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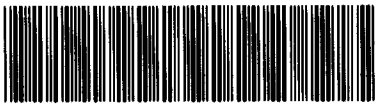

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3M

May 25, 2000

VIA EXPRESS MAIL

85000000014

Dr. Charles Auer
Director
Chemical Control Division
Office Of Pollution Prevention And Toxics
United States Environmental Protection Agency
401 M Street, Southwest
Room 403 East Tower (Mail Code 7405)
Washington, D. C. 20460

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Re: **Information On Perfluorooctanoic Acid And Supplemental Information On Perfluorooctane Sulfonates And Related Compounds**

Dear Charlie:

Pursuant to our recent communications, 3M is enclosing information on perfluorooctanoic acid. We also are enclosing information on perfluorooctane sulfonates and related compounds which supplements information submitted to you previously under cover of our April 21, 2000, May 4, 2000 and May 18, 2000 letters. We are providing this information on a voluntary basis as part of our continuing discussions with EPA regarding fluorochemistry.

The enclosed information on perfluorooctanoic acid includes the following:

⇒ Copies of post-1975 studies and certain other information relating to the following environmental science areas: (i) physical and chemical properties; (ii) environmental fate and transport; (iii) environmental monitoring; and (iv) ecotoxicity. For each study, 3M has prepared a summary in the HPV "robust summary" format.

⇒ Copies of post-1975 studies and certain other information relating to the following health effects areas: (i) acute toxicity; (ii) genotoxicity; (iii) repeated-dose toxicity; (iv) pharmacokinetics; (v) teratology; and (vi) medical surveillance and epidemiology. 3M has included a detailed index of this information subdivided by

each compound. We also have enclosed summaries for the medical surveillance and epidemiology studies and have included copies of certain published studies in this area in order to provide appropriate context.

⇒ Lists of all studies in progress and planned studies, along with study protocols or study plans, where available.

⇒ A bibliography of pre-1976 studies subdivided by each compound.

⇒ A bibliography of acute toxicity studies subdivided by each compound, except that we are providing copies of key acute studies (with reference to the HPV guidance).

⇒ A bibliography of published studies in 3M's possession.

3M is continuing its file review and will supplement the enclosed information on perfluorooctanoic acid as appropriate. As you review this information, we ask that you bear several points in mind:

⇒ The enclosed information spans several boxes. We have organized the information in each box with labeled file folders and indices to aid EPA's review. To ensure that you and your staff are able to access the most pertinent information, we also are attaching to this letter the indices covering studies and other information.

⇒ 3M provided the Agency with a list of all fluorochemical-related submissions made by 3M to the TSCA Section 8(e) docket under cover of our May 4, 2000 letter. This list included all submissions on perfluorooctanoic acid.

⇒ The enclosed information includes studies on perfluorooctanoic acid as well as on aqueous and/or solvent solutions of this material. Many of the studies refer to the test substance only by a 3M product identification number with a "T", "L", "FM" or "FC" prefix. Although analysis of the test substance has been included, where available, it is often not possible to determine from the study report itself the identity of the test substance. To assist in interpreting the studies, we have used 3M's historical product number records to provide composition information (*e.g.*, composition percentages; solvent content; purity grade, etc.) next to each study name on the index and/or on the study summary. Please note that some formulations contain a small amount of "perfluorochemical inerts" – a term which refers to a completely fluorinated carbon chain with no functionalized components. Finally, it should be recognized that product formulations have evolved over the years, and thus, some of the test substances do not constitute current products.

⇒ 3M understands that the Agency has requested information on perfluorooctanoic acid from duPont. For this reason, we are not providing copies of studies on perfluorooctanoic acid in 3M's files sponsored or conducted by duPont.

⇒ Consistent with the information previously provided on perfluorooctane sulfonates and related compounds, 3M has not provided all analytical chemistry reports on perfluorooctanoic acid. Rather, we have enclosed analytical chemistry reports which may prove useful to EPA in interpreting certain studies; understanding the details of analytical chemistry methods; or verifying human and biomonitoring data.

⇒ The enclosed information does not include a "Use And Exposure Information Profile" or "UEIP" for perfluorooctanoic acid. Our present intention is to provide you with completed a UEIP form for perfluorooctanoic acid by June 9, 2000.

⇒ The information on perfluorooctane sulfonates under cover of our May 4, 2000 letter included documents relating to ongoing mechanistic research by Dr. Ken Wallace of the University of Minnesota. Please note that this research also encompasses perfluorooctanoic acid. The comparative metabolism research by Dr. Marion Anders of the University of Rochester Medical Center also includes perfluorooctanoic acid; there are not documents yet available relating to this research.

3M looks forward to discussing the enclosed information with you and other EPA staff. In the meantime, please do not hesitate to contact me with any questions.

Very truly yours

William A. Weppner

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Enclosures

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

PFOA	

Acute Toxicity

1) Inhalation Toxicity Study of T-2305 CoC - Rat

   a) Final Report, An Acute Inhalation Toxicity Study of T-2305 CoC in the Rat, Bio/dynamics, Inc., Study No. 78-7184, May 3, 1979

   b) Technical Report Summary, Analysis of rat serum of FC-143, reported in terms of organic and inorganