYS	ADRENAL Sa	TESTES	HHAIN
PPR	A1R3518	556	15.12	1.623	1.318	3,413	9	4.523	2.15H
DPR	A1R3524	638	23.45	1.511	1.415	4.H45	27	↑15°E	2.046
Hdd 0	A1R3528	812	19.61	1.744	1.111	4.424	18	4.082	2.076
Mdd o	A1R3531	733	17.52	1.871	0.H70	3.842	2	3.574	2.121
0 PE	A1R3533	765	18.07	1.575	166.0	4.128	001	2.440	2.050
2 1	AIRBOAR	123	7.40	162.2	1.724	+ 	† 4 * ur	1 C	2.200
	MARKATA	706	18.4	1.667	1.148	4.670	73	3.52b	2.329
	A183554	511	14.19	1.547	1.135	3.461	HH.	3.628	1.990
0 C	A1R3557	612	17.71	1.786	1.106	4.718	7.0	4.123	2.45
Hed O	A1R3562	588	15.14	1.616	1.754	3.988	F.	3.475	2.063
0 PPR	A1R3564	576	16.20	1.674	1.396	3.745	643	3.328	2-223
O PPM	A183569	969	21.44	2.172	1.586	6.410	100	3.203	2.046
Mdd 0	A1H3573	159	22.41	1.025	0.407	5.011	113	3.561	1.861
	A1R3578	521	13.52	1.538	004.0	3.641	7.7	3.015	1.450
300 PPM	B1R3581	734	18.42	1.786	1.227	4.472	26	4.177	2-240
	A1R3585	929	21.42	1.465	1.447	4.64]	42	3.44 E	2.074
	R1R3591	044	14.04	1.427	0.662	3.831	59	2.631	2.091
_	B183594	174	23.83	1.486	1.237	5.013	92	3.967	2.210
	H1R3597	634	14.49	1.582	266.0	4. 032	47	4.050	2.134
	8183601	643	21.09	2.530	1.023	5.6H0	Ť	3.443	2.272
_	B1 83605	626	20.04	1.523	966.0	4.160	25	2.867	2.141
300 PPM	B1R3608	909	14.66	1.385	1.640	4.187	*	3.254	2.045
	81R3611	641	18.43	1.642	1.320	4.271	107	3.777	2.282
	A183618	100	18.91	1.574	0.740	4.342	7.7	3.849	2.123
_	B1R3623	622	20.26	1.803	1.217	750•۲	5	3,443	2.212
	B1R3630	507	15.62	1.443	0.H24	4.081	7.8	3.886	2.210
	B1R3633	632	24.81	1.666	1.A00	5.125	135	3.436	2.130
	R1R3636	564	16.44	1.585	1.067	4.222	£.8	2.114	2.247
	B1R3641	609	19.45	2.032	1.129	5.133	67	4	2.231
30 PPH	C183646	6.80	14.71	1.404	1.042	3.74R	99	3.149	2.218
	C1R3650	586	18.17	1.805	1.417	4.347	*	4.043	2.473
	C1H3654	704	21.84	2.020	1.108	5,309	83	5.371	2,317
	C163658	62A	16.67	1.293	0.837	4.197	÷	4.001	2.16#
	C1R3663	713	25.66	2.172	1.178	5.023	T	3.74x	2.220
	C1R3667	583	17.03	1.472	277.0	4.162	£	3.305	2.111
	C1R3670	653	E0.61	2.010	1.417	7.178	124	3.205	2.246
	C1H3672	616	16.77	1.025	1.082	4.400	7.3	2442	2.060
	C183676	539	54.00	2.326	1.414	10.404	143	3.209	2.150
_	C1H3679	921	23.86	2.120	0.962	7.664	9	4.544	2. 304
_	C183682	545	16.02	1.464	506.0	4.147	49	3.040	1.43H
30 PPM	C1R3684	772	16.98	2.022	1.151	034.4	7	4 • 104	7.145
30 PPM	C1R3689	164	13.94	1.416	0.773	4.170	62	H 40 P	2.312
	C1R3691	565	16.89	1.707	1.277	3. 448	=	3.832	エサン・へ
	C1R3694	269	16.58	1.631	1.033	4.626	142	4.179	050.5

Body weights and lorgan weights in grams. A Indicates adrenal weight in mg. NOTES:

J ¥0	TWO YEAR	DHAL	(01ET)	TOXICIT	Y-ONCOGENICITY
TUDY	OF.	FLUOR	UCARBON	FC-1+3	TUDY OF FLUORUCARBON PC-1+3 IN FEMALE HATS
	3	YEAR	INDIVIOL	JAL ONGA	TWO YEAR INDIVIDUAL ORGAN WEIGHTS

DOSE	ANIMAL	HODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS a	UTEAUS	HHAIR
	N 1845.83	464	15.99	1.174	1.032	3.308	H6	0.843	2.035
	N1R4586	460	11.86	1.215	0.483	2.824	43	1.065	2.069
	N1R4591	516	14.21	1.322	446.0	3.161	A.4	0.884	1.450
	N184595	455	11.98	1.415	0.740	2.708	104	0.729	2.049
	N1R4598	471	13.45	1.538	686.0	3.456		1.155	#\\rangle - 1
	N184603	184	14.31		160.0	3.218	* ,		*
E C	N1R4606	265	7. 4. 4. C	100.1	197	4.0	4 1 4	1,04	- A
	TOTALN	0 1	00.47	10001	727.0	3.366		0.5.0	0.00
	PTCPKIN	387	11.77	1.254	0.717	0.00	155	000	041.0
	N1R4626	353	10-28	040.0	0.581	494.2	7.8	0.354	2.032
	N1R4628	535	13.34	1.182	956.0	3.042	61	0.812	1.471
	N184634	567	19.23	1.523	C99-0	2.878	108	0.738	1.419
	N1R4630	260	19.57	1.180	0.933	3.261	85	0.746	1.874
	N184638	675	16.28	1.612	964.0	3,340	75	0.636	2.218
	0184644	468	14.35	1.208	609.0	2.832	76	0.466	1.55
	0184646	539	17.04	1.25H	0.946	3.688	¥6	0.767	2.236
	0184649	378	11.32	1.056	0.445	S-806	38	0.588	2010
	0184657	4 1 8	14.58	1.179	0.677	2.844	131	965.0	2.043
	0184659	519	15.84	1.308	1.134	3.293	102	1.465	2.016
	0184661	459	12.22	1.153	0.630	2.348	54	4540	2.045
	0184663	480	14.01	1.452	= £84	3.275	138	1.076	5.024
	0184672	380	10.92	1.403	446°C	Z•430	100	0.00	1.434
	0184679	55.	21.39	1.521	0.717	4.125	128	5.75	/ O # • [
	0184683	376	13.96	1.57	144.0	3.440	183	. t	
	0184588	375	13,32	1.334	40.4	3. H3	137	1.043	2.264
	0184693	4 H O		1.187	0.55	245.2	124	\$2 6. 0	A . C . C
	0184695	544	• !	1.610	174.0	3.737	175	1.532	2.031
	01R4697	354	11.60	1.122	0.724	× 93/	87	0.403	1.433
	0184701	542	13.98	1.288	0.549	3.194	112	625.0	# c c
	P184708	526	17.63	ط/s.1	0.457	3 - CE (C)	173	£ + £ • 0	
	P1R4711	559	22.66	1.456	1.016	3.0HS	123	714.0	1.927
		2.40 2.40	23.62	1.643	1.027	# C T . M	205	0.612	1.456
		404	70.01	1.544	797°C	2.7.5		100	37 X
	P184720	93.9		1 4 7	0.50	8 L . S	150	010.0	010-2
		U 4	10.40	1.432	1 057	0 1	C	1 0 4 5	2117
	02/4410		70.01	600.	7 4 5			100	
100	6574817	10 10 10 10 10 10 10 10 10 10 10 10 10 1	12.22	1.217	0.707	7	707	1.8.0	5.103
	• -	593	13.87	1.349	026.0	3.216	7.3	0+5.0	2.001
_	P184739	756	22+13	1.708	3,561		210	0.522	2.0Hh
	1847	428	14.03	1.464	0.824	3.670	111	0.774	2.047
	1R474	545	16.57	1.274	866.0	=	155	0.846	2,341
Œ.	P184752	575	15.09	1.538	U. H54	4.012	101	0.854	2.106
30 PPM	18475	487	14.88	1.210	1.157	2.B56	5 1	0.614	1.401
NOTES:	Body weigh	ts and	organ we	ights in	grams.				
	Indica	s adren	E						
	, t	2	: 3	; + ; c	ر د د	9 4 9 9 9 9 9		2	
	ייים ריים ריים ריים ריים ריים ריים ריים	, d	= 5 - 3 - -	- - - -	• nun -	ור מ <u>עי</u> ת	da c 1 y	י מ ה	
	- Indicate	SIIVEL	weight	not reco	rded 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

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

 $^{1 = 50 \}text{ rats/sex/group were at risk}$, % values derived from actual tissues examined

^{* =} Significantly different (= 0.05) from controls

TABLE 20

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

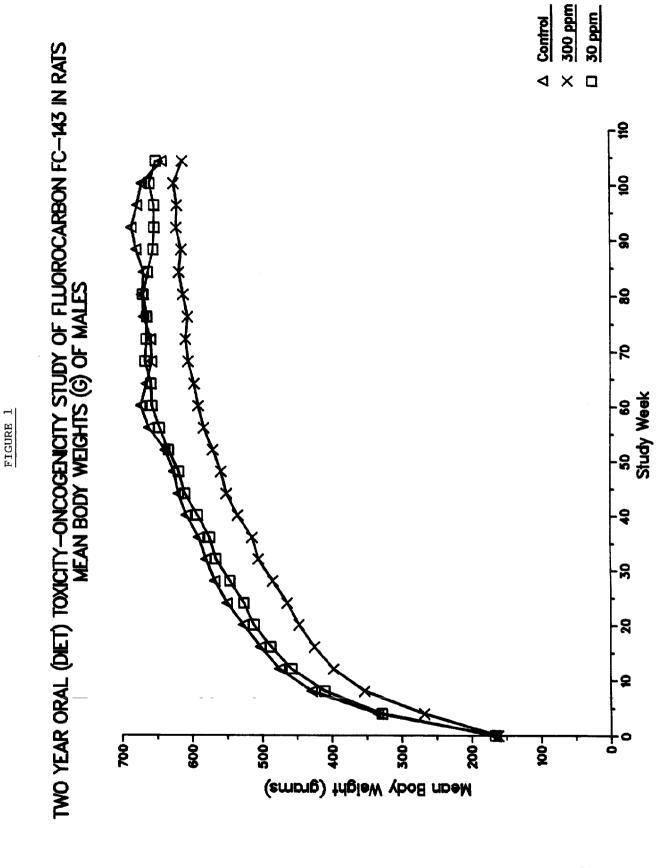
Summary of Major Microscopic Findings - Percent Incidence at 2 Years

NON-NEOPLASTIC LESIONS

		trols	Hig	<u>h</u>	Lo	W_
Organ/Lesion n = 1	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			~-	02	20	30
Myocarditis, Chronic	28	32	34	20	36	10*
Liver					33	10
Cystoid Degeneration	8	0	56*	2	14	2
Hepatocellular Alt. Basophi	1. 4	16	12	4	2	16
Hyperplastic Nodule	0	2	6	4	ō	0
Megalocytosis	0	0	80*	16*	12	2
Portal Mononuclear	74	38	96*	38	64	22
Cell Infil.				•	0 1	
Necrosis	6	10	10	4	10	12
Lung				•		12
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*

 $^{1 = 50 \}text{ rats/sex/group were at risk}$, % values derived from actual tissues examined

 $[\]star$ = Significantly different (= 0.05) from controls







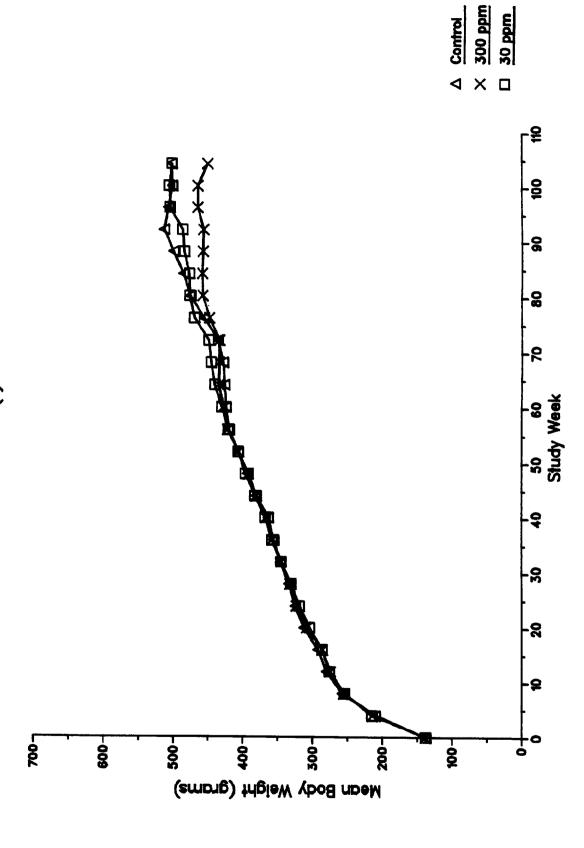
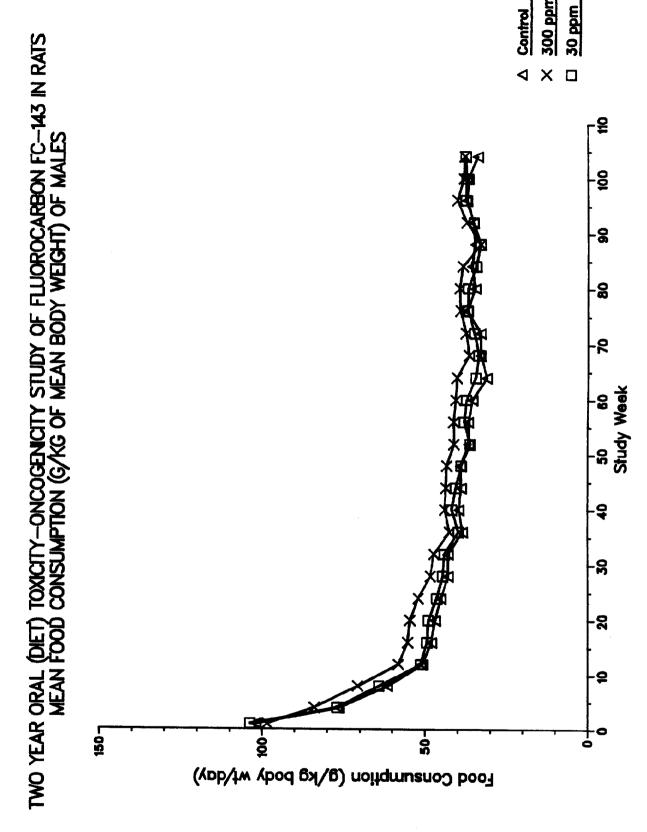
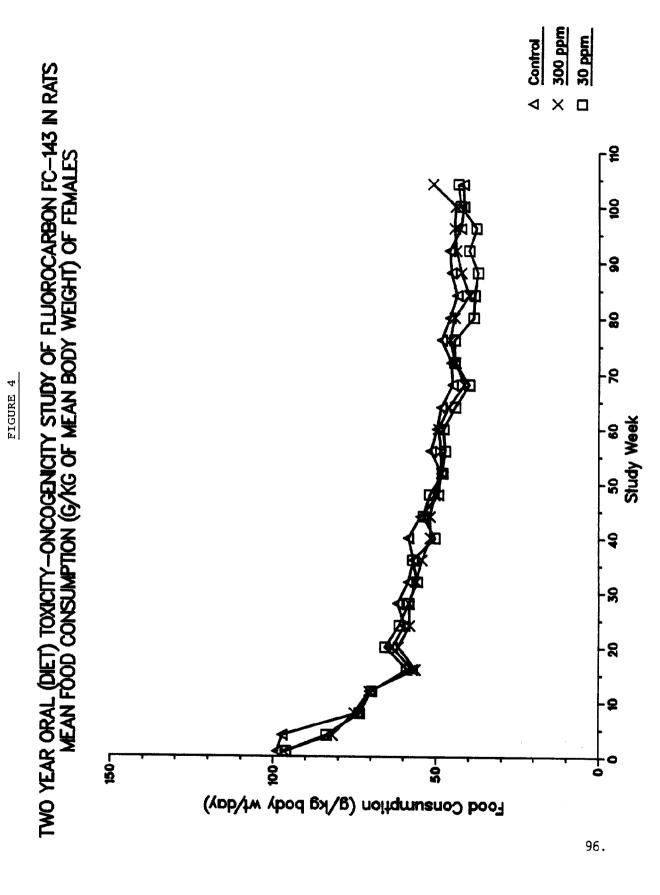


FIGURE 3





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

ro GM. 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



Summary

Air monitoring has been conducted in three animal treatment room 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 Analtyical Section of the 3M Central Research Laboratory. This laboratory has full accreditation as an Industrial Hygiene Laboratory by the American Industrial Hygiene Association.

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 of there are any questions.

. D Anen

SDS:cr

APPENDIX ITEM A

M. T. Case

-3-

August 27, 1981

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

Sample Number	Description	Time	Compound	Concentration, mg/m ³
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	۷0.001
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



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.

ament & shure

Appendix Item A

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



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

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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)

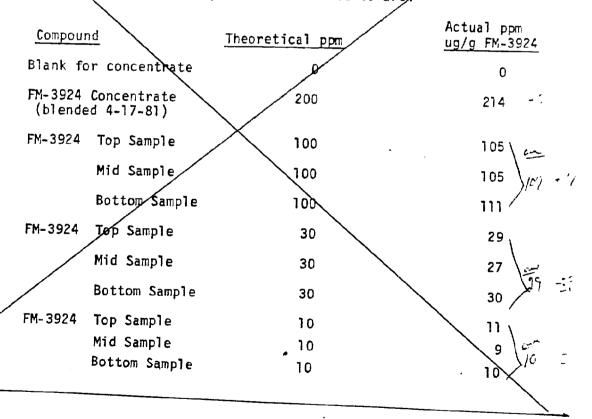
Date April 29, 1981

3

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



APPENDIX ITEM B

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

Compound	Theoretical ppm	Actual ppm (ug/g)FM-3924
Blank for 100 ppm level	0	0
Blank for 30 ppm level	0	0
Blank for 10 ppm level	0	0
The Tevel of ethanol in also checked and found	FM-3924 Concentrate (blende to be less than 1 ppm (ug/g)	d 4-17-78) was

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:

Theoretical ppm	Actual ppm (<u>ug/g)FC-143</u>
300	326
300	282
300	297
0	0
30	24
30	23
30	28/11
0	, 0
	300 300 300 0 30 30 30

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:

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

Compound	Theoretical ppm	Actual ppm (ug/g) FC-143
FC-143 Top Sample	30	31
Mid Sample	30	28
Bottom Sample	30	30 -1 ⁷
Blank for 30 ppm level LJS/mao cc: M. T. Case - 218-2	Colbert	0

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

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 1/229

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

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>	Theoretical ppm	Actual ppm <u>ug</u> /g FC-143
Blank for 300 ppm	. 0	0
FC-143 Top	300	, 303
Mid	300	-/ (1/ 305
Bottom	300	303 305 +6.3 295
Blank for 30 ppm	0	0
FC-143 Top	30	31
Mid	. 30	4/2. · C.: \(31\)
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

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



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

PJC/mao Paul D. Collert

dc: 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- 236-28

R. M. Payfer - 236-2B

G. W. Kirsch - 236-3A

COMMERCIAL CHEMICALS ANALYTICAL REPORT #289

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

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

GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND Subject: LAB CHOW (RIKER STUDY #2081ch0012)

Date:

November 30, 1981

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:

Sample	Theoretical PPM	Actual PPM ug/g FC-143	
Blank for 300	0	0	+1.3%
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

dc: M. T. Case - 21/8-2

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 - 236-28

L. D. Winter - 236-28 (2 copies)

Internal Correspondence

dc: M.T. Case - 218 2 G.W. Kirsch - 336-44 E.G. Lamprechi - 216-3 J.D. LaZerte - 236-1 W.C. McCormick - 220-2E-02

V. Pothapragada - 236-3A L.D. Winter - 236-23

> COMMERCIAL CHEMICALS ANALYTICAL REPORT #319

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

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

GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND

LAB CHOW (RIKER STUDY #2081 CR 0012)

Date: MARCH 5, 1982



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:

<u>Sample</u>	Theoretical PPM	Actual PPM ug/g FC-143
Blank for 300 PPM	0	O The state of the
300 PPM Top	300	165 - Survey June 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
300 PPM Middle	300	215 lund water was fine
300 PPM Bottom	300	215 June 15 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Blank for 30 PPM	0	ا ا
30 PPM Top	30	27
30 PPM Middle	30	33
30 PPM Bottom	30	24
Ruhard M. Payle		Remarks of

APPENDIX ITEM B

COMMERCIAL CHEMICALS ANALYTICAL REPORT #328

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

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

GLC RE-ANALYSIS OF FC-143 (T-2998 COC) BLENDED INTO Subject:

GROUND LAB CHOW (RIKER STUDY #2081 CROO12)

March 31, 1982

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

RMP/hc

Date:

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

APPENDIX ITEM B

COMMERCIAL CHEMICALS ANALTYICAL REPORT #340

L. J. SIBINSKI - 218-3-3

R. M. PAYFER - 236-2B From

Cather: GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND

LAB CHOW (RIKER STUDY #0281 CR0012)

May 28, 1982



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:

Sample	Theoretical PPM	Actual PPM ug/g FC-143
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

dc: M. T. Case - 218-2

RMP/nchand M. Payle

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

COMMERCIAL CHEMICALS ANALTYICAL REPORT #366

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

R. M. PAYFER - 236-28 From

GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND Subject:

LAB CHOW (RIKER STUDY #0281 CR0012) Sept. 13, 1982 Date:

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, 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 300 PPM Top 300 PPM Middle 300 PPM Bottom Blank for 30 PPM 30 PPM Top 30 PPM Middle 30 PPM Bottom	0 300 300 300 0 30 30 30	0 300 319 304 0 29.5 35 29.5

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

APPENDIX ITEM B

To: #1. L. Sibinski - 218-3

Commercial Chemicals
Analytical Report #384

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



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:

Samp!e	Theoretical ppm	Actual ppm µg/g FC-143
Blank for 300 ppm	0	0 s'
300 ppm Top	300	323 292 303
300 ppm Middle	300	292 کی کارک
300 ppm Bottom	300	303
Blank for 30 ppm	0	0
30 ppm Top	30	28 \ 11 28
30 ppm Middle	30	32 20,61 +20
30 ppm Bottom	30	28 32 - 10 10 00 + 200 32

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 - 236-28

V. Prothapragada - 236-GB

APPENDIX ITEM B

Commercial Chemicals Analytical Report #395

₩±. U. SIBINSKI = 218-3

From: G. W. KIRSCH - 236-2B

GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND Subject:

RODENT CHOW (RIKER STUDY #0281-CR0012)

MARCH 7, 1983 Date:

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:

Sample	Theoretical ppm	Actual ppm ug/g FC-143
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 3/Kinds

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

APPENDIX ITEM B

Commercial Chemicals Analytical Report #404

10 € 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

3N

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>	Theoretical ppm	Actual ppm ug/g FC-143
Blank for 300 ppm	0	0
300 ppm Top	300	326 (m) +9.4 (m)
300 ppm Middle	300	331 <i>33: / * * /</i>
300 ppm Bottom	300	328
Blank for 30 ppm	0	0
30 ppm Top	30	33 🤐
30 ppm Middle	30	34 5 5
30 ppm Bottom	30	33 //4 34 /23 / * / 32

GWK/hc G. Kirsch

dc: M. T. Case - 218-2 R. M J. D. LaZerte - 236-1 W. H W. C. McCormick - 220-2E L. D

R. M. Payfer - 236-2B W. H. Pearlson - 223-6SE 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/1
Aspartate Aminotransferase (AST)	20-60 International Units/1
Alkaline Phosphatase	50-200 International Units/1

50-150 International Units/l

Creatine Phosphokinase (CPK)

Appendix Item C

Methods Used for Hematology On Bleedings at 3 and 6 Months

Parameters	Units	Me thods
Hematology		
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,

%/100 WBC

Model MB

Microscope slide

International Equipment Co.

Differential

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

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 neutal 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
adrenals (2)
brain (3 sections including
    frontal cortex and basal
    ganglia, parietal cortex
    and thalamus; cerebellum
    and pons)
eyes
gonads
    ovaries (2)
    testes/epididymides (2)
heart
small intestine (3 sections)
large intestine
kidneys (2 sections)
```

```
liver (2 sections)
lung (2 sections)
lymph node (mesenteric)
mammary gland (females)
pancreas
pituitary
salivary gland
spinal cord/bone marrow (vertebrae)
spleen
stomach
thyroid/parathyroid/trachea/esophagus
urinary bladder
uterus or prostate
any tissue masses (suspected tumors)
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.

0281CR0012 (FC-143)

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

0231CR0012 (FC-143)

-2-

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 mimimal 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

0281CR0012 (FC-143)

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 occurence 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 occurence 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

0281CR0012 (FC-143)

-4-

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 $30\ \mathrm{ppm}$ group and decreased splenic hemosiderosis in females from the $300\ \mathrm{ppm}$ 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.

of Veterinary Pathologists

Diplomate, American College

9/27/f1-

0281CR0012 (FC-143)

TABLE OF CONTENTS

Table Num	ber	Page
1	Macroscopic Incidence for Males - 1 Year Interim	1 1 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	9-11
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		
Table Num	how	
Table Num		Page
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	210-241

0281CR0012 (FC-143)

Macroscopic Incidence for Males Rikar Laboratories, Inc. 3M

Table: 1

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

Project Mumber: 02010R0012 Species: Rat

Site/		
Description	Group 1	Group 5
No visible lesions	ي	S
Eye		
opacity		1
Pituitary		
Mass		1
Liver		
pala/tan color	2	3
Kesentery		
fat necrosis	1	
Kidhey		
nydranephrosis	1	
cystic lesion	1	
depressed area		1
Tastis		
small		1
Sidia		
nudule		1
Soft Tissue (leg)		
swollen foot	1	

Titles:

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

Macroscopic Incidence Page: 1

Macroscopic Incidence for Females Riker Laboratories, Inc. 3M

Table: 2

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
Mesentary		
Mass	1	
Kidney		
hydronephrosis	1	1
calculi		1
Ureter		
dilatation, calculi		1
Urinary Bladder		
distanded, 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 COO ppm * includes "possibly"

Macroscopic Incidence Page: 2

Macroscopic Incidence for Males Riker Laboratories, Inc. 3M

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

Project Number: 0231CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
No visible lesions	1.7	•	•
Brain	11	12	18
dark area	1		
Eye	7		
opacity/cloudy		1	4
hypopyon		1	'4
Pituitary		1	
mass/enlarged/raised lesion	7	3	11
dark/hemorrhagic/red foci	4	2	2
Thyroid	.4	۷	4
enlarged*	1	1	1
Adrenal	1	1	r
enlarged/mass	2	2	3
Throax (internal)	L	2	J
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 5 FC-143 30 ppm * includes "possibly"

Table: 3

Macroscopic Incidence Page: 3

Macroscopic Incidence for Males Riker Laboratories, Inc. 3M

Table 3

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

Project Number: 0231CR3012 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
Sp1een			
enlarged	3	2	3
raised lesion	1		
pale foci	2		
pale, depressed area	1		
srial1*		1	
Lymph node (mesenteric/abdominal)			
enlarged	2	2	2
greenish color			1
Mesentery			
nodular/enlarged/thickened vessels	1		2
mass		1	1
Kidney			
anlarged, pale, pitted	3	1	2
enlarged, pitted		1	
pala, 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	
Manmary Gland			
mass		1	2

Titles:

Group 5 FC-143 300 ppm Group 5 FC-143 300 ppm * includes "possibly"

Macroscopic Incidence Page: 4

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

Table: 3

Project Number: 0231CR0012 Species: Rat

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

Macroscopic Incidence for Females Riker Laboratories, Inc. 3M

Riker Laboratories, Inc. 3M Table: 4
FC-143: Two Year Oral Toxicity-Oncogenicity Study in Rats

Project Number: 0201CR0012 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	26	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	ő
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 3 FC-143 30 ppm

Macroscopic Incidence Page: 6

^{*} includes "possibly"

Macroscopic Incidence for Females Riker Laboratories, Inc. 3M

Table: 4

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

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
inass	1		1
dark area/lesion	2		1
hemorrhagic lesion			1
Nammary Gland			
mass/nodule	27	25	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 30 ppm * includes "possibly"

Macroscopic Incidence Page: 7

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/	Group 1	Group 5
Diagnosis/		
Modifier		
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
	(15)	(15)
Brain Within normal limits	15	15
	(15)	(15)
Esophagus	15	15
Within normal limits	(15)	(15)
Eye	15	13
Within normal limits	20	1
Cataract	0	1
Retinal atrophy minimal	0	i
••••	(15)	(15)
Heart Within normal limits	14	12
Myocardial fibrosis	0	2
minimal	0	- 1
mi }d	0	ī
Myocarditis, chronic nonsuppurative	1	2
minimal	ō	2
mild	1	٥
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
m ; t u		

Titles:

Group 1 CONTROL 0 ppm Group 5 FC-143 300 ppm () = Total Examined

Microscopic Incidence Page: 8

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: 0201CR0012 Species: Rat

Tissue/	Group 1	Group 5
Diagnosis/		
Modifier		
Kidney (continued)		
Pyelitis, acute	1	1
ninimal	1	O
mild	Э	1
Large Intestine	(15)	(15)
Within normal limits	15	14
Nematodiasis	0	1
Liver	(15)	(15)
Within normal limits	7	Э
Hepatocyte alteration, vacuolated	2	O
เล๋าท์เลลไ	1	0
mild	1	ð
Hepatocyte vacuolation	0	2
minimal	0	1
mild	0	1
Megalocytosis	Э	12
minimal	0	7
mild	0	3
moderate	9	2
Necrosis	٥	5
minimal	0	2
mild	0	4
Pigment, Kupfer cell	0	2
minimal	0	1
mild	C	1
Portal bile duct proliferation	5	1
minimal	1	Э
តារៀប	4	1
Portal mononuclear cell infiltrate	7	13
minimal	1	4
mild	ົວ	9
Lung	(15)	(15)
Within normal limits	1	2
Alveolar macrophages	3	5
mild	3	5
Atelectasis	1	C
mild	1	Э
Hemorrhage	6	3
mild	6	2
moderate	J	1
Hyperplasia, septal cell	1	0
mild	1	0
Titles:		
Group 1 CONTROL 3 ppm	() = Tot	al Examined
Group 5 FC-143 300 ppm		

Microscopic Incidence Page: 3

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: 0231CRO012 Species: Rat

Group 1 CONTROL 3 ppm

Group 5 FC-143 300 ppm

Tissue/	Group 1	Group 5
Diagnosis/		
Modifier		
Lung (continued)		
Perivascular mononuclear infiltrate	2	1
mild	2	1
Pneumonia, interstitial, chronic	3	2
minimal	1	- 3
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)	(5)
Within normal limits	3	, 3,
Mesentery	(1)	())
Necrosis, fat	1	(0)
marked	1	Ú
Steatitis, chronic	1	9
moderate	1	0
Pancreas	(15)	(15)
Within normal limits	11	15
Acinar atrophy	3	ij
mild	2	G
moderate	1	ő
Pancreatitis, chronic	3 .	9
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	Ü	1
Salivary Gland	(15)	(14)
Within normal limits	15	14
Small Intestine	(15)	(15)
Within normal limits	15	15
Titles:		
n 1 00117701 3	45	

Microscopic Incidence Page: 10

135

() = 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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group 1	Group 5
Diagnosis/	*********	
Modifier		
Spinal Cord	(14)	(15)
Within normal limits	14	15
Sp1een	(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

Microscopic Incidence Page: 11

Table: 5

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/	Group 1	Group 5
Diagnosis/ Modifier		
modifier		
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 mild	1	3 3
Cyst	1	0
mild	1	0
Hydronephrosis	1	1
moderate	1	. 0
marked	0	1
Hyperplasia, pelvic epithelium	1	0
mild	ī	Ö
Mineralization	Ō	1
mild	0	1

Titles:

Group 1 CONTROL 0 ppm Group 5 FC-143 300 ppm () = Total Examined

Microscopic Incidence Page: 12

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/	Group 1	Group 5
Diagnosis/		
Modifier		•
Kidney (continued)		
Pelvic mineralization	4	1
minimal	4	0
mild	٥	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
Galactocele	2	1

Titles:

Group 1 CONTROL 0 ppm Group 5 FC-143 300 ppm () = Total Examined

Microscopic Incidence Page: 13

Non-Neoplastic Incidence for Females (continued)

Riker Laboratories, Inc. 3M

FC-133: Two Year Oral Toxicity-Oncogenicity Study in Rats - One Year Interim

Table: 6

Project Number: 0231CR0012 Species: Rat

Tissue/	Group 1	Group 5
Diagnosis/		
Modifier		
Mesentary	(1)	(C)
Necrosis, fat	1	0
moderate	1	õ
Steatitis, chronic	1	Ö
aoderate	1	Ō
Ovary	(15)	(15)
Within normal limits	14	15
Cyst	1	0
Pancreas	(15)	(15)
Within normal limits	14	15
Pancreatitis, chronic	1	С
mild	1	0
Parathyroid	(6)	(9)
Within normal limits	5	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	C
Small Intestine	(15)	(15)
Within normal limits	15	15
Spinal Cord	(14)	(15)
Within normal limits	1.7	15
Splean	(15)	(15)
Within normal limits	14	15
Hemosiderosis	1	C
mild	1	Ü
Stonach	(15)	(15)
Within normal limits	15	15
Thyroid ,	(14)	(13)
Within normal limits	14	13
Trachea	(15)	(15)
Within normal limits	15	15
Urater	(6)	(1)
Calculus	0	1
Dilatation	0	1
marked	0	1
Inflammation, chronic	9 9	1
moderate	9	1

Titles:

Group 1 CONTROL J ppm Group 5 FC-143 300 ppm () = Total Examined

Microscopic Incidence Page: 1%

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/	Group 1	Group 5
Diagnosis/		
Modifier		
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

Microscopic Incidence Page: 15

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

Project Number: 0231CR0012 Species: Rat

Tissue/	Group) i	Group	5	Group	6
Diagnosis/						
Modifier	DOS	SAC	DO S	SAC	DOS	SAC
Adrenal	(15)	(34)	(6)	(44)	(14)	(36)
Within normal limits	6	13	2	12	8	18
Cortical degeneration	٥	C	0	0	0	2
moderate	0	0	ວ	0	Û	2
Cortical vacuolation	7	17	2	11	4	5
minimal	Ò	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

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		Э		0		2		J		0	
mild		1		4		l		4		0		3	
moderate		1		2		0		0		0		0	
Nodular hyperplasia, cortex		0		2		1		S		0		1	
minimal		٥		0		1		0		0		0	
mild		Э		1		0		7		0		0	
moderate		Э		1		0		1		0		1	
Sinusoidal actasia, 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		O.		0	
Necrosis		1		О		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		С		0		1		٥		1	
marked		0		2		0		0		٥		0	
Bone Marrow	(15)	(32)	(6)	(42)	(٥)	[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				D		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

Microscopic Incidence Page: 16

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group 1	Group 5	Group 6
Diagnosis/			
Modifier	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	- o - 9	- 1 0	- 0 9
Keratitis, chronic	0 0	0 1	0 1
mild	0 0	0 0	0 1
moderate	0 0	0 1	0 0
Phthsis 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
modera te	U 2	0 0	5 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)

142

Microscopic Incidence Page: 17

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Group	5	Group	6
Diagnosis/						
Modifier	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	ŋ
Papillary necrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Pelvic mineralization	1	3	Ŋ	3	4	8
minima l	0	1	0	1	0	1
mild	1	2	0	2	3	3
moderate	0	0	0	٥	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	٥	0	0	1	2
mild	0	D	0	0	1	2
Pyelonephritis, acute	1	٥	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	٥	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	ט	1
mild	0	2	1	22	2	4
moderate	0	1	0	3	0	0
Hematopoiesis, extramedullary	٥	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	9	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

Microscopic Incidence Page: 18

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

Project Number: 0281CR0012 Species: Rat

Table: 7

Tissue/	Group	1	Group	5	Group	6
Diagnosis/						
Modifier	DOS	SAC	DOS	SAC	DOS	SAC
Liver (continued)						
Hepatocyte vacuolation	3	14	2	10	б	2
minimal	0	1	1	1	Э	1
mild	4	13	0	8	3	1
moderate	2	0	1	1	3	0
marked	2	0	C	0	0	0
Hyperplasia, Kupffer cell	0	0	Э	0	0	1
moderate	0	0	0	0	0	1
Hyperplastic module	۵	٥	0	3	۵	0
Megalocytosis	0	ວ	2	33	٥	6
minimal	0	ວ	2	24	٥	6
mild	O	٥	0	10	0	Ü
moderate	0	0	0	4	0	0
Mononuclear cell infiltration	0	C	0	0	0	1
mild	0	O	0	0	0	1
Necrosis	2	1	2	3	2	3
minimal	Û	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	٥	a	1	0	0
mild	5	21	1	13	5	10
moderate	1	0	0	0	0	0
Portal mononuclear cell infiltrate	7	3 C	5	43	7	25
minimal	ð	2	0	2	0	С
mild	7	2 8	5	41	7	25
Lung	(15)	(34)	(5)	(44)	(14)	(35)
Within normal limits	0	1	0	o o	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	ō	0	1	9	0	С
Atelectasis	O	0	O.	0	1	٥
moderate	0	0	0	0	1	Э
Едета	3	o	c	0	0	0
mild	1	0	0	0	0	۵
moderate	1	ð	0	0	0	0
marked	1	0	0	0	0	0
Fibrosis	1	J	0	1	0	0
mild	1	0	0	0	0	0
moderate	Ē	0	0	1	0	0
	•					

Titles:

Group 1 CONTROL 3 ppm Group 5 FC-143 300 ppm Group 6 FC-143 30 ppm () = Total Examined DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

144

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

Project Number: 02810R3012 Species: Rat

Table: 7

Tissue/	Group	1 G	roup	5	Group	G
Diagnosis/					200	
Modifier	DOS S	AC D	os s	AC	DOS	SAC
Lung (continued)						
Granuloma	Û	3	3	1	5	0
Helasinhage	5	4	2	20	3	5
nild	2	1	0	5	3	₹,
moderate	1	2	1	13	.,}	2
manked	3	1	1	2	-)	0
Madial hypertrophy, arteries	9	3	1	15	j	Ö
moderate	Ü	•)	1	2	0)
Necrosis	1	S .	Ð	ŋ	0	9
marked	1	9	Ď.	j	0	Э
Peribronchial lymphoid hyperplasia	5	1	o c	ð	IJ	j
mild	0	1	5.	Э	3	Э
Perivascular mononuclear infiltrate	?	19	.)	7	Ô	3
minimal	ð	2	0	4	Ü	IJ
mild	2	14	.)	2	2	3
moderate	0	3	0	1	a	ō
Pneumonia, interstitial, acute)	0	Đ	ō	1	ð
moderate	ä	0	ĵ	0	1	0
Pneumonia, interstitial, chronic	•	14	1	ક	้	5
mild		11	1	5	J	5
moderate	1	3	3	n	0	õ
Thrombus	1	ΰ	1	3	3	3
Vascular mineralization	-	33	4	43	11	32
minimal	0	2	0	.0	0	9
mild	=	31	4	41	11	32
moderate	=	. J	Ċ	2	Û	0
Lymph Node (mesenteric)	(12)(δ) (_	0) (-
Within normal limits		29	5	33	. o, t	1
Granuloma	0	0	0	1	O O	5
moderate	ņ	0	0	1	Š	٥
Hemorrhage	2	4	0	4	0	S .
minimal	1	2	ĵ	1	٥	0
mild	1	1	e e	3	Ü	0
Sinusoidal ectasia	ů	0	Û	1	3	٥
mild	0	0	0	1	0	0
Mammary Gland	(0) (0) (0) (1) (-
Within normal limits	0	0, (0	0	1	0
Mesentery	(0) (2) (0) (0) (_	-
Polyarteritis	0, (2	ġ,	0, (1	1,
marked	0	2	9	ŋ	1	1
IIIQ1 KTU	Ū	۲.	J	,	1	_

Titles:

Group 5 FC-143 300 ppm Group 5 FC-143 300 ppm Group 5 FC-142 30 ppm () = Total Examined
DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

145

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

Project Number: 0281CR0012 Species: Rat

Tissue/

Pancreas

Parathyroid

Cyst Hyperplasia mild

Edema

Salivary Gland

Pituitary

Prostate

Diagnosis/

Modifier

Within normal limits
Acinar atrophy
minimal
mild
moderate
marked
Hyperplasia, acinar cell

mild
moderate
Hyperplasia, islet cell
mild
moderate
Polyarteritis
minimal
moderate
marked

Within normal limits

Within normal limits

Within normal limits

moderate
Prostatitis, acute
minimal
mild
moderate
marked

Within normal limits Sialadenitis, acute moderate marked

Sialadenitis, chronic

minimal

moderate

mild

- (Group) 	1		Group) 	5 		Grou	p 	6 	
I	200	:	SAC	1	200		SAC	1	200	,	SAC	
(-	(((-	((
	10		24		4		27	æ	10		21	_
	2		4	6	O		116	3/1	1		6	9
	0		0	(A)	0		1		1		1	A
	1		2		0		6	K	0		5	4
	1		1	H	0		4	M	0		2	W
	0		1	M	0		0	P	0		0	4
	0		0	Œ.	1		1	W)	. 0		2	U
	0		0		0		1		0		1	
	0		_0_	<u> </u>	_1_		<u> </u>	T	- <u>0</u>	<u>. </u>	_1	;
	0		2	•	1		3		1		1	
	0		0		0		0		1		1	
	0		2		1		3		0		0	
	Э		4		0		2		0		3	
	0		0		0		0		0		1	
	0		2		0		2		0		2	
	0		2	_	0		0		0		0	
(5)	(16)	(5)	(31)	(7)	(26)	
	6		16		5		29		7		26	
(15)	(33)	(5)	(((34)	
	7		13		3		28		3		20	
	2		2		0		2		1		4	
	0		2		0		0		0		2	
,	0	,	2	,	0	,	0	,	0	,	1	
(13)	-{	33) 27	(6) 5	(43) 40	(13) 11	(35) 35	
	10 1		0		0		0		0		22	
	1		0		0		0		0		0	
	3		5		1		3		2		1	
	0		0		0		1		0		0	
	1		2		0		0		1		1	
	1		3		0		1		. 0		ō	
	1		1		1		1		1		٥	
(12)	(32)	(5)	(41)	(10)	(34)	
•	12	•	31	•	4	•	25	•	10	•	21	
	0		0		0		1		0		1	
	0		0		0		1		0		0	
	0		0		0		0		0		1	

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Ti	+1	es	٠

Group 1 CONTROL 0 ppm Group 5 FC-143 300 ppm Group 6 FC-143 30 ppm () = Total Examined
DOS= Unscheduled Death(s)

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SAC= Protocol Scheduled Sacrifice(s)

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146

Microscopic Incidence Page: 21

Table: 7

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

Project Number: 0281CR0012 Species: Rat

Tissue/		Grou	m	1		Grou	p 5		Grou	_	,
Diagnosis/	_		-r 		_		р 5		Grou	þ	6
Modifier		DOS		SAC		DOS	SAC		DOS	SA	.c
Salivary Gland (continued)											
Sialadenitis, chronic											
marked		0		0		0	7		C		5
Skin	(8)	(-	(0)		(5)		4)
Abscess	•	0	•	0	`	0	0	•	1	-	4) 0
Pododermatitis, ulcerative		3		5		0	1		2		2
marked		3		5		0	i		2		2
ปไcer		1		o o		0	Ď		0		1
marked		1		٥		0	5		0		1
Small Intestine	1	14)	ŧ	-	(6)	(44)	ſ	1)		_
Within normal limits	•	13	•	32	'	5	44	1		•	0)
Polyarteritis		0		2		0	94		1		0
moderate		0		1		0	9		0		0
marked		0		1		0	0		0)
Spinal Cord	ŧ	15)	t		(6)	(42)	(-		3
Within normal limits	•	15	١	32	(5	421	ţ	0)	•))
Spl een	1		1	34)	(_	(44)	,	-	()	_
Within normal limits	,	5	,	20	`	1	25	1	14)		
Atrophy		0		0		1	0		0	35	
moderate		0		a		1	0		0	(
Fibrosis		0		1		0	0		0	0	
moderate		o		î		0	0		ŋ.	0	
Hematopoiesis, extramedullary, increased		4		0		1	1		1	0	
mild		2		٥		Ü	1		0	0	
moderate		1		0		1	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	_	
moderate		0		1		0	0		0	0	
Polyarteritis		0		Ô		0	0		0	0	
moderate		0		٥		0	_		-	1	
Stomach	(16)	ί.	33)	(-	0 (44)	,	0 14) :	1	,
Within normal limits		11	-	33, 33	'	5	43			35	ļ
Edema		3	•))		0	43 0		11	35	
moderate		J		-		9	Ü		0	0	

Titles:

U1cer

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

moderate

marked

Gastritis, acute

mild

marked

() = Total Examined DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

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147

Microscopic Incidence Page: 22

Table: 7

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

Project Number: 0281CR0012 Species: Rat

Τa	bl	_		7
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Tissue/ Diagnosis/	Group	l Gr	oup 5	Group	6
Modifier	DOS SA	DO	S SAC	DOS	SAC
Testis/Epididymis	(16) (3	3) (6) (44)	(14)	(36)
Within normal limits	13 20		5 23	7	26
Granuloma, spermatic	0 (0 0	1	0
Leydig cell hyperplasia	0 ()	0 1	1	1
mild	0 (ו	0 1	0	1
moderate	0 (0 0	1	ō
Mineralization	0 :	l	0 2	0	0
mild	0 :	l	0 2	0	0
Polyarteritis	1 9		0 2	1	5
mild	1 1	Į	0 0	٥	2
moderate	0 1	1	0 2	1	2
marked	0 3		0 0	5	1
Tubule atrophy, aspermatogenesis	3		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	5 0		0 9	3	0
mild	0 0		0 7	3	0
moderate	0 0		0 2	0	0
Thymus			1) (1)	(1)(-
Hemorrhage	0 0		0 1	0	0,
marked	0 0		0 1	0	0
Thyroid	(12) (31		5) (42)	(12) (
Within normal limits	11 25		4 33	10	26
Cyst, colloid	0 1		1 1	0	1
mi l d	0 1	-	1 0	0	ĵ
Follicular hyperplasia, cystic	0 1) 1	1	1
moderate	0 1		0 1	0	ĵ
marked	0 0		0 0	1	1
Hyperplasia, C cell	0 1) 1	1	5
mild	0 1) 1	1	3
moderate	0 0			ō	2
Ultimobranchial cyst	1 1	(3	1	2
Trachea	(15) (34) (6	5) (42)	(13)(_
Within normal limits	15 34			13	35
Urinary Bladder	(13) (33) (6	5) (44)		
Within normal limits	10 32			11	35
Calculus	0 0			1	0
Cystitis, acute	1 0			0	0
moderate	1 0	C) 0	0	0
Cystitis, chronic	0 0	C	0 0	1	0
minimal	0 0	C	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

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

Project Number: 0281CR0012 Species: Rat

Table: 7

Tissue/	Group	1	Group	5	Group	6
Diagnosis/						
Modifier	DOS	SAC	DOS	SAC	DOS	SAC
Urinary Bladder (continued)						
Epithelial hyperplasia, papillary	0	0	0	Q	1	0
mild	0	ð	0	o o	1	0
Epithelial hyperplasia, simple	2	1	1	3	3	٥
minimal	0	ŋ	9	1	0	0
mild	2	1	1	2	3	0
Hemorrhage	1	٥	0	1	0	0
minimal	0	0	Õ	1	0	0
marked	1	0	0	o o	0	0

Titles:

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

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

149

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

Project Number: 0291CR0912 Species: Rat

Tissue/	Group	1	Group	5	Group 6
Diagnosis/ Modifier	DOS	SAC	DOS	SAC	DOS SAC
Modifier	003	SAL	ъоз	SAC	DUS SAC
Adrenal	(25)	(25)	(20)	(29)	(26) (24)
Within normal limits	2	ŋ	4	2	3 1
Cortical atrophy	0	0	1	2	C 0
moderate	0	0	1	2	0 0
Cortical degeneration	2	5	1	С	4 4
mild	1	o o	0	J	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	٥	0	0	1 1
mild	3	0	0	0	0 0
moderate	1	0	0	0	0 1
marked	0	0	0	0	I 0
Hemosiderosis	0	0	0	0	1 0
mild	3	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	9	0	0 0
marked	2	0	0	0	0 0
Nodular hyperplasia, cortex	0	Э	0	1	1 2
moderate	C	0	0	1	1 2
Sinusoidal ectasia, cortex	19	23	16	25	?1 22
minimal	J	1	0	1	1 0
mild	3	4	9	6	7 3
moderate	5	3	3	7	7 13
marked	5	9	4	11	5 5
Aorta	(21)	(23)	(19)	(27)	(0)(0)
Within normal limits	17	23	19	27	O C
Mineralization	2	0	0	0	0 0
mild	2	Э	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	20	0 0
Esophagus	(15)	(21)	(9)	(15)	(23) (22)
Within normal limits	14	21	9	15	23 22

Titles:

Group 1 CONTROL 3 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

Microscopic Incidence Page: 25

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Group 5	Group 6
Diagnosis/ Modifier	DOS	SAC	DOS SAC	DOS SAC
riod () lei	003	JAC	DO3 3AC	003 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	O	0 0	1 0
Panophthalmitis	O	1	0 0	ũ n
marked	0	1	0 0	0 0
Phthsis bulbi	0	1	0 0	0 0
moderate	ð	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)	(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	ο ο
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	9	o c	1 0
mild	2	0	0 0	0 0
moderate	0	0	0 0	1 0
Nephrosis	7	0	0 9	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)

151

Microscopic Incidence Page: 26

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Group	5	Group	6
Diagnosis/						
Modifier	DOS	SAC	200	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	С
moderate	0	0	0	υ	0	2
Polyarteritis	0	0	O	ű	0	1
minimal	0	0	0	0	0	1
Protein resorption droplets	0	0	1	0	1	1
mild	0	0	ე	0	0	1
marked	0	0	1	0	1	0
Pyelitis, acute	O	0	2	0	0	0
mild	C	0	1	0	0	0
moderate	2	0	1	0	0	0
Pyelonephritis, acute	1	0	0	0	0	0
moderate	1	0	0	0	0	n
Vacuolation, conv. tub. epitheium	1	0	0	0	0	ŋ
moderate	1	0	0	0	0	0
Large Intestine	(24)	(23)	(17)	(29)	(0)	(0)
Within normal limits	22	22	17	27	٥	0
Nematodiasis	1	1	0	2	0	0
Liver	(25)	(25)	(21)	(29)	(25)	(24)
Within normal limits	1	0	4	4	7	7
Atrophy	0	0	ū	J	1	o
moderate	0	0	0	0	1	0
Cystoid degeneration	0	0	0	1	1	J
minimal	0	0	0	1	0	0
mild	0	0	0	O	1	Ü
Hematopoiesis, extramedullary	3	0	1	0	5	2
minimal	0	0	0	٥	3	1
mild	3	0	C	0	2	1
moderate	0	0	1	0	J	ŋ
Hepatocyte alteration, basophilic	1	7	0	2	S	3
minimal	0	0	0	1	ŋ	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	3	0	9	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)

152

Microscopic Incidence Page: 27

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

Project Number: 0281CR0012 Species: Rat

Ta	ы	e	:	8

Tissue/ Diagnosis/	Group	1	Group	5	Group	5
Modifier	DOS	SAC	DOS	SAC	DOS	SAC
Liver (continued)						
Hepatocyte alteration, vacuolated						
marked	0	О	o	0	1	0
Hepatocyte vacuolation	15	15	8	13	7	9
minima?	1	1	0	3	2	2
mild	9	13	5	10	2	7
moderate	3	1	2	0	2	0
marked	2	o o	1	3	1	0
Hyperplastic nodule	0	1	ō	2	0	0
Megalocytosis	0	ō	1	7	o o	1
minimal	0	0	1	6	0	1
mild	0	0	0	1	0	0
Mitotic activity, increased	1	0	0	ō	Ö	Ô
moderate	1	0	0	9	0	0
Mononuclear cell infiltration	0	Ü	1	0	0	0
mild	ð	o.	1	0	0	0
Necrosis	4	1	2	0	6	0
minimal	ġ	ō	c	0	1	0
mild	1	1	1	o o	3	0
moderate	1	ō	0	0	0	0
marked	2	0	1	0	2	ŗ
Pigment, Kupfer cell	0	9	1	0	0	3
mild	0	0	1	0	ð	0
Portal bile duct proliferation	4	13	5	9	1	4
m ild	3	12	5	3	i	4
moderate	0	1	0	1	0	ð
marked	1	ō	Ö	ō	e e	0
Portal mononuclear cell infiltrate	10	9	4	15	5	5
minimal	1	0	Ö	2	0	2
តារៀd	8	9	4	12	5	4
moderate	1	0	Ö	1	0	0
Telangiectasis	1	٥	0	0	0	0
mild	1	G	0	ō	Ö	õ
Lung	(25) (25}	(21)((26) (
Within normal limits	2	3	1	3	2	2
Abscess	1	0	0.	Ċ	0	0
Alveolar macrophages	5	9	6	13	3	7
minimal	1	0	2	0	o o	1
mild	4	9	4	12	3	6
moderate	Ĵ	Ĵ	0	1	0	Ö
Atelectasis	0	0	0	0	1	0
ធា រ l d	0	0	ō	0	1	0
					=	-

Titles:

Group 1 CONTROL 3 ppm Group 5 FC-143 330 ppm Group 6 FC-143 30 ppm

() = Total Examined

DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

153

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Group	5	Group	6
Diagnosis/ Modifier	DOS	SAC	DOS	SAC	DOS	SAC
PIDUTTICT	003	JAC	003	SAC	D 03	JAC
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	C
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	O
mild	4	3	1	5	0	3
marked	0	0	1	0	0	0
Vascular mineralization	12	10	15	11	19	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	٥	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	O

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)

154

Microscopic Incidence Page: 29

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

Project Number: 0281CR0012 Species: Rat

Tissue/		Grou	ıp	1		Grou	р :	5	Grou	р 6
Diagnosis/ Modifier	•	DOS		SAC	-	DOS	 SA(;	DOS	SAC
Lymph Node (mesenteric) (continued)										0.1.0
Pigment, brown		0		0		0			•	
minimal		0		0		0	5		0	0
mild		0		0		0	2		0	0
moderate		0		0		0	2		-	0
Sinusoidal ectasia		1		0		0			0	0
moderate		1		0		0	2		0	0
marked		0		0		0	_		0	0
Mammary Gland	,	23)	(-	,		1		0	0
Within normal limits	ı	4	1	23)	·	17) 7			(23)	(22)
Fibrosis		0		0		0	9		4	7
mild		0		•		•	1		0	O
Galactocele		5		0 4		0	1		0	0
Lobular hyperplasia		4		3		2	1		7	2
moderate				-		2	1		2	1
Ovary	,	1	,	0	,	2	0		0	. 5
Within normal limits	(25)	((18)				(24)
Cyst		19		17		11	16		23	11
Tubular hyperplasia		3		3		0	5		2	7
mild		0		0		7	8		0	7
moderate		0		0		0	2		0	1
marked		0		0		5	б		0	б
Pancreas		0		0		1	0		0	0
Within normal limits	(24)	(25)	(-	(28) ((22)	(21)
Acinar atrophy		22		16		15	24		18	17
minimal		0		6 į	,	2		4	3	25
mild		0		1		0	1		1	1
moderate		0		. 2		2	1		1	0
marked		0		3		0	0		0	1
Cyst		0		0		0	0		1	0
Edema		0		1		0)		0	0
moderate		0		0		1	0		0	0
Hyperplasia, islet cell		0		0		1	0		0	0
mild		0		0		0	1		0	1
Pancreatitis, chronic		0		0		0	1		0	1
moderate		0		0		1	0		0	0
Polyarteritis		0		0		1	0		0	0
minimal		0		0		0	0		0	1
Parathyroid	,	0	,	0	,	0	0		0	1
Within normal limits	((0)	(14)	(15) (,
100 Mar. 1 Mar 63		5		0		9	14		15	15

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Titles:
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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)

155

Microscopic Incidence Page: 30

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

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/	Group	1	Group 5	Group 6
Modifier Modifier	DOS S	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	o c	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	O.	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)	(13) (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 9
marked	0	0	0 0	1 0
Spinal Cord	(25) ((21) (29)	
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)((21) (29	
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	9	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)

156

Microscopic Incidence Page: 31

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

Titles:

Group 1 CONTROL 0 ppm

Group 5 FC-143 300 ppm

Group 6 FC-143 30 ppm

fissue/	Group	1	Group 5	Group 6
Diagnosis/				
Modifier	DOS	SAC	DOS SAC	DOS SAC
Spleen (continued)				
Hemosiderosis				
marked	0	0	0 0	1 0
Stomach	(25)	(25)	(20) (29)	(26) (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	ō	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		
mild	0	0		
	•	_		2 (
hyroid	(25)		(15) (26)	
Within normal limits	20	23	14 22	22 21
Follicular hyperplasia, cystic	1	0	0 0	0 0
mild	1	0	0 0	o 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
rachea		(25)	(20) (25)	(24) (23
Within normal limits	25	25	2 0 2 3	24 23
rinary Bladder	(25) ((25)	(16) (26)	(25) (22
Within normal limits	17	25	15 2 5	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	O 0	0 0
Hypertrophy	0	0	0 1	0 0
mild	0	0	0 1	0 0
terus	(25)		(19) (29)	
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	ō	1	1 2	1 1
		_	_	

() = Total Examined DOS= Unscheduled Death(s)

SAC= Protocol Scheduled Sacrifice(s)

157

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/	Group 1	Group 5
Diagnosis/		
Modifier		
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

160

Neoplastic Incidence for Males Riker Laboratories, Inc. 3/1

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group 1 Group 5 Group 6	,
Diagnosis/	DOS SAC DOS SAC DOS SAC	
Modifier	003 3AC 003 3AC 003 3AC	
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	i
Hemolymphoreticular neoplasm present	0 0 1 0 0)
Bone Marrow	(15) (32) (6) (42) (0) ())
Hemolymphoreticular neoplasm present	0 0 1 0 0)
Brain	(16) (34) (6) (44) (0) (1	1)
Astrocytoma, benign	0 1 0 0 0 1	l
Oligodendroglioma, benign	1 0 0 0 0)
Hemolymphoreticular neoplasm present	0 0 1 0 0)
Eye	(12) (33) (6) (44) (2) (3	3)
Hemolymphoreticular neoplasm present	0 0 1 0 0)
Heart	(15) (34) (6) (44) (14) (36	S)
Hemolymphoreticular neoplasm present	1 0 0 0 0	3
Kidney	(16) (34) (5) (44) (14) (36	5)
Hemolymphoreticular neoplasm present	1 0 1 0 1	0
Liver	(16) (34) (6) (44) (14) (36	5)
Hepatocellular carcinoma	2 1 1 4 1	3
Hemolymphoreticular neoplasm present	2 1 1 1 1	0
Lung	(20)	6)
Hemolymphoreticular neoplasm present	J 1 1 1	0
Lymph Node (abdominal)		0)
Hemolymphoreticular neoplasm present	• • •	C
Lymph Node (mesenteric)	(12) (00) (0) (11)	1)
Hemangiosarcoma	3 3	0
Hemolymphoreticular neoplasm present		0
Pancreas	1 201 1 001 1 01 1 001	4)
Adenocarcinoma	, , ,	1
Islet cell adenoma		J
Hemolymphoreticular neoplasm present		0
Parathyroid	(0) (20) (0) (02) (=	5)
Adenoma		0
Pituitary	(13) (33) (0) (12) (20) (1	4)
Adenoina		3
Salivary Gland	1 12/ 1 02/ 1 0/ 1 12/ 1 22/ 1	4)
Carcinoma		0
Skin	(0) ()) (0) (0)	4)
Fibroma	<u> </u>	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

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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Grou	ıp 5	Group	6
Diagnosis/	DOS	SAC	DOS	SAC	DOS	SAC
Modifier	עטט	SAC	003	SAC	903	JAG
Skin (continued)						
Keratoacanthoma	1	2	0	1	O	0
Liposarcoma	1	0	0	0	0	0
Papilloma	0	1	0	0	٥	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	Ü
Small Intestine	(14)	(34)	(6) (44)	(1)	(0)
Hemolymphoreticular neoplasm present	1	C	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	Û
Sp1een	(16)	(34)	(6) (44)	(14)	(36)
Hemangiosarcoma	0	1	0	0	0	0
Homolymphoreticular neoplasm present	1	1	1	0	1	0
Stomach	(16)	(33)	(6) (44)	(14)	(35)
Adenocarcinoma	0	0	0	1	0	٥
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)	(O)
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	С	2	0	0	0	0
Follicular adenoma	О	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	Q	0	1	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)

162

Microscopic Incidence Page: 37

Neoplastic Incidence for Females Riker Laboratories, Inc. 3M

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

Project Number: 0281CR9012 Species: Rat

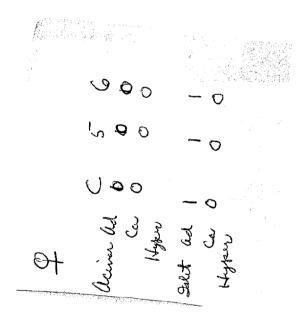
Tissue/	Group 1	Group 5	Group 6
Diagnosis/ Modifier	DOS SAC	DOS SAC	DOS SAC
Adrena1	(25) (25)	(20) (29)	(25) (24)
Adenoma, cortical	0 0	0 1	0 1
Carcinoma, cortical	0 0	0 0	1 0
Pheochromocytoma, benign	0 2	0 0	0)
Pheochromocytoma, malignant	o o	1 0	0 0
Hemolymphoreticular neoplasm present	2 0	0 0	0 0
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	ງ ງ
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 6	0 0	0 0
Harderian Gland	(0)(0)	(0)(0)	(1)(0)
Adenocarcinoma	0 0	9 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
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	ე ე	0 Э	1 0
Mammary Gland	(23) (23)	(17) (27)	(23) (22)
Adenocarcinoma	4 3	2 3	9 5
Adenoma	2 1	0 0	0 0
Carcinoma	0 1	0 0	0 0
Fibroadenoma	6 4	5 16	8 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: 38



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

Project Number: 0281CR0012 Species: Rat

Tissue/	Group	1	Group	5	Group 6
Diagnosis/ Modifier	DOS S	SAC	DOS	SAC	DOS SAC
modifiler	505	,,,,	500	0.10	
Mesentery	(0) (0}	(0)	(0)	(2)(0)
Mesothelioma, malignant	O	0	0	0	1 0
Hemolymphoreticular neoplasm present	υ	0	0	0	1 0
Ovary	(25)(23)	(18)	(29)	(26) (24)
Granulosa cell tumor, benign	0	0	0	0	0 1
Leiomyoma	1	0	Э	0	0 0
Tubular adenoma	0	4	0	1	0 0
Hemolymphoreticular neoplasm present	2	C	Э	0	1 0
Pancreas	(24)(25)	(19)	(28)	(22) (21)
Islet cell adenoma	0	1	0	1	1 0
Islet cell carcinoma	o	1	0	1	0 0
Hemolymphoreticular neoplasm present	2	C	0	0	1 0
Pituitary	(22)(24)	(21)	(29)	(23) (24)
Adenoma	16	17	14	22	20 19
Skin	(3)(3)	(2)	(0)	(6)(4)
Fibroma	1	2	1	0	4 1
Fibrosarcoma	۵	Û	O	٥	1 1
Small Intestine	(24)(25)	(18)	(29)	(1)(1)
Leiomyosarcoma	0	0	0	Э	9 1
Spinal Cord	(25) (23)	(21)	(29)	(0)(0)
Hemolymphoreticular neoplasm present	1	C	Э	0	0 0
Spleen	(25)(25)	(21)	(29)	(24) (23)
Hemolymphoreticular neoplasm present	3	0	Û	0	1 0
Stomach	(25) (25)	(20)	(29)	(26) (24)
Hemolymphoreticular neoplasm present	1	0	0	0	C 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	٥	1 0
Uterus	(25) (25)	(19)	(29)	(26) (23)
Adenoma	0	1	0	0	0 0
Hemangioma	С	0	0	0	1 0
Leiomyoma	0	Ü	0	0	0 1
Polyp	С	1	0	1	2 1
Hemolymphoreticular neoplasm present	2	0	0	0	0 0
Hemolymphoreticular System [# affected]	[5] [0]	[1]		[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)

164

Microscopic Incidence Page: 30

JOSEPHOND ST. 1 SOMETHINGS.

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

Table: 1

Anisal Number: 1R-3516 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 53) 1 Year Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Lung

Lymph Node (mesenteric) --Pancreas

Pancreas Parathyroid Small Intestine -Not examined, missing -Acinar atrophy, mild -Not examined, missing -Within normal limits

Thyroid

Fewer than protocol number
-Not examined, missing

-Chronic progressive nephropathy, mild -Vascular mineralization, minimal

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 O ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Lung Parathyroid Thyroid -Chronic progressive mephropathy, minimal -Vascular mineralization, mild

-Not examined, missing

-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 O ppm

Fate: (Week= 53) 1 Year Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Simusoidal ectasia, cortex, bilateral,

moderate

Kidney

-Chronic progressive nephropathy, minimal

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 1

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

Table: 1

Animal Number: 18-3520 Sex: Male Group: (1) CONTROL 0 pps Fate: (Week= 53) 1 Year Interim Sacrifice Microscopic Observations (continued): Liver -Hepatocyte alteration, vacuolated, focal, minimal -Vascular mineralization, minimal Lung 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. Sex: Male Animal Number: 1R-3522 Group: (1) CONTROL O ppm Fate: (Week= 53) 1 Year Interim Sacrifice Macroscopic Observations: liver -Light (pale) tan in color. Microscopic Observations: Kidnev -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 Mode (mesenteric), Pancreas, Salivary Gland, Eye. Animal Number: 1R-3527 Sex: Male Group: (1) CONTROL O 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

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

Table: 1

Animal Number: 1R-3527 Sex: Male Group: (1) CONTROL 0 pps Fate: (Week= 53) 1 Year Interia 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 O ppm Fate: (Week= 53) 1 Year Interia Sacrifice Macroscopic Observations: -Area of fat necrosis, 2 x 3 x 0.5 cm. Mesentary Microscopic Observations: Lung -Alveolar macrophages, multifocal, mild Atellectasis, focal, mild -Necrosis, fat, marked Mesentary 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 O 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 -Vascular mineralization, minimal Lung 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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 3

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

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 Stomach -Perivascular mononuclear infiltrate, mild

-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 O 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 Pancreas -Vascular mineralization, mild -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 Bland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 4

FC-143: Two Year Bral 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

Lung

-Portal mononuclear cell infiltrate. mild

Portal bile duct proliferation, sild

-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, Thursday, Branch Branch Branch Branch Branch Branch

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 Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Pancreas -Chronic progressive mephropathy, mild -Pancreatitis, chronic, focal, mild

Acinar atrophy, focal, mild

Parathyroid -Not examined, not in plane of section

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 5

FC-143: Two Year Bral Toxicity-Oncogenicity Study in Rats - One Year Interia

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 pps

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal Lung

-Cortical vacuolation, multifocal, mild -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: Kidnev

-Chronic progressive nephropathy, minimal -Vascular mineralization, minimal Alveolar macrophages, multifocal, mild Hemorrhage, focal, mild

-Cyst, pars distalis

Lung

Pituitary

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: 0281CR0012

Summarized STAR Page: 6

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

Table: i

Animal Number: 1R-3580 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Kidney

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

Microscopic Observations:

Bone Marrow

Kidney

-Not examined, missing

-Chronic progressive nephropathy, mild

Cyst, cortical, unilateral

Lung

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

mild

Pancreas Parathyroid Spinal Cord -Pancreatitis, chronic, focal, mild
-Not examined, not in plane of section

-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 O ppm

Fate: (Week= 53) 1 Year Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

-Pelvic mineralization, minimal

Lymph Node (mesenteric)

Parathyroid

-Not examined, missing
-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 Bland, Pituitary, Adrenal,
Thyroid, Trachea, Esophagus, Pancreas, Salivary Bland, Eye.

Animal Number: 1R-4582 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 53) I Year Interim Sacrifice

Macroscopic Observations:

Mesentary

-Yellow nodular mass, 1 x 0.5 cm.

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative, focal,

minimal

Kidnev

-Calculus, pelvic, unilateral

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 7

9 Tre Course

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

Table: 1

Animal Number: 18-4582 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Large Intestine

Lung

-Not examined, missing

-Pneumonia, interstitial, chronic, multifocal,

Hemorrhage, local areas, mild

Perivascular mononuclear infiltrate, mild

-Necrosis, fat, nodular, moderate Steatitis, chronic, moderate

-Not examined, not in plane of section Parathyroid

Urinary Bladder -Not examined, missing

Uterus

Mesentary

-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.

Sex: Female Group: (1) CONTROL O ppm Animal Number: 1R-4585

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, focal, unilateral,

mild

Kidney

Liver

-Pelvic mineralization, minimal

-Portal mononuclear cell infiltrate, minimal -Vascular mineralization, mild

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, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Manmary Gland, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 8

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

Table: 1

Animal Number: 1R-4588 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 53) 1 Year Interia Sacrifice

Macroscopic Observations:

Skin Adrenal -Hair loss, neck. -Left enlarged

Microscopic Observations:

Adrenal

Kidney

-Sinusoidal ectasia, cortex, unilateral,

marked

Cortical degeneration, unilateral, wild -Hyperplasia, pelvic epithelium, mild

Calculus, pelvic, unilateral Cyst, medullary, mild

rer -Henatocyte vacu

-Hepatocyte vacuolation, multifocal, mild

-Hemorrhage, diffuse, moderate

-Not examined, missing -Hemosiderosis, mild

Liver Lung Spinal Cord Spleen

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 Interia Sacrifice

Macroscopic Observations:

Pituitary

-Slightly enlarged

Microscopic Observations:

Liver

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

-Galactocele

Mammary Gland 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 Bland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 9

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

Table: 1

Animal Number: 1R-4590 Sex: Female Group: (1) CONTROL O pom

Fate: (Week= 53) 1 Year Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Luna

-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, Massary Gland, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4601 Sex: Female Group: (1) CONTROL 0 ppg

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Kidney

-Hydronephrosis, unilateral

Microscopic Observations:

Kidney

-Hydronephrosis, unilateral, moderate

Calculus, unilateral, mild

Liver Lung

-Hepatocyte vacuolation, multifocal, minimal

-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:

Ilterus

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

Liver

Microscopic Observations:

Lung

Lymph Node (mesenteric)

Uterus

-Hepatocyte vacuolation, multifocal, minimal

-Hemorrhage, multifocal, mild -Not examined, missing

-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

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

Table: 1

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Animal Number: 1R-4610 Sex: Female Group: (1) CONTROL O ppm
Fate: (Week= 53) 1 Year Interim Sacrifice
     Macroscopic Observations:
          Pituitary
                                                  -Slightly enlarged
          Uterus
                                                  -Slightly enlarged
     Microscopic Observations:
                                                  -Sinusoidal ectasia, cortex, mild
          Adrenal
          Large Intestine
                                                  -Nematodiasis
         Lung
                                                  -Alveolar macrophages, multifocal, mild
          Pancreas
                                                  -Pancreatitis, chronic, focal, mild
          Parathyroid
                                                  -Not examined, not in plane of section
          literus
                                                   -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, Kidney, Heart, Stomach, Small Intestine,
Urinary Bladder, Aorta, Ovary, Mammary Gland, Pituitary, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.
Animal Number: 1R-4620
                          Sex: Female Group: (1) CONTROL O pps
Fate: (Week= 53) 1 Year Interim Sacrifice
     Macroscopic Observations:
         Eve
                                                  -Atrophy, right eye.
     Microscopic Observations:
         Eye
                                                  -Panophthalmitis, unilateral, marked
                                                   Atrophy, unilateral, marked
          Kidnev
                                                   -Pelvic mineralization, minimal
         Lung
                                                  -Hemorrhage, multifocal, mild
          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,
Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Adrenal, Thyroid, Parathyroid,
Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.
Animal Number: 1R-4629
                          Sex: Female Group: (1) CONTROL O ppm
Fate: (Week= 53) 1 Year Interia Sacrifice
     Macroscopic Observations:
          Skin
                                                  -Hair loss, head, neck, face.
     Microscopic Observations:
          Adrenal
                                                  -Cortical degeneration, focal, unilateral,
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 11

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

Animal Number: 1R-4629 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 53) 1 Year Interia 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. Microscopic Observations: Kidnev -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 O ppm Fate: (Week= 53) | 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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 12

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

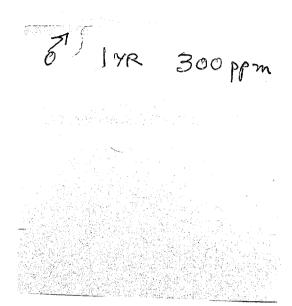
Table: 1

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Animal Number: 1R-4631
                          Sex: Female Group: (1) CONTROL O 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 O ppm
Fate: (Week= 53) 1 Year Interim Sacrifice
     Macroscopic Observations:
          Pituitary
                                                   -Slightly enlarged with a dark red focus on
                                                     surface.
                                                   -Small spherical mass, 1.2 cm dia., containing
          Massary Gland
                                                     dark red fluid, left inguinal.
     Microscopic Observations:
          Adrenal
                                                   -Sinusoidal ectasia, cortex, focal, unilateral,
          Kidney
                                                   -Chronic progressive nephropathy, mild
          Liver
                                                   -Hepatocyte vacuolation, multifocal, mild
          Luno
                                                   -Hemorrhage, multifocal, mild
          Mammary Sland
                                                   -Balactocele
                                                     Chronic inflammation and hemorrhage in cysts.
                                                   -Cyst, unilateral
          Dvary
          Pituitary
                                                   -Adenosa
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
                                                   -Hemprihage, 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.
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Species: Rat

Project Number: 0281CR0012

Sussarized STAR Page: 13



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 Interia

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 Liver

-Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild

Megalocytosis, moderate

Lung

Necrosis, focal, minimal -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 Liver

-Chronic progressive nephropathy, minimal -Portal mononuclear cell infiltrate, mild

Megalocytosis, mild Necrosis, multifocal, mild -Vascular mineralization, mild

Lung 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 Mode (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat

Project Number: 0281CR0012

Sussarized STAR Page: 14

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

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: -Not examined, missing Aorta -Portal mononuclear cell infiltrate, mild Liver Megalocytosis, mild -Vascular mineralization, mild Lung 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: IR-3592 Sex: Hale Group: (5) FC-143 300 ppm Fate: (Week= 53) 1 Year Interia 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 Alveolar macrophages, multifocal, mild 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, 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 Interia Sacrifice Macroscopic Observations: -No visible lesions.

Species: Rat

Project Number: 0281CR0012

Microscopic Observations:

Heart

Summarized STAR Page: 15

-Myocarditis, chronic nonsuppurative,

aultifocal, minimal

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

Table: 1

Group: (5) FC-143 300 ppm Sex: Male Animal Number: 1R-3598

Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Kidnev Liver

-Chronic progressive mephropathy, minimal -Portal mononuclear cell infiltrate, mild

Megalocytosis, minimal

Necrosis, multifocal, minimal

Lung

-Alveolar macrophages, multifocal, mild -Not examined, not in plane of section

Parathyroid

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 pps

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta

Heart Kidnev

Liver

Lung

Parathyroid Salivary Gland -Not examined, missing

-Myocardial fibrosis, focal, mild -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild

Megalocytosis, minimal Necrosis, multifocal, mild -Vascular mineralization, mild

Alveolar macrophages, multifocal, mild

Hemorrhage, local areas, mild -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, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 16

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

Table: i

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 -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

Microscopic Observations:

Kidney -Mineralization, multifocal, cortical

Pyelitis, acute, unilateral, mild
Liver -Megalocytosis, minimal

Lung —Alveolar macrophages, multifocal, mild Lymph Node (mesenteric) —Hemorrhage, minimal

Lyaph Node (mesenteric) -Hemorrhage, minimal -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

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

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 Kidney Liver -Not examined, missing

-Chronic progressive nephropathy, minimal -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 Interio Sacrifice

Macroscopic Observations:

Eye Testis -Ocular opacity, bilateral.

-Left testis small.

Microscopic Observations:

Eye Kidney Liver

Lung

-Cataract, bilateral

-Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, minimal

Megalocytosis, minimal

Pigment, Kupfer cell, brown, minimal -Vascular mineralization, minimal

Pneumonia, interstitial, chronic, multifocal,

aild

Lymph Node (mesenteric)

Parathyroid Prostate -Hemorrhage, mild

-Not examined, not in plane of section

-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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 18

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

Table: 1

Animal Number: 1R-3626 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 53) 1 Year Interia 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, intersititial, 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 Luna -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 -Hemorrhage, local areas, moderate Lung Lymph Node (mesenteric) -Not examined, missing

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 19

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 Prostate -Not examined, missing -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

-Nematodiasis

Large Intestine Liver

-Megalocytosis, mild

Lymph Node (mesenteric)

-Not examined, missing -Not examined, missing

Parathyroid 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: Hale 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 Liver -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild

Megalocytosis, moderate
Necrosis, multifocal, mild

Luna

Necrosis, multifocal, mild

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

mild

Perivascular mononuclear infiltrate, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 20



FC-143: Two Year Oral Toxicity-Encogenicity Study in Rats - One Year Interia

Table: 1

Broup: (5) FC-143 300 ppm Animal Number: 1R-3643 Sex: Male

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 Interia Sacrifice

Macroscopic Observations:

Eve Uterus

Microscopic Observations:

Eye

Kidney.

Large Intestine

Liver

Parathyroid

Uterus

-Atrophy, right eye.

-Both horns enlarged, filled with clear fluid.

-Panophthalmitis, unilateral, marked

Atrophy, unilateral, marked

-Chronic progressive nephropathy, mild

-Nematodiasis

-Hepatocyte vacuolation, multifocal, mild

-Not examined, not in plane of section

-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.

Sex: Female Group: (5) FC-143 300 ppm Animal Number: 1R-4652

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

Liver

Parathyroid

-Chronic progressive mephropathy, mild -Hepatocyte vacuolation, multifocal, mild

-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

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

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 Interia Sacrifice Macroscopic Observations: -No visible lesions. Microscopic Observations: Kidney -Chronic progressive nephropathy, mild Mineralization, multifocal, cortical, mild -Hepatocyte vacuolation, multifocal, mild Liver -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: Massary 61 and -Subcutaneous mass, 3.5 cm dia., left inquinal Microscopic Observations: -Hepatocyte vacuolation, multifocal, mild Liver 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

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

Table: i

Animal Number: 1R-4664 Sex: Female Group: (5) FC-143 300 ppm

Fate: (Week= 53) 1 Year Interia 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 Interia 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 Luna

Mammary Gland

-Hepatocyte vacuolation, multifocal, mild

-Hemorrhage, multifocal, mild

-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, Dvary, 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 Interia Sacrifice

Macroscopic Observations:

Massary Gland

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

Microscopic Observations:

Kidney

-Pelvic mineralization, mild Calculus, pelvic, mild

Species: Rat

Project Number: 0281CR0012

Sussarized STAR Page: 23

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

Table: 1

Sex: Female Group: (5) FC-143 300 ppm Animal Number: 1R-4671

Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Liver

Luna

Manmary Gland

Parathyroid

-Hepatocyte vacuolation, multifocal, minimal

-Hemorrhage, multifocal, mild

-Fibroadenoma

-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.

Sex: Female Group: (5) FC-143 300 ppm Animal Number: 1R-4674

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Aorta Esophagus Large Intestine

Lung Parathyroid

-Not examined, missing -Not examined, missing -Not examined, missing

-Hemorrhage, multifocal, mild

-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

Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Mammary Gland

-Two subcutaneous masses in both inquinal areas, 1.5 and 2 cm dia. Left side milk cyst, right side cyst filled with rust colored fluid.

Microscopic Observations:

Adrenal Heart

-Sinusoidal ectasia, cortex, mild

-Myocarditis, chronic nonsuppurative, focal,

mild

-Calculus, pelvic Kidney

-Hepatocyte vacuolation, multifocal, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 24

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

Animal Number: 1R-4676 Sex: Female Group: (5) FC-143 300 pps

Fate: (Week= 53) 1 Year Interim Sacrifice

Microscopic Observations (continued):

Mammary Gland

-Alveolar macrophages, multifocal, mild

-Salactocele

Galactocele

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

Kidney

-Bilateral marked hydronephrosis with numerous

calculi in the pelvic area.

Microscopic Observations:

Esophagus Kidney

Mammary Gland

Parathyroid

Urinary Bladder

Ureter

Uterus

-No diagnosis, inadequate section

-Hydronephrosis, bilateral, marked Pyelitis, chronic, moderate

-Not examined, missing

-Not examined, not in plane of section

-Calculus

Inflammation, chronic, diffuse, moderate

Dilatation, marked

-Epithelial hyperplasia, simple, diffuse, mild

Cystitis, chronic, diffuse, moderate

-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: 0281CR0012

Summarized STAR Page: 25

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

Table: 1

```
Animal Number: 1R-4689 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Neek= 53) 1 Year Interia Sacrifice
    Macroscopic Observations:
                                                 -Right eye atrophied.
         Eve
         Liver
                                                 -Pale tan in color.
         Lymph Node (mesenteric)
                                                 -Hemorrhagic
    Microscopic Observations:
         Adrenal
                                                 -Sinusoidal ectasia, cortex, mild
                                                 -Atrophy, unilateral, marked
         Eve
                                                 Panophthalmitis, chronic, unilateral, marked
                                                 -Hepatocyte vacuolation, multifocal, mild
         Liver
                                                 -Hemorrhage, local areas, mild
         Lung
                                                 -Hemorrhage, marked
         Lymph Node (mesenteric)
                                                 -Not examined, not in plane of section
         Parathyroid
         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 Interia Sacrifice
     Macroscopic Observations:
                                                 -No visible lesions.
     Microscopic Observations:
         Luna
                                                 -Hemorrhage, local areas, moderate
                                                 -Not examined, missing
         Lymph Node (mesenteric)
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, Bvary, 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
                                                 -Negatodiasis
         Large Intestine
                                                 -Hepatocyte vacuolation, multifocal, mild
         Liver
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 26

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

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 Interia Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

-Cortical degeneration, focal, unilateral,

aild

Liver

Lung

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

-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 Bland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 27

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

Table: 2

Animal Number: 18-3518 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Raised inflammed lesion on right rear Skin footpad. Microscopic Observations: -Cortical vacuolation, multifocal, mild Adrenal Medullary cell hyperplasia, multifocal, mild -Myocarditis, chronic nonsuppurative, Heart local areas, moderate -Chronic progressive nephropathy, minimal Kidney Pelvic mineralization, minimal -Portal mononuclear cell infiltrate, minimal Liver Portal bile duct proliferation, mild -Vascular mineralization, minimal Luna Pneumonia, interstitial, chronic, multifocal, Perivascular mononuclear infiltrate, moderate -Not examined, missing Parathyroid -Adenosa Pituitary -Pododermatitis, ulcerative, hindleg, marked Skin -Not examined, missing Thyroid 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. Group: (1) CONTROL 0 ppm Sex: Male Animal Number: 1R-3519 Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -No visible lesions. Microscopic Observations: -Sinuspidal ectasia, cortex, multifocal, mild Adrenal Cortical vacuolation, multifocal, mild -Not examined, missing Esophagus -Myocarditis, chronic nonsuppurative, Heart multifocal, mild -Chronic progressive nephropathy, mild Kidney -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, multifocal, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 28

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

Table: 2

Sex: Male Group: (1) CONTROL O pps Animal Number: 1R-3519

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

-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 O ppm

Fate: (Week= 92) Sacrificed in extremis

Macroscopic Observations:

Skin

Liver

Spleen

Microscopic Observations:

Adrenal

Heart Kidney Liver

Lung

Parathyroid

Skin Spleen

Stomach

-Both hind footpads ulcerated.

-Pale

-Enlarged

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

-Myocardial fibrosis, multifocal, mild -Chronic progressive nephropathy, moderate -Hepatocyte vacuolation, centrilobular,

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, local areas,

mild

Edema, local areas, mild Fibrosis, pleural, mild

Thrombus

-Not examined, missing

-Pododermatitis, ulcerative, hindleg, marked -Henatopoiesis, extramedullary, increased,

moderate

-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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 29

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

Table: 2

Animal Number: 18-3523 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.

-Wall edematous with possible ulceration in cardia.

Microscopic Observations:

Adrenal

Stosach

Heart Kidney Liver

Lung

Prostate Skin

Deactato

Stonach

-Cortical vacuolation, multifocal, mild

Sinusoidal ectasia, cortex, diffuse, mild -Myccardial fibrosis, multifocal, mild -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild

-Vascular mineralization, mild Hemorrhage, focal, mild Alveolar macrophages, mild

-Prostatitis, acute, suppurative, marked

-Fibrosarcoma, thorax

Well differentiated, highly cellular with

moderate collagen formation.

-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

Microscopic Observations:

Adrenal Kidney

Large Intestine Liver -Small red lesion.

-Medullary cell hyperplasia, multifocal, mild -Chronic progressive nephropathy, moderate

Pelvic mineralization, mild

-Nematodiasis, colon

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

Species: Rat

Project Number: 0281CR0012

Sugmarized STAR Page: 30

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

Animal Number: 18-3524 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice Microscopic Observations (continued): -Vascular mineralization, mild Lymph Node (mesenteric) -Not examined, missing -Not examined, not in plane of section Parathyroid -Adenoma Pituitary Thyroid -Follicular hyperplasia, cystic, unilateral, 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: IR-3525 Sex: Male Group: (1) CONTROL 0 ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: Rone -Joints of right forelimb and right hindlimb swollen. -Raised pale circular lesion, 2 cm dia., in Liver medial lobe. Microscopic Observations: -Cortical vacuolation, local areas, moderate Adrenal Bone -Arthritis, synovitis; joints, foreleg, hindleg, marked -Myocarditis, chronic nonsuppurative, Heart local areas, mild Kidney -Chronic progressive nephropathy, moderate -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild Hepatocellular carcinoma Large, poorly differentiated, anaplastic, infiltrative. Adenoid areas. Multiple tumor emboli in lung. Luna -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,

Species: Rat

Project Number: 02B1CR0012

Summarized STAR Page: 31

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

Table: 2

Animal Number: 1R-3525 Sex: Male Group: (1) CONTROL O 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 O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Liver -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild

-Vascular mineralization, mild

Lung

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 O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney

Microscopic Observations:

Adrenal

Kidney

Liver

Lung

Pituitary

-Hydronephrosis

-Cortical vacuolation, focal, mild

-Chronic progressive nephropathy, moderate Hydronephrosis, unilateral, moderate

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

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

mild

-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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 32

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

Table: 2

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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 O 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
     Microscopic Observations:
         Adrenal
                                                 -Cortical vacuolation, multifocal, mild
          Kidnev
                                                 -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 O ppm
Fate: (Week= 106) Terminal Sacrifice
    Macroscopic Observations:
                                                -No visible lesions.
    Microscopic Observations:
         Heart
                                                -Myocarditis, chronic nonsuppurative, focal,
         Kidnev
                                                -Chronic progressive nephropathy, mild
         Liver
                                                -Portal mononuclear cell infiltrate, mild
                                                 Portal bile duct proliferation, mild
                                                 Cystoid degeneration, focal, moderate
                                                 Hepatocyte alteration, vacuolated, mild
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 33

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

Table: 2

Animal Number: 1R-3530 Sex: Male Broup: (1) CONTROL 0 ppm

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lune

Spleen

-Vascular mineralization, mild

Peribronchial lymphoid hyperplasia, 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, 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 O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Liver

-Chronic progressive nephropathy, sild -Hepatocyte vacuolation, multifocal, mild Portal mononuclear cell infiltrate, minimal -Vascular mineralization, mild

Lung

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. _______________________________

Sex: Male Group: (1) CONTROL O ppm Animal Number: 18-3532

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary

Kidney

-Raised red mass, 0.4 cm dia.

-Fluid filled cyst, 1 cm dia., in right kidney

Microscopic Observations:

Eye Heart

Kidney

Liver

Lung

-Retinal atrophy, focal, mild -Myocardial fibrosis, focal, mild

-Chronic progressive mephropathy, moderate

Cyst, cortical, marked -Portal mononuclear cell infiltrate, mild

Portal bile duct proliferation, mild

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

Hemorrhage, local areas, mild

Perivascular mononuclear infiltrate, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 34

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

Animal Number: 1R-3532 Sex: Male Group: (1) CONTROL 0 ppm

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lymph Node (mesenteric)

Pituitary

Spleen

-Adenoma

-Hemosiderosis, mild

-Hemorrhage, 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, Fancreas, Salivary Bland.

Animal Number: 1R-3533 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Spleen

Microscopic Observations:

Eve Heart

> Kidney Liver

Lung

Prostate Spleen

-Pale circular depressed area, 0.4 cm dia.

Table: 2

-No diagnosis, inadequate section -Myocarditis, chronic nonsuppurative, multifocal, mild

-Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

Perivascular mononuclear infiltrate, mild -Prostatitis, acute, suppurative, mild

-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 O ppm

Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations:

Thypus Pancreas -Enlarged

-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

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 35

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

Table: 2

Animal Number: 1R-3534 Sex: Male Broup: (1) CONTROL O ppm

Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations (continued):

Pancreas (continued)

Kidnev

Testis/Epididymis

Liver

-Pale and pitted.

-liver lobes.

-Right testis small.

-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 mephropathy, moderate

Malignant lymphoma, histiocytic

Liver Lung

-Hepatocyte vacuolation, diffuse, earked -Hemorrhage, diffuse, marked

Malignant lymphoma, histiocytic

Lymph Node (mesenteric)

-Hemorrhage, mild

Malignant lymphoma, histiocytic -Malignant lymphoma, histiocytic Pancreas

Parathyroid

Pituitary Small Intestine

Spleen Stomach

Testis/Epididymis

-Not examined, missing -Adenoma

-Malignant lymphoma, histiocytic -Malignant lymphoma, histiocytic -Malignant lymphoma, histiocytic

-Tubule atrophy, aspermatogenesis, unilateral,

marked

Thyeus

-Malignant lymphoma, histiocytic Multiple sections of tumor from thymic and

mediastinal areas.

Thyroid

Urinary Bladder

-Not examined, missing -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 36

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

Table: 2

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Sex: Male Group: (1) CONTROL O ppm
Animal Number: 1R-3536
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
                                                -Chronic progressive nephropathy, minimal
         Kidney
      -Portal bile duct proliferation, multifocal,
                                                 mild
                                                 Portal mononuclear cell infiltrate, mild
                                                 Hepatocyte vacuolation, multifocal, minimal
                                                -Vascular mineralization, mild
         Lung
                                                 Perivascular mononuclear infiltrate, mild
                                                -Keratoacanthoma
         Skin
                                                  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 Bland, Eye, Urinary Bladder.
Animal Number: 1R-3537 Sex: Male Group: (1) CONTROL O 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 inquinal
                                                -Hemorrhagic mass, 0.7 cm dia.
         Pituitary
    Microscopic Observations:
         Eve
                                                -Not examined, missing
         Heart
                                                -Malignant lymphoma, histiocytic
                                                -Hepatocyte vacuolation, diffuse, marked
         Liver
                                                 Malignant lymphoma, histiocytic
                                                -Malignant lymphoma, histiocytic
         Luna
                                                 Hemorrhage, local areas, moderate
         Lyaph Node (mesenteric)
                                                -Not examined, missing
         Pancreas
                                                -Not examined, missing
                                                -Not examined, missing
         Parathyroid
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 37

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

Table: 2 Animal Number: 18-3537 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 73) Found Dead Microscopic Observations (continued): Pituitary -Adenona -Malignant lymphoma, histiocytic Skin Mass from inquinal area was malignant lymphoma. There was extensive necrosis in -Hemosiderosis, mild Soleen -Not examined, missing Thyroid 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. _____ Group: (1) CONTROL O ppm Animal Number: 1R-3538 Sex: Male Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Small hemorrhagic area, 0.2 cm dia. Pituitary -Multiple pale foci, all lobes. Liver -Enlarged Spleen Microscopic Observations: -Certical vacuolation, focal, mild Adrena1 -Chronic progressive nephropathy, mild Kidney -Malignant lymphoma, histiocytic Liver -Vascular mineralization, mild Lung Alveolar macrophages, mild Malignant lymphoma, histiocytic Perivascular mononuclear infiltrate, mild -Hemorrhage, minimal Lymph Node (mesenteric) Parathyroid -Not examined, not in plane of section -Prostatitis, acute, suppurative, marked Prostate -Malignant lymphoma, histiocytic Spleen -Epithelial hyperplasia, simple, diffuse, mild Urinary Bladder 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.

Species: Rat

Project Number: 0281CR0012

Sugmarized STAR Page: 38

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

Table: 2

Animal Number: 1R-3539 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney

Large Intestine

Liver

Lunc

-Nematodiasis, colon

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

-Chronic progressive nephropathy, mild

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

Perivascular mononuclear infiltrate, mild -Not examined, not in plane of section

Parathyroid -Cyst, pars distalis Pituitary -Hemosiderosis, mild Spleen 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 Bland, Eye.

Sex: Male Group: (1) CONTROL O ppm Animal Number: 1R-3540

Fate: (Week= 64) Found Dead

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Bone Marrow

Liver

Lung

Prostate Spinal Cord Thyroid Urinary Bladder

-Not examined, missing

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

-Vascular mineralization, mild Alveolar macrophages, mild

-Not examined, missing -Not examined, missing -Ultimobranchial cyst -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 39

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

Table: 2

Animal Number: 18-3541 Sex: Male Group: (1) CONTROL O ppe 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 Hemorrhage, diffuse, marked Perivascular mononuclear infiltrate, mild Prostate -Not examined, missing Skin -Pododermatitis, ulcerative, hindleg, marked Testis/Epididymis -Not examined, missing Uninary Bladder -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 Bland, Eye. Animal Number: 1R-3542 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: Testis/Epididymis -Both testes small. Microscopic Observations: Kidney -Chronic progressive mephropathy, moderate Liver -Hepatocyte vacuolation, multifocal, mild -Vascular mineralization, minimal Lung Lymph Node (mesenteric) -Hemorrhage, minimal Pancreas -Hyperplasia, islet cell, moderate Testis/Epididymis -Tubule atrophy, aspermatogenesis, bilateral, marked Polyarteritis, 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, Adrenal, Parathyroid, Trachea, Salivary Gland, Eye,
Esophagus.

-Not examined, missing

Species: Rat

Project Number: 02B1CR0012

Thyroid

Summarized STAR Page: 40

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

Table: 2 Animal Number: 1R-3544 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: Pituitary -Hemorrhagic lesion, 0.7 cm dia. -Both enlarged, pale and pitted. Kidney -Left testis small. Testis/Epididymis Microscopic Observations: -Cortical vacuolation, multifocal, moderate Adrenal Sinusoidal ectasia, cortex, moderate -Chronic progressive nephropathy, marked Kidnev -Hepatocyte vacuolation, multifocal, mild Liver -Vascular mineralization, mild Luna Alveolar macrophages, mild Pancreas -Acinar atrophy, mild Polyarteritis, moderate Parathyroid -Not examined, not in plane of section Pituitary -Adenoma Soleen -Hemosiderosis, mild Testis/Epididyais -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 O ppa Fate: (Week= 104) Found Dead Macroscopic Observations: -Circular lesions, 2.5 cm dia. on both hind Skin footpads. -Slightly pale Liver Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, moderate Cortical vacuolation, multifocal, moderate Eye -Not examined, missing Heart -Myocardial fibrosis, local areas, mild -Chronic progressive nephropathy, mild Kidney -Vascular mineralization, mild Lung Alveolar macrophages, mild -Acinar atrophy, moderate Pancreas

Species: Rat

Project Number: 0281CR0012

Pituitary

Summarized STAR Page: 41

205

-Adenoma

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

Table: 2 Animal Number: 1R-3545 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 104) Found Dead Microscopic Observations (continued): -Pododermatitis, ulcerative, hindleg, bilateral, marked Spleen -Hematopoiesis, extramefullary, 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, Eschhagus, Lyoph Node (mesenteric), Salivary Sland. ______ Animal Number: 18-3547 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 -Sinuscidal ectasia, cortex, moderate Brain -Oligodendroglioma, benigm Large necplasm composed of large, fairly uniform polyhedral cells in cerebral cortex. Kidney -Chronic progressive nephropathy, minimal Pyelônephritis, acute, mild -Portal mononuclear cell infiltrate, mild Liver 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 O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -No visible lesions.

Species: Rat

Project Number: 0281CR0012

Microscopic Observations:

Summarized STAR Page: 42

-Cortical vacuolation, multifocal, mild

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

Table: 2

Animal Number: 1R-3548 Sex: Male Group: (1) CONTROL O 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 O 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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 43

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

Table: 2 Group: (1) CONTROL 0 ppm Animal Number: 1R-3552 Sex: Male Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Circular raised lesion, 1.2 cm dia. Spleen Microscopic Observations: -Cortical vacuolation, multifocal, mild Adrenal Medullary cell hyperplasia, local areas, moderate -Chronic progressive nephropathy, moderate Kidney -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild -Vascular mineralization, mild Lung Pneumonia, interstitial, chronic, multifocal, aild Pancreas -Acinar atrophy, mild -Not examined, not in plane of section Parathyroid -Adenoma Pituitary -Prostatitis, acute, suppurative, mild Prostate -Hemandiosarcoma Spleen 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 Bland, Eye. Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 88) Found Dead Macroscopic Observations: -Left enlarged by a 1 cm dia. mass. Adrenal Microscopic Observations: -Sinuspidal ectasia, cortex, mild Adrenal Pheochromocytoma, benign, unilateral -Not examined, missing Eye -Myocarditis, chronic nonsuppurative, Heart multifocal, mild -Chronic progressive mephropathy, mild Kidney -Not examined, missing Large Intestine -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, moderate Hepatocyte vacuolation, multifocal, mild

Species: Rat

Project Number: 0281CR0012

Lymph Node (mesenteric)

Summarized STAR Page: 44

Necrosis, multifocal, mild -Vascular mineralization, mild -Not examined, missing

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

Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 88) Found Dead

Microscopic Observations (continued):

Pancreas Pituitary Salivary Gland Small Intestine -Not examined, missing -Cyst, pars distalis -Not examined, missing -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: 18-3554 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations: Kidney

Liver

Lung

-Chronic progressive nephropathy, moderate -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild -Alveolar macrophages, multifocal, moderate Perivascular mononuclear infiltrate, moderate

Table: 2

Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

moderate

-Not examined, not in plane of section Parathyroid -Prostatitis, acute, suppurative, moderate Prostate

The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Acrta, Testis/Epididymis, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lyaph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 18-3555 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 102) Sacrificed in extremis

Macroscopic Observations:

Kidney Urinary Bladder -Pale, enlarged; wild hydronephrosis. -Enlarged, fluid filled, wall appears

hemorrhagic.

Microscopic Observations:

Adrenal

-Cortical vacuolation, local areas, moderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 45

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 O 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 Parathyrpid -Not examined, not in plane of section Prostate -Prostatitis, acute, suppurative, mild Edema, intersititial, moderate Small Intestine -Within normal limits Fewer than protocol number Spleen -Hemosiderosis, mild Stomach -Edema, submucosal, moderate Uninary 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 Bland, Eye. Animal Number: 1R-3556 Sex: Male Group: (1) CONTROL O 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, wild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 46 210

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

Table: 2 Sex: Male Group: (1) CONTROL O pom Animal Number: 1R-3556 Fate: (Week= 106) Terminal Sacrifice Microscopic Observations (continued): -Pneumonia, interstitial, chronic, multifocal, Lung ∎ild Metastatic neoplasm Perivascular mononuclear infiltrate, mild Vascular mineralization, mild -Not examined, not in plane of section 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/Epididyeis, 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, 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 C ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Raised mass, 0.9 cm dia. Pituitary Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, mild -Chronic progressive nephropathy, mild Kidney Calculus, pelvic, minimal -Cystoid degeneration, focal, minimal

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 47

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

Table: 2

Animal Number: 1R-3558 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid

Pituitary Spleen

-Not examined, not in plane of section

-Adenona

-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.) -Dark red diffuse mottling, all lobes; red

frothy exudate at trachea.

-Pale, appears enlarged.

-Hepatic and renal nodes enlarged.

Lung

Spleen

Lymph Node (abdominal)

Liver

Microscopic Observations:

Brain

Liver Lung

Lymph Node (mesenteric) Small Intestine

Soleen

-Abscess, mild

-Enlarged

Hemorrhage, multifocal, moderate -Malignant lymphoma, histiocytic -Malignant lymphoma, histiocytic Hemorrhage, diffuse, marked Necrosis, local areas, marked

-Hemorrhage, minimal -Within normal limits

Fewer than protocol number

-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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 48

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

Table: 2 Animal Number: 1R-3561 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Right and left hindpaw and right forepaw Soft Tissues (leg) swollen. -Right kidney polycystic. Kidney Microscopic Observations: -Cortical vacuolation, multifocal, mild Adrenal Medullary cell hyperplasia, multifocal, mild Bone -Arthritis, synovitis; joints, hindleg, foreleg, marked Bone Marrow -Not examined, missing Kidney -Chronic progressive mephropathy, mild Pelvic mineralization, mild Cyst, cortical, unilateral, marked -Nematodiasis, colon Large Intestine -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild -Perivascular mononuclear infiltrate, mild Lung Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, Hemorrhage, local areas, moderate -Not examined, missing Parathyroid -Adenoma Pituitary Spinal Cord -Not examined, missing -Hemosiderosis, mild Spleen -Tubule atrophy, aspermatogenesis, moderate Testis/Epididymis 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 O ppm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Raised ulcerated inflammed lesion, right rear Skin footpad. -Several pale foci. Spleen

Species: Rat

Project Number: 0281CR0012

Microscopic Observations:

Adrenal

Summarized STAR Page: 49

-Nodular hyperplasia, cortex, unilateral,

213

moderate

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

Table: 2

Anigal 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

Preumonia, interstitial, chronic, mild Perivascular mononuclear infiltrate, mild

Parathyroid -Not examined, not in plane of section

Pituitary -Adenoma
Salivary Bland -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 O 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 spindelate.
-Myocarditis, chronic nonsuppurative.

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, local areas, moderate

Lung -Vascular mineralization, mild

Perivascular mononuclear infiltrate, mild

Pancreas -Acinar atrophy, marked

Pituitary -Adenoma

Prostate -Prostatitis, acute, suppurative, anderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 50

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

Table: 2

Animal Number: 1R-3563 Sex: Male Group: (1) CONTROL 0 pps

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Skin Thyroid -Keratoacanthoma, back -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 Bland, Eye.

Animal Number: 1R-3564 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney

Microscopic Observations:

Adrenal

Liver

Lung

-Pale area in cortex of one kidney.

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

noderate

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. Portal bile duct proliferation, mild

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

-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.

Species: Rat

· Project Number: 0281CR0012

Summarized STAR Page: 51 215

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

Table: 2

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Animal Number: 1R-3565 Sex: Male Group: (1) CONTROL O 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
         Aprta
                                                -Not examined, missing
                                               -Not examined, missing
         Esophagus
                                               -No diagnosis, inadequate section
         Ey₽
                                               -Chronic progressive nephropathy, mild
         Kidney
         Large Intestine
                                                -No diagnosis, inadequate section
         Liver
                                               -Hepatocyte vacuolation, multifocal, mild
                                                Necrosis, multifocal, moderate
                                               -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 O ppm
Fate: (Week= 106) Terminal Sacrifice
    Macroscopic Observations:
                                               -Small dark lesion.
         Pituitary
    Microscopic Observations:
         Adrenal
                                               -Nithin normal limits
                                               One of pair present
                                               -Chronic progressive nephropathy, wild
         Kidney
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 52

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

Group: (1) CONTROL 0 ppm Animal Number: 1R-3566 Sex: Male Fate: (Week= 106) Terminal Sacrifice Microscopic Observations (continued): -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild -Vascular mineralization, mild Lung Perivascular mononuclear infiltrate, mild -Polyarteritis, moderate Fancreas -Not examined, not in plane of section Parathyroid -Hemosiderosis, mild Spleen 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. Group: (1) CONTROL 0 pos Animal Number: 1R-3567 Sex: Male Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Raised papilloma type mass on back; raised Skin inflammed lesion, right rear footpad. -Two pale foci. Spleen Microscopic Observations: -Cortical vacuolation, multifocal, mild Adrenal Modular hyperplasia, cortex, focal, mild -Chronic progressive nephropathy, moderate Kidney -Portal mononuclear cell infiltrate, mild Liver

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.

-Vascular mineralization, mild

Alveolar nacrophages, minimal

-Necrosis, local areas, moderate

-Papilloma, back

Perivascular mononuclear infiltrate, minimal

Pododermatitis, ulcerative, hindleg, marked

Species: Rat

Project Number: 0281CR0012

Lung

Skin

Spleen

Summarized STAR Page: 53

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

Table: 2 Animal Number: 18-3569 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 Kidnev -Chronic progressive nephropathy, marked -Portal mononuclear cell infiltrate, mild Liver Hepatocyte vacuolation, multifocal, mild -Vascular mineralization, mild Lung Perivascular mononuclear infiltrate, mild -Hyperplasia, focal, pars distalis, mild Pituitary -Polyarteritis, moderate Testis/Epididyais 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: -Pale Liver Kidney -Pale, pitted, enlarged. -Mesenteric vessels thickened Mesentery Microscopic Observations: -Cortical vacuolation, focal, minimal Adrenal -Myocarditis, chronic nonsuppurative, Heart multifocal, minimal -Chronic progressive nephropathy, marked Kidney -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild -Vascular mineralization, mild Lung Perivascular mononuclear infiltrate, minimal Mesentery -Polyarteritis, marked -Polyarteritis, marked Pancreas -Not examined, not in plane of section Parathyroid -Not examined, missing Pituitary

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 54

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

Sex: Male Group: (1) CONTROL 0 ppm Animal Number: 1R-3571

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Small Intestine

-Polyarteritis, mesentery, marked

Table: 2

Spleen Testis/Epididymis

-Hemosiderosis, mild -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 O ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney Liver

-Chronic progressive nephropathy, minimal -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild -Vascular mineralization, mild

Lung Pancreas Parathyroid Stomach

-Hyperplasia, islet cell, moderate -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, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Bland, Eye.

Animal Number: 1R-3573 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pancreas

Microscopic Observations:

Adrenal

Kidney

Large Intestine

Liver

-Small circular pale mass, 0.5 cm dia.

-Cortical vacuolation, multifocal, mild Pheochromocytoma, benign, unilateral -Chronic progressive nephropathy, mild

-Nematodiasis, colon

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

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 55

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

Animal Number: 1R-3573 Sex: Male Sroup: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung -Vascular mineralization, mild

Perivascular mononuclear infiltrate, mild

Table: 2

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,
Aprta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Trachea, Esophagus,
Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 99) Bacrificed 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

Unitorm 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

Portal bile duct proliferation, mild -Pneumonia, interstitial, chronic, diffuse,

moderate

Perivascular mononuclear infiltrate, mild

Edema, local areas, marked

Lyaph Node (mesenteric) -Not examined, missing

Pancreas —Acinar atrophy, mild

Parathyroid -Not examined, not in plane of section

Species: Rat

Project Number: 0281CR0012

Lung

Summarized STAR Page: 56

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

Table: 2

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL O ppm Fate: (Week= 99) Sacrificed in extremis Microscopic Observations (continued): Pituitary -Cyst, pars intermedia Prostate -Prostatitis, acute, suppurative, moderate -Not examined, missing Salivary Gland Skin -Fibroma, subcutaneous, inquinal Pododernatitis, ulcerative, hindleg, marked Testis/Epididymis -Tubule atrophy, aspermatogenesis, bilateral, 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 O 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 Liver No fisible legions:

-Chronic progressive mephropathy, moderate
-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Hepatocyte vacuolation, multifocal, mild
Cystoid degeneration, multifocal, mild
Hepatocyte alteration, vacuolated, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 57

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

Table: 2

Animal Number: 1R-3577 Sex: Male Group: (1) CONTROL O ppm

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

-Vascular mineralization, mild -Polyarteritis, marked Mesenterv -Polyarteritis, marked Pancreas

-Polyarteritis, mesentery, moderate Small Intestine

-Hemosiderosis, mild Soleen -Cyst, colloid, mild Thyroid

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: 18-3578 Sex: Male Group: (1) CONTROL 0 pps

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-Hemorrhagic mass, 0.7 cm dia. Pituitary Skin

-Raised ulcerated inflammed lesion, 1.5 cm dia., left hind footpad.

Microscopic Observations:

-Chronic progressive nephropathy, mild Kidney Hydronephrosis, unilateral, moderate

Calculi present in wreter of hydronephrotic

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

-Vascular mineralization, mild

Lung Hemorrhage, local areas, moderate

-Adenona Pituitary

-Prostatitis, acute, suppurative, moderate Prostate

-Sialademitis, chronic, minimal Salivary Gland

Very minimal lesion, only one duct affected. -Pododermatitis, ulcerative, hindleg, marked Skin

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.

Species: Rat

Project Number: 0281CR0012

222 Summarized STAR Page: 58

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

Table: 2

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Animal Number: 1R-3579 Sex: Male Group: ( 1) CONTROL O ppm
Fate: (Week= 86) Sacrificed in extremis
     Macroscopic Observations:
                                                  -Raised mass, 0.8 cm dia.
          Pituitary
                                                   -Raised pale 2 cm dia. mass in right lateral
          Liver
                                                    lobe.
                                                   -Mass seen clinically on right side appears to
          Skin
                                                    be healed lesion.
     Microscopic Observations:
                                                   -Chronic progressive nephropathy, marked
          Kidney
                                                   -Portal bile duct proliferation, mild
          Liver
                                                    Hepatocellular carcinoma
                                                    Portal mononuclear cell infiltrate, mild
                                                   -Perivascular mononuclear infiltrate, mild
          Lung
                                                   -Not examined, not in plane of section
          Parathyroid
          Pituitary
                                                   -Adenosa
                                                   -Keratoacanthoma
          Skin
                                                    Skin lesion from right side.
                                                   -Within normal limits
          Small Intestine
                                                   Fewer than protocol number
                                                   -Hemosiderosis, mild
          Soleen
                                                   -Tubule atrophy, aspermatogenesis, unilateral,
          Testis/Epididymis
                                                    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 Broup: ( 1) CONTROL O ppm
Fate: (Week= 25) Sacrificed in extremis
     Macroscopic Observations:
                                                   -Enlarged; mottled yellow color.
                                                   -Enlarged
          Lymph Node (bronchial)
                                                   -Pale
          Lung
                                                   -Enlarged
          Spleen
                                                   -Red patchy areas on aucosa.
          Stomach
                                                   -Enlarged and reddened.
          Lyeph Node (mesenteric)
     Microscopic Observations:
                                                   -Sinuspidal ectasia, cortex, mild
          Adrenal
                                                   -Malignant lymphoma, lymphocytic
          Bone Marrow
                                                   -Malignant lymphoma, lymphocytic
          Kidney
                                                   Mineralization, cortical, mild
```

Species: Rat

Project Number: 02B1CR0012

Summarized STAR Page: 59

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

Table: 2

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Animal Number: 1R-4576 Sex: Female Group: ( 1) CONTROL O ppm
Fate: (Week= 25) Sacrificed in extremis
     Microscopic Observations (continued):
                                                -Malignant lymphoma, lymphocytic
         Liver
                                                -Malignant Lymphoma, lymphocytic
         Luno
                                                 Hemorrhage, multifocal, mild
                                                -Malignant lymphoma, lymphocytic
          Lymph Node (mesenteric)
                                                -Malignant lymphoma, lymphocytic
          Pancreas.
                                                -Not examined, missing
          Salivary Gland
                                                -Malignant lymphoma, lymphocytic
         Spinal Cord
                                                -Malignant lymphoma, lymphocytic
          Spleen
          Stomach
                                                -Epithelial hyperplasia, simple, diffuse, mild
          Urinary Bladder
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:
                                                 -Hemorrhagic mass, O.B cm dia.
          Pituitary
                                                 -Multilobular mass, 4.5 x 3.5 x 2 cm, in right
          Manmary Gland
                                                   axilla.
      Microscopic Observations:
                                                 -Sinusoidal ectasia, cortex, moderate
          Adrenal
                                                 -Pelvic mineralization, mild
          Kidney
                                                  Nephrosis, tubular, marked
                                                 -Portal mononuclear cell infiltrate, mild
          Liver
                                                  Portal bile duct proliferation, mild
                                                  Hepatocyte vacuolation, multifocal, mild
                                                 -Not examined, missing
          Lymph Node (mesenteric)
                                                 -Lobular hyperplasia
          Mammary Gland
                                                 -Hemorrhage, marked
          Pituitary
                                                  Necrosis, moderate
                                                 -Hemosiderosis, mild
           Spleen
                                                 -Cystic glands, moderate
          Uterus
 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.
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 60

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

Table: 2 Animal Number: 1R-4579 Sex: Female Broup: (1) CONTROL O ppm Fate: (Week= 84) Sacrificed in extremis Macroscopic Observations: -Raised mass, 0.5 cm dia. Pituitary -Raised thickened lesion with scab on right Skin side. -Slightly pale Liver -Somewhat reddened Stomach -Fluid filled cyst in left kidney. Kidney Microscopic Observations: Adresal -Sinusoidal ectasia, cortex, wild Aorta -Mineralization, multifocal, mild Heart -Myocarditis, chronic nonsuppurative, multifocal. moderate -Nephrosis, tubular Kidney Pelvic mineralization, marked Cyst. cortical, moderate Hyperplasia, pelvic epithelium, diffuse, mild -Hepatocyte vacuolation, multifocal, mild Liver -Vascular mineralization, mild Lung -Not examined, missing Lymph Node (mesenteric) -Not examined, not in plane of section Parathyroid Pituitary -Adenona -Ulcer, marked Skin Skin lesion from side. -Hemosiderosis, mild Spleen -Mineralization, aucosal, mild Stomach The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Small Intestine, Large Intestine, Urinary Bladder, Uterus, Ovary, Mammary Sland, Trachea, Thyroid, Esophagus, Pancreas, Salivary Bland, Eye. _____ Sex: Female Group: (1) CONTROL 0 ppm Animal Number: 18-4580 Fate: (Week= 52) Sacrificed in extremis Macroscopic Observations: -Enlarged; dark red mass, 0.5 cm dia. Pituitary Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, mild Aortá -Not examined, missing -Not examined, missing Esophagus -Not examined, missing Lymph Node (mesenteric) Mammary Gland -Galactocele Parathyroid -Not examined, not in plane of section

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 61

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 Bland, Eye.

Animal Number: IR-4581 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland

-Ulcerated mass, 6 x 6 x 3 cm behind right

shoulder.

Liver Soleen -Possibly slightly pale and swollen.

-Enlarged

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex

Liver

-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, basophilic, mild

Hematopoiesis, extramedullary, mild -Vascular mineralization, mild

Lung

Pneumonia, interstitial, chronic, multifocal,

mild

Mammary Sland -Adenocarcinoma

Parathyroid Spleen -Not examined, not in plane of section -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 Bland, Eye.

Animal Number: 1R-45B3 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye

-Extensive post bleeding inflammation of right

eye.

Manuary Gland

-Firm nodular mass, 6 x 5 x 3 cm, left

inguinal.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 62

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

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

Table: 2

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 O 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 -Phthsis bulbi, anderate

Heart -Myocarditis, chronic nonsuppurative,

multifocal, mild

Kidney -Chronic progressive mephropathy, mild

Liver -Portal bile duct proliferation, mild

Hepatocyte vacuolation, multifocal, mild

-Pneumonia, interstitial, chronic, multifocal,

mild Perivascular mononuclear infiltrate, mild

Hemorrhage, local areas, mild

Parathyroid -Not examined, not in plane of section

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 63

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

Table: 2 Animal Number: 1R-4584 Sex: Female Broup: (1) CONTROL 0 pps Fate: (Week= 105) Terminal Sacrifice Microscopic Observations (continued): -Adenoma Pituitary -Hemosiderosis, mild Spleen 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 O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: Pituitary -Raised dark mass, 0.3 cm dia. -Dark area, 0.5 x 0.5 cm, in left horn near Uterus cervix. Microscopic Observations: -Sinusoidal ectasia, cortex, mild Adrenal -Chronic progressive nephropathy, mild Kidney Pelvic mineralization, mild -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild -Perivascular mononuclear infiltrate, minimal Luna -Not examined, missing Overv Pancreas -Acinar atrophy, moderate -Not examined, not in plane of section Parathyroid -Adenoma Pituitary -Cystic clands, marked Uterus 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:

Species: Rat

Project Number: 0281CR0012

Maggary Gland

Summarized STAR Page: 64

-Small nodular mass, 3 x 2 cm, axillary; large

mass. 8 x 8 x 3 cm. throat area.

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

Table: 2

Sex: Female Group: (1) CONTROL O ppm Animal Number: 18-4587 Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal Heart

-Sinusoidal ectasia, cortex, marked -Myocarditis, chronic nonsuppurative, multifocal, mild

Kidney

-Chronic progressive nephropathy, mild Pelvic mineralization, minimal

Liver

Massary Sland Parathyroid Salivary Gland

Skin Soleen Uterus

-Hepatocyte vacuolation, multifocal, minimal -Lobular hyperplasia

-Not examined, not in plane of section -Not examined, missing

-Fibroma, subcutaneous -Heapsiderosis. mild -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, Brinary Bladder, Aorta, Ovary, Pituitary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-4591 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

Kidney Liver

Lung Lymph Node (mesenteric)

Pancreas Parathyroid Pituitary

-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, minimal -Chronic progressive mephropathy, minimal -Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild

-Vascular mineralization, mild

-Not examined, missing

-Acinar atrophy, focal, minimal -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, Trachea, Thyroid, Esophagus, Salivary Gland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 65

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= 8B) Found Dead

Macroscopic Observations:

Pituitary

-Enlarged, 0.9 x 1 cm.

Microscopic Observations:

Adrenal Kidnev Liver Lung

-Sinusoidal ectasia, cortex, moderate -Chronic progressive mephropathy, minimal -Hepatocyte vacuolation, multifocal, mild

-Vascular mineralization, mild

Perivascular mononuclear infiltrate, mild

Lymph Node (mesenteric) Mammary Gland Parathyroid Pituitary Spleen

-Not examined, missing -Lobular hyperplasia, moderate -Not examined, not in plane of section

-Adenoma

-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: 18-4593 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal Liver

-Sinusoidal ectasia, cortex, marked -Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild

Lunc Parathyroid -Vascular mineralization, mild -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 66

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

Table: 2

Animal Number: 1R-4594 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 79) Found Dead

Macroscopic Observations:

Kidney

Urinary Bladder

Pituitary

Microscopic Observations:

Adrenal

Aorta

Kidney

Liver Lune

Lymph Node (mesenteric)

Ovary

Pancreas

Parathyroid Pituitary

Small Intestine

Spleen Urinary Bladder

-Right kidney appears slightly enlarged; filled with yellow milky fluid.

-Enlarged, 4.5 x 2 cm; filled with large, hard

calculi.

-Hemorrhagic mass, 0.9 x 0.6 cm

-Sinusoidal ectasia, cortex, moderate

One of pair present -Not examined, missing

-Pyelonephritis, acute, bilateral, moderate Hydronephrosis, bilateral, moderate Nephrosis, tubular, bilateral, moderate -Hepatocyte alteration, vacuolated, mild

-Vascular mineralization, mild

-Not examined, missing -Within normal limits One of pair present -Not examined, missing

-Not examined, not in plane of section

-Adenoma

-Not examined, missing -Hemosiderosis, moderate

-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 O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary Mammary Sland -Hemorrhagic mass, 0.8 cm dia.

-Small lobular mass, 2.7 x 1.5 x 1.8 cm, left

Pancreas

-Small lobular mass, 1 x 0.7 cm, in area of

pancreas.

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, moderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 67

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

Sex: Female Group: (1) CONTROL O ppm Animal Number: 18-4595

Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Kidney

Liver

Mammary Gland Pancreas

Parathyroid Pituitary Uterus

-Chronic progressive nephropathy, minimal

Table: 2

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

-Alveolar macrophages, mild -Lobular hyperplasia

-Islet cell carcinoma

-Mass, 0.8 x 0.6 cm.

-Pale, bilaterally

-Very pale

Partially encapsulated with invasion of capsule. Well differentiated. -Not examined, not in plane of section

-Adenoma -Adenoma

Small circumscribed papillary lesion.

-Mass, 2.5 x 2 x 1.5 cm, in left axilla.

-Bilaterally pale and pitted; slightly

-Cortical vacuolation, focal, moderate

enlarged; 0.4 cm dia. cyst in right.

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, Thyrold, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye, Ovary.

Animal Number: IR-4596 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 78) Sacrificed in extremis

Macroscopic Observations:

Pituitary

Mammary Gland

Liver Kidney

Aorta

Kidney

liver

Adrenal Microscopic Observations:

Adcenal

Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild Cortical degeneration, local areas, moderate

-Mineralization, mild Mineralization also in media of an elastic artery in section of mesentery submitted for mesenteric lymph node.

-Chronic progressive nephropathy, marked

Cyst, cortical, moderate

-Hepatocyte vacuolation, diffuse, marked

Species: Rat

Project Number: 0281CR0012

232 Summarized STAR Page: 68

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

Table: 2

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Anigal Number: 1R-4596 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 78) Sacrificed in extremis
    Microscopic Observations (continued):
                                                  -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 Bland
                                                  -Not examined, missing
                                                  -Hemosiderosis, moderate
         Soleen
                                                  -Epithelial hyperplasia, simple, diffuse, mild
         Urinary Bladder
```

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 O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations: Adrenal -Right adrenal enlarged. Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, marked Medullary cell hyperplasia, focal, mild -Chronic progressive nephropathy, minimal Kidney Pelvic mineralization, mild -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild -Alveplar macrophages, mild Luna Perivascular mononuclear infiltrate, mild Lymph Node (mesenteric) -No diagnosis, inadequate section -Tubular adenoma, unilateral Ovary -Cyst Pancreas Parathyroid -Not examined, not in plane of section -Hemosiderosis, mild Spleen

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Masmary Gland, Pituitary, Trachea, Thyroid, Esophagus, Salivary Gland,
Eye.

-Within normal limits
Fewer than protocol number

Species: Rat

Project Number: 0281CR0012

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Summarized STAR Page: 69 233

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

Table: 2

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_____
Animal Number: 1R-4598 Sex: Female Group: (1) CONTROL O ppm
Fate: (Week= 105) Terminal Sacrifice
    Macroscopic Observations:
        Pituitary
                                              -Mass, 0.7 cm dia.
                                              -Left adrenal greatly enlarged.
         Adrenal
    Microscopic Observations:
         Adrenal
                                              -Sinusoidal ectasia, cortex, marked
         Brain
                                              -Oligodendroglioma, benign
                                              -Myocarditis, chronic nonsuppurative,
        Heart
                                               aultifocal, mild
                                              -Chronic progressive nephropathy, moderate
        Kidney
                                               Pelvic mineralization, mild
                                               Hyperplasia, pelvic epithelium, local areas,
                                              -Hepatocyte vacuolation, multifocal, mild
        Liver
                                               Hepatocyte alteration, basophilic, mild
                                              -Vascular mineralization, mild
        Lung
                                               Perivascular mononuclear infiltrate, mild
                                              -Tubular adenoma
         Ovary
                                              -Acinar atrophy, moderate
         Pancreas
                                              -Not examined, not in plane of section
         Parathyroid
         Pituitary |
                                              -Cystic glands, moderate
         Uterus
The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Aprta, 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:
                                              -Subcutaneous mass, 2.5 x 2 x 1 cm, in
         Mammary Gland
                                                perineal area.
                                              -Appears mottled
         Liver
                                              -Areas of enlongated ulceration.
         Stomach
                                             -Thickened walls; mass 1.5 x 1 cm, with
         Urinary Bladder
                                               adhesions to abdominal wall.
                                              -No tissue taken due to postmortem changes
         Eye
    Microscopic Observations:
                                              -Sinusoidal ectasia, cortex, marked
         Adrenal
                                              -Malignant lymphoma, histiocytic
         Aorta
                                              -Malignant lymphoma, histiocytic
         Esophagus
                                              -Not examined, missing
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 70 234

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

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Table: 2
                         Sex: Female Group: (1) CONTROL 0 pps
Animal Number: 1R-4599
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
                                                -Malignant lymphoma, histiocytic
         Liver
                                                 Necrosis, local areas, marked
         Lung
                                                -Malignant lymphoma, histiocytic
                                                Hemorrhage, multifocal, mild
                                                -Malignant lymphoma, histiocytic
         Lymph Node (mesenteric)
         Mammary Gland
                                                -Malignant lymphoma, histiocytic
         Ovary
                                                -Malignant lymphoma, histiocytic
         Pancreas
                                                -Malignant lymphoma, histiocytic
         Parathyroid
                                                -Not examined, not in plane of section
         Pituitary
         Spleen
                                                -Remosiderosis, mild
                                                -Necrosis, aucosal, moderate
         Stomach
                                                -Malignant lymphoma, histiocytic
         Thyroid
                                                -Malignant lymphoma, histiocytic
         Uninary Bladder
                                                 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 O 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
                                                -Not examined, missing
         Eye
                                               -Myocarditis, chronic nonsuppurative,
         Heart
                                                multifocal, mild
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 71

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

Table: 2 Animal Number: 1R-4600 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 99) Found Dead Microscopic Observations (continued): -Chronic progressive nephropathy, mild Kidney 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 -Vascular mineralization, mild Lung Mammary Gland -Adenoma, papillary Lobular hyperplasia -Cyst, unilateral Ovary Parathyroid -Not examined, not in plane of section -Adenoma Pituitary -Hemosiderosis, mild Soleen 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. Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: -Cornea appears cloudy. Eye Pituitary -Raised mass, 1 cm dia. Adrenal -Right adrenal enlarged. Kidney -Pale and pitted. Microscopic Observations: -Sinusoidal ectasia, cortex, marked Adrenal Cortical decemeration, diffuse, marked -No diagnosis, inadequate section Eve -Myocarditis, chronic nonsuppurative, Heart multifocal, mild -Chronic progressive nephropathy, marked Kidney Pelvic mineralization, mild Cyst, cortical Liver -Hepatocyte alteration, basophilic, mild -Hemorrhage, local areas, moderate Lung -Not examined, not in plane of section Parathyroid

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 72

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

Table: 2

Animal Number: (R-4602 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Spleen Uterus

-Hemosiderosis, mild -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 O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Liver

lateral lobe.

Skin

Microscopic Observations:

Adrenal

Heart

Kidney

Liver

Lung

Mammary Sland Parathyroid

Pituitary

Skin Spleen -Circular raised lesion, 0.6 cm dia., left

-Hair loss on forelimbs.

-Sinuspidal ectasia, cortex, moderate Cortical degeneration, diffuse, moderate -Myocarditis, chronic nonsuppurative,

multifocal, mild

-Pelvic mineralization, mild

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

-Galactocele

-Not examined, not in plane of section

-Adenosa

-Acanthosis. 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, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 73

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

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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
          Anrta
                                                   -Not examined, missing
                                                   -Not examined, missing
          Escohagus
          Kidnev
                                                   -Chronic progressive mechropathy, mild
                                                   Pelvic mineralization, mild
                                                   -Not examined, missing
          Large Intestine
                                                   -Portal bile duct proliferation, mild
         Liver
                                                    Hepatocyte vacuolation, multifocal, mild
                                                    Hyperplastic nodule
                                                   -Cyst, unilateral
          Ovary
                                                   -Not examined, not in plane of section
          Parathyroid
          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,
                          Sex: Female Group: (1) CONTROL O ppm
Animal Number: IR-4605
Fate: (Week= 77) Sacrificed in extremis
     Macroscopic Observations:
                                                   -Slightly pitted
          Kidney
                                                   -Right apical lobe consolidated and somewhat
          Lung
                                                     enlarged; possibly tumor, mass,
                                                     chronic pneumonia.
     Microscopic Observations:
          Adrenal
                                                   -Necrosis, local areas, moderate
                                                    Hematopoiesis, extramedullary, multifocal,
          Heart
                                                   -Myocarditis, chronic nonsuppurative,
                                                    multifocal, moderate
                                                    Malignant lymphoma, lymphocytic
                                                   -Chronic progressive mephropathy, moderate
         Kidney
                                                    Pelvic mineralization, minimal
                                                   -Hepatocyte vacuolation, midzonal, moderate
         Liver
                                                    Malignant lymphoma, lymphocytic
          Lung
                                                   -Vascular mineralization, mild
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 74

Malignant lymphoma, lymphocytic

necrosis.

Large circumscribed mass with extensive

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

Sex: Female Group: (1) CONTROL 0 ppm Animal Number: 1R-4605

Fate: (Week= 77) Sacrificed in extremis

Microscopic Observations (continued):

-Cyst, unilateral Ovary

Parathyroid -Not examined, not in plane of section

Pituitary -Adendaa

Spinal Cord -Malacia, local areas, moderate

Soleen -Hemosiderosis, mild

-Epithelial hyperplasia, simple, diffuse, Urinary Bladder

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 Bland, Eye.

Animal Number: 1R-4606 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-Small mass, 1.4 cm dia., left lateral area. Mammary Gland Pituitary -Enlarged; circular dark lesion, 0.4 cm dia. Uterus

-Dark fluid filled lesion, 0.5 x 0.6 cm, right

Table: 2

horn.

Microscopic Observations:

Heart

Adrenal -Sinuspidal ectasia, cortex, mild

Cortical degeneration, bilateral, moderate

Pheochromocytoma, benign, unilateral -Myocarditis, chronic nonsuppurative,

multifocal, mild

Kidney -Chronic progressive nephropathy, mild

Pelvic mineralization, mild

-Hepatocyte vacuolation, multifocal, mild Liver

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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 75

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

Table: 2

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Sex: Female Group: (1) CONTROL 0 ppm
Animal Number: 1R-4506
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.
                           Sex: Female Group: ( 1) CONTROL 0 ppm
Animal Number: 18-4607
Fate: (Week= 40) Sacrificed in extremis
     Macroscopic Observations:
                                                   -Reddened gland like structures, possibly
          Soft Tissues (neck)
                                                     enlarged lymph nodes or salivary
                                                     clands.
                                                    -Enlarged axillary, hepatic, mesenteric and
          Lyaph Node
                                                     internal iliac lymph nodes.
                                                    -Possibly slightly pale.
          Liver
                                                   -Considerably enlarged.
          Spleen
     Microscopic Observations:
                                                    -Malignant lymphoma, lymphocytic
          Adrenal
                                                    -Malignant lymphoma, lymphocytic
           Aorta
                                                    -Malignant lymphoma, lymphocytic
           Bone Marrow
                                                    -No diagnosis, inadequate section
           Esophagus
                                                    -Malignant lymphoma, lymphocytic
           Eye
                                                    -Malignant lymphoma, lymphocytic
           Kidney
                                                    -Malignant lymphoma, lymphocytic
           Liver
                                                    -Malignant lymphoma, lymphocytic
           Lung
                                                     Hemorrhage, local areas, mild
                                                     Abscess
                                                    -Hemorrhage, moderate
           Lymph Node (mesenteric)
                                                     Malignant lymphoma, lymphocytic
                                                      Massive enlargment of node by mature
                                                      appearing lymphocytes. All other nodes
                                                      examined were similarily involved.
                                                     -Malignant lymphoma, lymphocytic
           Manmary Gland
                                                    -Malignant lymphoma, lymphocytic
           Ovary
                                                     -Not examined, not in plane of section
           Parathyroid
                                                     -Not examined, missing
           Salivary Gland
                                                     -Malignant lymphoma, lymphocytic
           Soleen
                                                     -Hemorrhage, submucosal, moderate
           Stomach
                                                     Malignant lymphoma, lymphocytic
                                                     -Malignant lymphoma, lymphocytic
           Thyroid
                                                     -Malignant lymphoma, lymphocytic
           Uterus
  The following tissues were found to be within normal limits:
 Brain, Spinal Cord, Heart, Small Intestine, Large Intestine, Urinary Bladder, Pituitary,
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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 76

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

Animal Number: 1R-4607 Sex: Female Group: (1) CONTROL O 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 O pom 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:

Lung

Adrenal -Sinusoidal ectasia, cortex, moderate Heart -Myocarditis, chronic nonsuppurative, multifocal, mild

Kidney -Chronic progressive nephropathy, mild Pelvic mineralization, moderate

Large Intestine -Not examined, missing

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

Hepatocyte vacuolation, multifocal, mild -Pneumonia, interstitial, chronic, multifocal,

Table: 2

mild Mannary Gland -Carcinoma

Highly cellular very undifferentiated tumor.

Pancreas -Acinar atrophy, moderate

Parathyroid -Not examined, not in plane of section

Pituitary -Adenoma

Spleen -Hemosiderosis, mild -C cell adenoma Thyroid 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.

Species: Rat

Project Number: 0281CR0012

241 Summarized STAR Page: 77

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

Table: 2

Animal Number: 1R-4611 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland

-Large lobular mass, 10 x 7.5 x 5 cm.

Microscopic Observations:

Adrenal

Liver

-Sinusoidal ectasia, cortex, marked

Cortical degeneration, local areas, moderate

-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, eosinophilic, mild

-Hemorrhage, multifocal, mild _..._Lung ... _...

Alveolar macrophages, multifocal, mild

-Fibroadenoma

Mammary Gland -Not examined, not in plane of section Parathyroid

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 Bland, Eye.

Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary

Mammary Gland

-Raised mass, 0.7 cm dia.

-Mass, 3 cm dia., left axilla; 4 cm dia.,

right axilla;

 $7 \times 6 \times 2$ cm, right side.

Microscopic Observations:

Adrenal Eve

Liver

Lung

Uterus

-Sinusoidal ectasia, cortex, moderate

-No diagnosis, inadequate section

-Hepatocyte vacuolation, multifocal, mild

-Hemorrhage, diffuse, marked Alveolar macrophages, mild

-Balactocele Mammary Gland

Fibroadenosa Fibroadenoma

Two tumors present.

Parathyroid Pituitary

-Not examined, not in plane of section

-Adenoma

-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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 78

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

Table: 2

Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL Oppm 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 Bland.

Animal Number: 1R-4613 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 89) Sacrificed in extremis

Macroscopic Observations:

Pituitary Mammary Gland

Mammary Gland

Liver

Microscopic Observations:
Adrenal

Esophagus Kidnev

Kidney

Large Intestine

Liver

Lung

Mammary Bland Parathyroid Pituitary

Spleen

Urinary Bladder

Uterus

-Somewhat enlarged

-Mass, 10 x 8 x 5 cm, inguinal area; surface ulcerated.

-Appears pale

-Hematopoiesis, extramedullary, mild Sinusoidal ectasia, cortex, mild Cortical vacuolation, focal, mild

-Not examined, missing -Pelvic mineralization, mild

Hyperplasia, pelvic epithelium, local areas,

mild

-Not examined, missing

-Hepatocyte vacuolation, periportal, mild

Necrosis, multifocal, mild Hematopoiesis, extramedullary, mild

-Henorrhage, multifocal, mild

Pneumonia, interstitial, chronic, multifocal,

mild

-Lobular hyperplasia ,

-Not examined, not in plane of section

-Adenoma

-Hematopoiesis, extramedullary, increased,

moderate

-Epithelial hyperplasia, simple, diffuse, mild

-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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 79

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

Table: 2 Animal Number: 1R-4614 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: Mammary Gland -Mass in perineal area; possible milk cyst. -Large gelatinous cervical mass, 2 cm dia. literus Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, moderate Kidnev -Pelvic mineralization, minimal Chronic progressive mephropathy, mild -Hepatocyte vacuolation, multifocal, mild Liver Mammary Gland -Adenocarcinosa -Acinar atrophy, mild Pancreas Parathyroid -Not examined, not in plane of section Pituitary -No diagnosis, inadequate section Spinal Cord -Hemosiderosis, mild Spleen 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. Sex: Female Group: (1) CONTROL 0 ppm Animal Number: 1R-4615 Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: -No visible lesions. Microscopic Observations: -Sinusoidal ectasia, cortex, marked Adrenal 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 -Not examined, not in plane of section Parathyroid Soleen -Hemosiderosis, mild

Species: Rat

Project Number: 0281CR0012

Uterus

Summarized STAR Page: 80 244

-Within normal limits

Fewer than protocol number

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

Table: 2

Animal Number: 1R-4615 Sex: Female Group: (1) CONTROL O ppa

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 O ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

Heart

Kidney

Liver

Lung

Mammary Gland Ovary Parathyroid Spleen

-Cortical degeneration, unilateral, marked -Myocardial fibrosis, focal, mild Myocarditis, chronic nonsuppurative, multifocal, mild

-Chronic progressive nephropathy, mild Pelvic mineralization, minimal

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

Vascular mineralization, mild

Alveolar macrophages, mild -Not examined, missing -Cyst, unilateral

-Not examined, not in plane of section

-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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 81

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

Liver

-Hemorrhagic mass, 5 cm dia., left ovary. -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

Mammary Gland

Ovary

-Vascular mineralization, mild

-Not examined, missing

-Leiomyoma

Large well differentiated neoplasm, mostly necrotic, probably arises from an oviduct. -Not examined, not in plane of section

Parathyroid

Pituitary

-Not examined, missing

The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Spless, 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 O ppm

Fate: (Week= 93) Sacrificed in extremis

Macroscopic Observations:

Pituitary

Mammary Gland

-Raised mass, 1.1 cm dia.

-Large ulcerated mass, 10 x 7 x 9 cm, right axillary area.

Microscopic Observations:

Adrenal

Esophagus

Kidney

Liver Lung -Sinuspidal ectasia, cortex, mild

-Not examined, missing

-Pelvic mineralization, minimal

-Portal mononuclear cell infiltrate, mild

-Vascular mineralization, mild Alveolar macrophages, mild

Perivascular mononuclear infiltrate, mild

Mammary Bland -Not examined, missing

Parathyroid -Not examined, not in plane of section

Pituitary -Aden

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 82

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

Animal Number: 1R-4618 Sex: Female Group: (1) CONTROL O 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

Table: 2

present in section. -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 pps

Fate: (Week= 64) Found Dead

Thyroid

Macroscopic Observations:
Soleen -Slightly enlarged

Liver -Pale with an irregular surface on all lobes.

Pituitary -Enlarged with hemorrhagic foci.

Microscopic Observations:

Lung

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 -Vascular mineralization, mild Malignant lymphoma, histiocytic

Lymph Node (mesenteric) -Hemorrhage, mild

Manmary Gland -Salactocele

Parathyroid -Not examined, not in plane of section

Pituitary -Adenoma

Salivary Gland -Sialadenitis, chronic, moderate
Spleen -Malignant lymphoma, histiocytic

Hematopoiesis, extramedullary, increased,

noderate

Stonach -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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 83

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

Animal Number: IR-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 O 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 Sinuspidal ectasia, cortex, marked Esophagus -Not examined, missing Heart -Myocarditis, chronic nonsuppurative, multifocal, mild -Chronic progressive nephropathy, mild Kidney 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 Balactocele Parathyroid -Not examined, not in plane of section Pituitary 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 Sland, Eye.

Species: Rat

Project Number: 02B1CR0012

Summarized STAR Page: 84

Table: 2

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

Table: 2

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Sex: Female Group: (1) CONTROL O ppm
Animal Number: 1R-4622
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 #ass.
          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,
          Liver
                                                   -Hepatocyte vacuolation, periportal, moderate
          Lung
                                                   -Alveolar macrophages, mild
          Mammary Gland
                                                   -Galactocele
          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 O ppm
Fate: (Week= 96) Sacrificed in extremis
     Macroscopic Observations:
                                                   -Opacity, right eye.
          Manmary 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
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 85

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

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Animal Number: 1R-4623
                           Sex: Female Group: (1) CONTROL 0 pps
 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
                                                   -Adenona
          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 Bland.
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
                                                    inquinal area.
         Lung
                                                  -Raised circular nodule, 0.6 cm dia., in left
    Microscopic Observations:
         Adrenal
                                                  -Sinuspidal 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 manmary adenocarcinoma.
        Mammary Gland
                                                 -Fibroadenosa
                                                  Adenocarcinoma
                                                 -Cyst, unilateral
```

Species: Rat

Project Number: 0281CR0012

250 Summarized STAR Page: 86

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

Animal Number: 1R-4624 Sex: Female Group: (1) CONTROL O ppm Fate: (Neek= 100) Sacrificed in extremis

Microscopic Observations (continued):

Parathyroid -Not examined, not in plane of section
Pituitary -Adenoma
Spleen -Hematopoiesis, extramedullary, increased,

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.

Anisal Number: 1R-4625 Sex: Female Group: (1) CONTROL 0 pps

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

Contical 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

Hepatheyte vacuotation, moithfular,

Lung -Hemorrhage, local areas, moderate

Mammary Bland -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, Acrta, Uterus, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 87

Table: 2

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

Sex: Female Group: (1) CONTROL 0 ppm Animal Number: 1R-4626 Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: -Raised mass, 0.9 cm dia. Pituitary Microscopic Observations: Adrenal -Pheochromocytoma, benign, unilateral -Chronic progressive mephropathy, moderate Kidney 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 Soleen -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: iR-4627 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: Pituitary -Mass. 1 x 0.6 cm. -Firm mass, 5.5 x 4 x 3.5 cm, right lateral Mammary Sland area; lobular mass, 7 x 6 x 5 cm, left axilla. Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild -Myocarditis, chronic nonsuppurative, Heart multifocal, mild -Chronic progressive mephropathy, moderate Kidney Liver -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, moderate Hepatocyte alteration, basophilic, moderate -Vascular mineralization, mild Lung Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild -Adenocarcinoma Manmary Gland Neoplasm arises in several places in a fibroadenoma. Ovary -Tubular adenoma, unilateral

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 88

252

Cyst, bilateral

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

Table: 2

Anigal Number: 1R-4627 Sex: Female Group: (1) CONTROL 0 ppm Fate: (Week= 105) Terminal Sacrifice Microscopic Observations (continued): Pancreas -Islet cell adenoma -Not examined, not in plane of section Parathyroid -Adenona Pituitary -Fibroma, subcutaneous Skin -Cystic glands, mild Uterus 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 O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: Pituitary -Mass, 1.2 cm dia. Mammary Gland -Small module, 1.5 cm dia., right axilla; possible milk cyst. Microscopic Observations: Adrenal -Sinuspidal ectasia, cortex, moderate Esophagus -Not examined, missing Kidney -Pelvic mineralization, minimal -Portal bile duct proliferation, mild Liver Hepatocyte alteration, vacuolated, mild Hepatocyte vacuolation, multifocal, mild Lung -Vascular mineralization, mild -Galactocele Mammary Gland Adenoma, papillary Small highly cellular neoplasm lying adjacent to several large galactocoels. -Not examined, not in plane of section Parathyroid Pituitary -Adenona The following tissues were found to be within normal limits:

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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 89

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

Animal Number: 1R-4633 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 63) Sacrificed in extremis

Macroscopic Observations:

liver

Spleen

Mammary Gland

-Very pale

-Slightly enlarged

-Large subcutaneous mass, 6 x 10 x 2.5 cm,

with necrotic areas, containing dark brown fluid, ventral abdomen.

Microscopic Observations:

Adrenal

Aorta Esophacus Kidney

Liver

Lung

Mammary Gland

Parathyroid Salivary Bland

Spleen

-Hematopoiesis, extramedullary, cortical, mild Sinusoidal ectasia, cortex, mild

-Not examined, missing -Not examined, missing

-Chronic progressive nephropathy, minimal Vacuolation, conv. tub. epitheium, moderate -Hepatocyte vacuolation, centrilobular, marked

-Vascular mineralization, mild Hemorrhage, multifocal, mild

-Adenocarcinoma

Well differentiated, ductular pattern, areas of moderate mitotic activity, large areas of

necrosis.

-Not examined, not in plane of section

-Not examined, missing

-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,

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL 0 ppm

Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary

Mammary Gland

-Mass, 0.7 cm dia.

-Lobular mass, 8 x 6 x 4 cm, right axilla; lobular mass, 9 x 7 x 3.5 cm, left

inguinal.

Microscopic Observations:

Adrenal

Esophagus Heart

-Sinuspidal ectasia, cortex, moderate

-Not examined, missing

-Myocarditis, chronic nonsuppurative,

multifocal, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 90

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

Table: 2

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Microscopic Observations (continued): Kidney -Pelvic mineralization, minimal -Portal mononuclear cell infiltrate, mild Liver Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, moderate Hepatocyte alteration, eosinophilic, mild -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 -Adenona Soleen -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 Sland, Eye.

Animal Number: 1R-4635 Sex: Female Group: (1) CONTROL O pps

Fate: (Week= 94) Found Dead

Macroscopic Observations:

Small Intestine -Jejunum appears inflammed with reddish fluid;

ileum appears inflammed near

Mammary Gland -Mass, 7 x 7.5 x 2 cm, multilobular and

ulcerated, right inquinal; mass, light beige in color, spherical, 2 cm dia.,

in left axilla.

Microscopic Observations:

Adrenal

-Sinuspidal ectasia, cortex, mild Hematopoiesis, extramedullary, cortical,

moderate

Esophagus -Not examined, missing Eye -Not examined, missing

-Chronic progressive nephropathy, mild Kidney Pelvic mineralization, minimal

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 91

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

Table: 2

Sex: Female Group: (1) CONTROL O pps Animal Number: 1R-4635 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 -Adenona Adenocarcinosa Extensive necrosis. Parathyroid -Not examined, not in plane of section -Not examined, missing Pituitary Salivary Gland -Not examined, missing -Hematopoiesis, extramedullary, increased, Spleen 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. Sex: Female Group: (1) CONTROL 0 ppm Animal Number: 1R-4636 Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: -Mass in right axilla appears to be milk cyst. Mammary Gland -Slightly raised dark mass, 0.6 cm dia., left Liver lateral lobe. Microscopic Observations: -Cortical vacuolation, focal, mild Adrenal Sinusoidal ectasia, cortex, mild Heart -Myocardial fibrosis, multifocal, mild Kidney -Chronic progressive nephropathy, mild -Nematodiasis, colon Large Intestine -Hepatocyte vacuolation, multifocal, mild Liver Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild Lung -Vascular mineralization, mild Alveolar macrophages, mild -Lobular hyperplasia Mammary Gland Pancreas -Acinar atrophy, mild Parathyroid -Not examined, not in plane of section Pituitary -Adenoma

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 92

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

Table: 2 Animal Number: 1R-4636 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Microscopic Observations (continued): -Hemosiderosis, mild Spleen 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 O ppm Fate: (Week= 82) Sacrificed in extremis Macroscopic Observations: -Reddened mass, 1 cm dia. Pituitary -Focal areas of consolidation in anterior part Lung of right and left lung. -Possibly pale liver Microscopic Observations: Eye -Keratitis, acute, marked -Pelvic mineralization, mild Kidney Mineralization, cortical, mild Chronic progressive nephropathy, mild Liver -Hepatocyte vacuolation, periportal, moderate -Pneumonia, acute exudative, local areas, Lung moderate Hemorrhage, multifocal, mild Mammary Gland -Galactocele 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, Lyaph Node (mesenteric), Pancreas, Salivary Bland. Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Macroscopic Observations: Pituitary -Mass, 0.5 cm dia. Microscopic Observations: Adrenal -Sinusoidal ectasia, cortex, mild -Not examined, missing Esophagus

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 93

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

Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL O ppm Fate: (Week= 105) Terminal Sacrifice Microscopic Observations (continued): -Chronic progressive mephropathy, mild Kidney -Portal bile duct proliferation, mild Liver Hepatocyte vacuolation, multifocal, moderate Lung -Vascular mineralization, mild Mammary Gland -Not examined, missing

Parathyroid -Not examined, not in plane of section -No diagnosis, inadequate section Pituitary Spleen -Hemosiderosis, mild -Cystic glands, marked Uterus

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 Mode (mesenteric), Pancreas, Salivary Gland,

Eye, Ovary.

Animal Number: 18-4639 Sex: Female Group: (1) CONTROL O ppm

Fate: (Week= 56) Sacrificed in extremis

Macroscopic Observations: Skin -Midsternal subcutaneous mass. 8 x 8 x 3 cm.

Liver -Slightly pale

Microscopic Observations: -Pelvic mineralization, mild Kidney

Chronic progressive nephropathy, mild

-Nematodiasis, colon Large Intestine

-Portal mononuclear cell infiltrate, mild Liver Lung

-Hemorrhage, multifocal, mild

-Fibroadenoma

Mamsary Sland Salivary Gland -Not examined, missing Spleen -Hemosiderosis. mild

Uterus -Within normal limits Fewer than protocol number

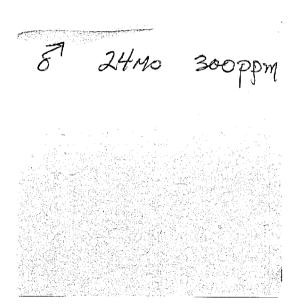
The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Uninary Bladder, Abrta, Ovary, Pituitary, Trachea, Adrenal, Thyroid, Parathyroid, Esophagus, Lyaph Nide (aesenteric), Panireas,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 94

Table: 2



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

Table: 2

Animal Number: 1R-3581 Sex: Male Group: (5) FC-143 300 pps Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -Raised mass, 0.5 cm dia. Pituitary Microscopic Observations: Adrenal -Pheochromocytoma, benign Kidney -Chronic progressive meanropathy, mild -Portal mononuclear cell infiltrate, mild Liver Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, minimal -Vascular mineralization, mild Lung Hemorrhage, multifocal, moderate Pituitary -Adenona -Hemosiderosis, mild Spleen -C cell adenoma Thyroid 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: -Ulcerated mass, 2.8 cm dia., dorsal. Skin Pituitary -Hemorrhagic lesion, 0.2 cm dia. -Pale Kidney -Left adrenal enlarged, 0.7 cm dia. mass. Adrenal Testis/Epididymis -Testes small, bilateral. Microscopic Observations: Adrenal -Pheochromocytoma, benign, unilateral -Retinal atrophy, diffuse, marked Eye Heart -Myocarditis, chronic nonsuppurative, multifocal, mild Kidney -Chronic progressive nephropathy, moderate Liver -Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild -Vascular mineralization, wild Lung Parathyroid -Not examined, missing Pituitary -Adenoma Salivary Gland -Not examined, missing -Keratoacanthoma, back

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 95

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):

Soleen

Testis/Epididymis

-Hemosiderosis, mild

-Tubule atrophy, aspermatogenesis, bilateral,

mild

Thyroid

-Not examined, missing

The following tissues were found to be within normal limits:

Brain, Spinal Cord, Bone Marrow, Stonach, 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.

Microscopic Observations:

Adrenal Kidney Liver

-Sinusoidal ectasia, cortex, moderate -Chronic progressive nephropathy, mild

-Hepatocellular carcinoma Megalocytosis, mild

Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild

Lung

-Vascular mineralization, mild Alveolar macrophages, mild -Leydig cell adenoma, unilateral Vascular mineralization, mild

Testis/Epididymis

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.

Microscopic Observations:

-Chronic progressive nephropathy, wild Kidney

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 96

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

Table: 2

Animal Number: 18-3585 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

liver

Lung

-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Malignant lymphoma, lymphocytic

Hepatocyte alteration, basophilic, moderate

Megalocytosis, minimal

-Vascular mineralization, mild Fibrosis, pleural, moderate

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 Eladder, 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

Testis/Epididymis

Microscopic Observations:

Adrenal

Heart Kidney Liver

Lung Pancreas Salivary Gland Testis/Epididymis -Possible pale foci on one lobe.

-Pale mass, 1 cm dia.

-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, mild

-Myocarditis, chronic nonsuppurative, mild -Chronic progressive nephropathy, moderate -Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, moderate

Megalocytosis, mild

-Vascular mineralization, mild -Acinar atrophy, moderate

-Sialadenitis, chronic, moderate

-Tubule atrophy, aspermatogenesis, moderate
Mineralization tubular, mild

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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 97

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

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Table: 2
 Animal Number: iR-3587
                            Sex: Male
                                       Group: ( 5) FC-143 300 ppm
 Fate: (Week= 106) Terminal Sacrifice
      Macroscopic Observations:
           Eve
                                                    -Hypopyon, right eye.
      Microscopic Observations:
          Adrenal
                                                    -Sinusoidal ectasia, cortex, minimal
           Eye
                                                    -Phthsis 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, basephilic, 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 Bland
                                                   -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:
         Thyeus
                                                   -Enlarged, 1.5 x 1.5 x 0.3 cm, dark red.
         Liver
                                                   -Enlarged, brown/yellow mottling.
         Soleen
                                                  -Markedly enlarged, 8 x 2 x 1 cm.
         Lyaph 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
```

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 98

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 -Malignant lymphoma, lymphocytic Bone Marrow Brain -Malignant lymphoma, lymphocytic Ey€ -Malignant lymphona, lymphocytic Kidney -Malignant lymphoma, lymphocytic -Malignant lymphoma, lymphocytic Liver Parenchyma almost completely replaced by diffuse noeplastic 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 Uninary 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 ppe Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: -No visible lesions. Microscopic Observations: Admenal -Sinusoidal ectasia, cortex, mild Esophagus -No diagnosis, inadequate section Kidney -Chronic progressive mephropathy, minimal Liver -Portal mononuclear cell infiltrate, mild Cystoid degeneration, moderate Hepatocyte alteration, basophilic, moderate Megalocytosis, minimal Lung -Vascular mineralization, mild Alveolar macrophages, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 99

Hemorrhage, local areas, moderate

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., interior caudate lobe.

Microscopic Observations: Kidnev

Liver

Lung

Parathyroid

Thyroid

-Chronic progressive nephropathy, mild -Megalocytosis, minimal

Portal mononuclear cell infiltrate. mild Cystoid degeneration, multifocal, mild Hepatocellular carcinoma

Well differentiated, trabecular pattern, moderate mitotic activity, vascular invasion.

-Vascular mineralization, mild Alveolar macrophages, mild

-Not examined, not in plane of section

-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, Brinary 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: (Neek= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

Microscopic Observations:

Adrenal

Heart

-Pale foci throughout.

-Sinusoidal ectasia, cortex, moderate -Myocarditis, chronic nonsuppurative,

multifocal, minimal

-Chronic progressive mephropathy, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 100

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. Alveolar macrophages, moderate Parathyroid -Not examined, not in plane of section Pituitary -Adenoma Testis/Epididveis -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 Broup; (5) FC-143 300 pcm Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: Manmary Gland -Firm mass, 3 x 2 x 1.5 cm, right axilla. Pituitary -Hemorrhagic mass, 0.5 x 0.7 cm. Microscopic Observations: Adrenal -Sinuspidal 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 -Adenona Salivary Gland -Sialadenitis, acute, moderate Mass described at necropsy as mammary gland was apparently the enlarged, inflammed

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 101

salivary gland. No mammary tissue was

present on any slide.

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

Table: 2

Animal Number: 18-3595 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Spinal Cord Spleen

-Not examined, missing -Hemosiderosis, wild

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

Microscopic Observations:

Adrenal

Heart

Kidney

Liver

Lung

Pituitary Testis/Epididymis -Pale, enlarged and pitted, bilateral.

-Cortical vacuolation, multifocal, minimal Medullary cell hyperplasia, focal, mild -Myocarditis, chronic nonsuppurative, multifocal, mild

-Chronic progressive nephropathy, marked

Cyst, cortical, moderate

-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild

Megalocytosis, mild

-Vascular mineralization, mild Hemorrhage, local areas, marked

-Adenona

-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 Bland, Eye.

Animal Number: 1R-3597 Sex: Male Group: (5) FC-143 300 ppm

Fate: (Neek= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart

-Myocarditis, chronic nonsuppurative,

multifocal, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 102

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

Table: 2

Animal Number: 1R-3597 Group: (5) FC-143 300 ppm Sex: Male

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Kidney Liver

Luna

-Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild

Megalocytosis, minimal -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: 18-3599 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidnev

Microscopic Observations:

Kidney

Liver

Lung

-Hydronephrosis, right kidney.

-Chronic progressive nephropathy, mild Pelvic mineralization, mild

Hyperplasia, pelvic epithelium, multifocal,

moderate

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

Cystoid degeneration, multifocal, mild

Megalocytosis, mild

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

mild

Alveolar macrophages, mild Hemorrhage, local areas, moderate -Sialadenitis, chronic, moderate

-Hemosiderosis, mild

Salivary Gland Spleen

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.

Species: Rat

Project Number: 0281CR0012

267 Summarized STAR Page: 103

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

Table: 2 Animal Number: 1R-3600 Sex: Male Broup: (5) FC-143 300 ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations: Liver

Microscopic Observations:

Adrenal Bone Marrow

Heart

Kidney Liver

Lung

Lymph Node (mesenteric) Pituitary

Spinal Cord Spleen

Testis/Epididymis

-Mottled

-Cortical vacuolation, mild -Not examined, missing

-Myocarditis, chronic nonsuppurative,

multifocal, mild

-Chronic progressive mephropathy, mild -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild

Megalocytosis, moderate -Vascular mineralization, mild Alveolar macrophages, mild

Hemorrhage, local areas, moderate

-Hemorrhage, minimal -Not examined, missing -Not examined, missing -Hemosiderosis, mild

-Vascular mineralization, mild

The following tissues were found to be within normal limits: Brain, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Acrta, 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

Lymph Node (mesenteric) Stomach

Microscopic Observations:

Adrenal Reart

Kidnev Liver

-Mottled; yellow raised lesions, 0.7 and 0.9

ce dia., posterior caudate lobes.

-Enlarged

-Enlarged gastric rugae

-Cortical vacuolation, multifocal, moderate -Myocarditis, chronic nonsuppurative,

multifocal, minimal

-Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, moderate Hepatocyte alteration, vacuolated, mild

Megalocytosis, moderate

Hepatocyte alteration, basophilic, moderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 104

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

Table: 2

Sex: Male Group: (5) FC-143 300 ppm Animal Number: 1R-3601 Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung

Lymph Node (mesenteric)

Pancreas Pituitary Stomach

-Vascular mineralization, mild Hemorrhage, local areas, marked

-Hemorrhage, mild Hemangiosarcoma

-Acinar atrophy, moderate -Cyst, pars distalis -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, Aprta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland. Eye.

Animal Number: 18-3602 Sex: Male Group: (5) FC-143 300 ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

Heart

Kidney Liver

Lung

Lymph Node (mesenteric) Pancreas . Spleen

Testis/Epididyais

Thyroid

-Nodular hyperplasia, cortex, focal, mild Medullary cell hyperplasia, focal, mild -Myocarditis, chronic nonsuppurative,

multifocal, mild

-Chronic progressive mephropathy, mild -Portal mononuclear cell infiltrate, mild

Megalocytosis, minimal

-Vascular mineralization, mild Alveolar macrophages, mild

-Hemorrhage, mild -Islet cell adenoma -Hemosiderosis, mild

-Vascular mineralization, mild

-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.

Species: Rat

Project Number: 0281CR0012

269 Summarized STAR Page: 105

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

Luno

-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

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 Bland, 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,

asild

Alveolar macrophages, moderate

Perivascular mononuclear infiltrate, moderate

Salivary Gland

Spleen

-Sialadenitis, chronic, moderate

-Hematopoiesis, extramedullary, increased,

mild

Hemosiderosis, mild

Testis/Epididymis

-Tubule atrophy, aspermatogenesis, unilateral,

marked

Vascular mineralization, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 106

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,
April, 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 Kidney

Liver

Lung Parathyroid Spleen -Nodular hyperplasia, cortex, focal, mild -Chronic progressive nephropathy, minimal

Pyeloneohritis, acute, mild

-Portal mononuclear cell infiltrate, mild

Megalocytosis, minimal

-Vascular mineralization, mild -Not examined, not in plane of section

-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: 18-3607 Sex: Male Group: (5) FC-143 300 ppm

Fate: (Week= 104) Terminal Sacrifice

Macroscopic Observations:

Microscopic Observations:

Adrenal

Pituitary

Kidney

Liver Lung

Pancreas

-Hemorrhagic mass, 1 x 0.7 cm.

-Cortical vacuolation, multifocal, moderate Pheochromocytoma, benign, unilateral -Chronic progressive nephropathy, mild

Pyelonephritis, acute, moderate
Hyperplasia, pelvic epithelium, diffuse, mild
-Portal mononuclear cell infiltrate, mild

-Vascular mineralization, mild Alveolar macrophages, mild

-Acinar atrophy, mild

Hyperplasia, islet cell, moderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 107

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

Arimal Number: 1R-3607 Sex: Male Group: (5) FC-143 300 ppm

Arimal Number: 1R-3607 Sex: Male Group: (5) FC-143 300 pps Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid -Adenosa Pituitary -Adenosa

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: 18-3608 Sex: Male Group: (5) FC-143 300 ppm

Animal Number: 18-3508 Sex: Male Broup: (3) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin -Raised inflammed lesion, left hind footpad.
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

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 Bland, Eye.

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Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 108 272

Table: 2

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 Kidney Liver -Nodular hyperplasia, cortex, focal, mild -Chronic progressive nephropathy, minimal -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Megalocytosis, mild

Lung

-Vascular mineralization, mild Hemorrhage, local areas, moderate

Lyaph Node (mesenteric)

-Sinusoidal ectasia, mild -Acinar atrophy, moderate Polyarteritis, moderate

Pancreas

-Not examined, not in plane of section

Parathyroid 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
Microscopic Observations:

-Testes appear somewhat small.

Adrenal Kidney Liver

-Pheochromocytoma, benign, unilateral
-Chronic progressive mephropathy, mild
-Portal mononuclear cell infiltrate, mild
Hepatocyte vacuolation, multifocal, mild
Cystoid degeneration, multifocal, mild

Megalocytosis, minimal

Lung

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

8110

Perivascular mononuclear infiltrate, minimal

Hemorrhage, local areas, moderate

Pancreas

Testis/Epididymis

-Acinar atrophy, mild -Mineralization, tubular, mild

Tubule atrophy, aspernatogenesis, bilateral,

marked

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 107

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

Table: 2

Animal Number: 1R-3610 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Thyroid

-C cell adenoma

Follicular hyperplasia, cystic, 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, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivery Gland, Eye. ------

Animal Number: 1R-3611 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Few pale foci; raised pale lesion, 0.7 cm dia., in median lobe.

Microscopic Observations:

Adrenal

-Sinuscidal ectasia, cortex, mild Cortical vacuolation, focal, minimal -Not examined, missing

Esophagus 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

Lung

-Vascular mineralization, mild Hemorrhage, local areas, moderate

Pancreas Parathyroid Salivary Gland

-Acinar atrophy, mild -Not examined, missing

-Sialadenitis, chronic, marked

Extensive squamous metaplasia of duct epithelium with some ducts occluded by hyperplastic, metaplastic epithelium.

Thyroid -Not examined, missing

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 110

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

Table: 2

Animal Number: 1R-3611 Sex: Male Broup: (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: 18-3612 Sex: Male Broup: (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 Kidney Liver -Cortical vacuolation, focal, minimal
-Chronic progressive mephropathy, marked
-Portal mononuclear cell infiltrate, mild
Portal bile duct proliferation, mild
Henatorellular carringma

Hepatocellular carcinoma
Well differentiated, trabecular pattern,
large areas of necrosis within tumor.
-Vascular mineralization, mild

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 Microscopic Observations: Kidney

Liver

-Pale masses of various sizes in both testes.

-Chronic progressive mephropathy, mild -Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, minimal

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 111

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

Table: 2

Animal Number: 18-3614 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung

Prostate Soleen

Testis/Epididymis

-Vascular mineralization, mild Alveolar macrophages, mild -Not examined, missing -Hemosiderosis, mild

-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 Testis/Epididymis

Microscopic Observations:

Adrenal Kidney

Liver

Lung

Parathyroid Pituitary

Salivary Bland

Spleen

Testis/Epididymis

-Mass, 0.8 cm dia.

-Right testis small.

-Sinusoidal ectasia, cortex, mild

-Chronic progressive nephropathy, moderate -Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild

Megalocytosis, minimal

-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, mild

-Not examined, not in plane of section

-Sialadenitis, chronic, marked

Extensive hyperplasia and metaplasia of duct

epithelium. -Hemosiderosis, mild

-Tubule atrophy, aspermatogenesis, 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, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 112

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 Liver

Lung

Pancreas

Pituitary

Spleen

-Chronic progressive mephropathy, minimal -Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, minimal Cystoid degeneration, multifocal, mild

Necrosis, multifocal, moderate

-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, diffuse, marked

-Hyperplasia, acinar cell, moderate

-Adenoma

-Not examined, missing Salivary Gland -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/Epididygis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3618 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Appears pale; pale raised mass, 1 cm dia.,

Microscopic Observations:

Adrenal

Kidnev Liver

Lung

caudate lobe.

-Cortical vacuolation, multifocal, mild Sinusoidal ectasia, cortex, mild -Chronic progressive nephropathy, mild -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.

-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,

Species: Rat

Project Number: 0281CR0012

277 Summarized STAR Page: 113

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

Table: 2

Sex: Male Group: (5) FC-143 300 ppm Animal Number: 1R-3618 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 Kidney

Urinary Bladder

-Hydronephrosis, left kidney.

-Distended into abdomen, filled with dark colored fluid.

-Raised lesions, 2 x 1.5 cm, median lobes.

Microscopic Observations:

Adrenal

Kidney

Liver

Lung

Salivary Gland Urinary Bladder -Sinusoidal ectasia, cortex, mild

Modular hyperplasia, cortex, focal, moderate -Chronic progressive nephropathy, minimal

Hydronephrosis, bilateral, mild

-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild

Megalocytosis, mild Hepatocellular carcinoma

Poorly differentiated, adenoid and trabecular patterns, moderate mitotic activity.

-Vascular mineralization, mild Hemorrhage, local areas, moderate

-Not examined, missing

-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 mephropathy, minimal

Species: Rat

Project Number: 0281CR0012

Sugmarized STAR Page: 114

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

Sex: Male Group: (5) FC-143 300 ppm Animal Number: 1R-3621 Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver

-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild

Megalocytosis, mild

Lung Parathyroid Salivary Gland -Vascular mineralization, mild -Not examined, not in plane of section -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.

Group: (5) FC-143 300 ppm Animal Number: 18-3623 Sex: Male

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal

Kidney

Liver

Lung

Lymph Node (mesenteric)

Pituitary Prostate

Salivary Gland Testis/Epididymis

-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, moderate -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild

Hepatocyte vacuolation, mild Necrosis, multifocal, mild Megalocytosis, minimal

-Vascular mineralization, mild

Pneumonia, interstitial, chronic, multifocal,

Alveolar macrophages, mild

-Hemorrhage, mild -Not examined, missing

-Prostatitis, acute, suppurative, moderate

-Sialadenitis, chronic, marked -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 115

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

Table: 2

Animal Number: IR-3624 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 90) Sacrificed in extremis Macroscopic Observations: Pituitary -Remorrhagic 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, Alveolar macrophages, multifocal, mild Pituitary -Adenona Prostate -Prostatitis, acute, suppurative, marked Spleen -Headsiderosis, mild Testis/Epididymis -Tubule atrophy, aspermatogenesis, bilateral, The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Brinary 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 neoplasm Thrombus Large thrombus containing tumor cells from salivary gland tumor. Multiple small

Species: Rat

Project Number: 0281ER0012

Summarized STAR Page: 116 280

metastases of salivary tumor throughout lung.

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

-Carcinosa

Highly cellular, anaplastic tumor. Appears to have arisen in parotid gland duct. Small rim of salivary gland tissue around mass.

-Hematopoiesis, extramedullary, increased,

Spleen -

rnal limits:

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 Kidney Liver -Cortical vacuolation, focal, moderate
-Chronic progressive nephropathy, moderate
-Portal mononuclear cell infiltrate, mild
Fortal bile duct proliferation, mild
Cystoid degeneration, multifocal, mild
Megalocytosis, minimal

Lunc

-Vascular mineralization, moderate Alveolar macrophages, mild Hemorrhage, local areas, moderate -Not examined, not in plane of section

Parathyroid

Spleen

-Kemosiderosis, 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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 117

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

Heart

-Sinusoidal ectasia, cortex, mild -Myocardial fibrosis, local areas, mild Myocarditis, chronic nonsuppurative,

local areas, mild

Liver -Portal mononuclear cell infiltrate, mild

Cystoid degeneration, multifocal, mild

Megalocytosis, minimal

tung -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 118 282

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 -Chronic progressive nephropathy, mild

Kidnev 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 -Sialadenitis, chronic, marked

Salivary Gland

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: 18-3632 Sex: Male Group: (5) FC-143 300 ppm

Fate: (Week= 10A) Terminal Sacrifice

Macroscopic Observations:

Liver Testis/Epididymis -Few pale foci. -Pale mass, 1.5 cm dia.

Microscopic Observations:

Kidnev Liver

-Chronic progressive mephropathy, moderate -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

pultiple cytoplasmic vacuoles. -Vascular mineralization, mild Alveolar macrophages, mild

Hemorrhage, focal, mild

Lung

-Hyperplasia, islet cell, moderate

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 119

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

Table: 2

Sex: Male Group: (5) FC-143 300 ppm Animal Number: 1R-3632

Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued): Testis/Epididymis

-Tubule atrophy, aspermatogenesis, unilateral, Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits: Brain, Spinal Cord, Bone Marrow, Spieen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Pituitary, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus,

Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 18-3433 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations: Eve Kidney

Microscopic Observations:

Adrenal

-Sinusoidal ectasia, cortex, mild Ganglioneuroma

-Opacity, right eye.

-Bilaterally pale and pitted.

-Keratitis, chronic, moderate

Large, well differentiated tumor arising in medulla of one gland. Composed of nerve fibers and large ganglion cells.

Ey₽ Heart

-Myocarditis, chronic nonsuppurative, local areas, mild -Chronic progressive nephropathy, marked

Kidney

One of pair present Liver

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

Lung

Megalocytosis, moderate -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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 120 284

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= 104) Terminal Sacrifice

Macroscopic Observations: Testis/Epididymis

Mesentery Microscopic Observations:

Liver

Lung

Pancreas

Parathyroid Spleen Testis/Epididyais -Pale masses, 1 cm dia., in each testis. -Mass, 3 x 1.5 cm in area of pancreas.

-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Hepatocyte alteration, vacuolated, moderate Megalocytosis, minimal

-Vascular mineralization, mild Alveolar macrophages, mild -Adenocarcinoma

Large, highly cellular, well differentiated neoplasm with high mitotic index. Lymphatic

-Not examined, not in plane of section

-Hemosiderosis, mild

-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 Microscopic Observations:

Adrenal Kidney Liver

Lung

Pituitary Salivary Gland -Hemorrhagic area, 0.5 x 0.2 cm.

-Medullary cell hyperplasia, focal, minimal -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, mild Megalocytosis, minimal

-Vascular mineralization, mild Alveolar macrophages, mild

Perivascular mononuclear infiltrate, minimal

-Adenosa

-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,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 121

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

Table: 2

Animal Number: 1R-3635 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, Acrta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3636 Sex: Male Broup: (5) FC-143 300 ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Bone

-Swollen metatarsal joints, bilateral hind liabs.

Testis/Epididymis -Both testes appear small.

Microscopic Observations:

Bone

Lung

-Arthritis, synovitis; joints, hindleg,

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

-Vascular mineralization, mild Alveolar macrophages, mild -Granuloma, multifocal, moderate

Lymph Node (mesenteric) 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.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 122

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

Animal Number: 1R-3637 Sex: Male Group: (5) FC-143 300 ppm Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Thyroid

Pituitary Thymus

Microscopic Observations:

Heart

Kidney Liver

Lung

Pancreas Pituitary Salivary Gland Thymus

-Possibly slightly enlarged.

-Mass. 0.5 cm dia.

-Slightly enlarged and hemorrhagic.

-Myocarditis, chronic nonsuppurative,

multifocal, minimal

-Chronic progressive nephropathy, minimal -Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Necrosis, multifocal, moderate

-Vascular mineralization, mild Hemorrhage, local areas, moderate

-Acinar atrophy, minimal

-Adenoma

-Not examined, missing -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 Group: (5) FC-143 300 ppm Sex: Male

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary Adrenal

Microscopic Observations:

Adrenal

Kidney Liver Luno

-Raised dark mass, 0.7 cm dia. -Enlarged, right adrenal

-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, marked Medullary cell hyperplasia, focal, mild

-Mineralization, cortical, mild

-Portal mononuclear cell infiltrate, minimal

-Vascular mineralization, mild Alveolar macrophages, mild

Perivascular mononuclear infiltrate, mild

Hemorrhage, local areas, moderate

Granuloma

Fragment of unidentified foreign material in

granuloma.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 123

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: 18-3639 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 Sroup: (5) FC-143 300 ppm Fate: (Week= 72) Sacrificed in extremis

Macroscopic Observations: Spleen

Abdomen (internal)

Eye Microscopic Observations:

Adrenal Eve

Kidney Liver

Lung

Spleen

Stomach

-Possibly smaller than normal.

-Gastrointestinal tract from stomach to cecum distended with gas.

-Right eye slightly atrophied

-Nodular hyperplasia, cortex, focal, minimal

-Keratitis, acute, marked

Lesion in right eye. Extensive corneal ulceration.

-Calculus, pelvic, mild

-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal

-Vascular mineralization, mild Alveolar macrophages, mild

-Hemosiderosis, mild Atrophy, moderate

-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, Lyaph Node (mesenteric), Pancreas, Salivary Bland.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 124 288

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

Animal Number: 1R-3641 Sex: Male Group: (5) FC-143 300 ppm

Macroscopic Observations:

Fate: (Week= 106) Terminal Sacrifice

Liver

-Yellowish foci, 0.3 cm dia., median lobe.

Microscopic Observations:

Adrenal Heart

-Medullary cell hyperplasia, local areas, mild

Table: 2

-Myocarditis, chronic nonsuppurative,

multifocal, mild

Kidney Liver

Lung

-Chronic progressive nephropathy, moderate -Portal mononuclear cell infiltrate, mild

Cystoid degeneration, multifocal, mild Megalocytosis, minimal

Hyperplastic module

Circumscribed, expansive lesion with

preservation of normal architecture. Portal

areas present. Cells in module more

basophilic, vacuolated.

-Vascular mineralization, mild

Hemorrhage, focal, mild -Acinar atrophy, moderate

-Hemosiderosis, mild

-Leydig cell adenoma, unilateral

Pancreas

Spleen Tootie/Enididum

Testis/Epididymis

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,
Acrta, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric),
Salivary Sland, Eye.

Animal Number: 18-3644 Sex: Male Group: (5) FC-143 300 ppm

Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver

-Appears mottled; small pale area in median

lobe.

Microscopic Observations:

Adrenal

Heart

Kidney Liver -Cortical vacuulation, focal, mild

Nodular hyperplasia, cortex, focal, mild -Myocarditis, chronic nonsuppurative,

multifocal, mild

-Chronic progressive mephropathy, minimal -Portal momonuclear cell infiltrate, mild

Portal bile duct proliferation, mild

Megalocytosis, minimal Hyperplastic nodule

Cells of nodule have slightly more basophilic

cytoplasm; many are vacuolated.

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 125 289

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

Group: (5) FC-143 300 ppm Animal Number: 1R-3644 Sex: Male Fate: (Week= 106) Terminal Sacrifice Microscopic Observations (continued): -Vascular mineralization, mild Luna 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 Group: (5) FC-143 300 ppm Sex: Male Fate: (Week= 106) Terminal Sacrifice Macroscopic Observations: Testis/Epididymis -Pale mass, 1.3 cm dia., in left testis. Microscopic Observations: Adrenal -Nodular hyperplasia, cortex, multifocal, mild Acrta -Metastatic neoplasm Esophagus -Metastatic neoplasm Kidney -Chronic progressive nephropathy, mild -Portal mononuclear cell infiltrate, minimal Liver Portal bile duct proliferation, minimal Megalocytosis, minimal Lung -Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, Alveolar macrophages, mild Hemorrhage, focal, mild Pancreas -Acinar atrophy, mild Parathyroid -Adenoma Salivary Sland -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 neoplasm Urinary Bladder -Epithelial hyperplasia, simple, diffuse,

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 126

290

minimal

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

Table: 2

Animal Number: 1R-3645 Sex: Male Broup: (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 inquinal 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 Esophagus Kidney

Kidney Liver

Lung

Mammary Gland Ovary Salivary Gland -Sinusoidal ectasia, cortex, marked

-Not examined, missing

-Chronic progressive mephropathy, minimal
-Portal bile duct proliferation, mild
Hepatocyte alteration, vacuolated, focal,

minimal

-Hemorrhage, local areas, mild

Alveolar macrophages, multifocal, mild

-Fibroadenoma

-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, Urinary Bladder, Aorta, Uterus, Pituitary, Trachea, Thyroid, Farathyroid, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 18-4643 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 Kidnev -Not examined, missing

-Pelvic mineralization, mild

Liver -Hepatocyte vacuolation, diffuse, mild

Species: Rat

Project Number: 0281CR0012

Summarized STAR Page: 127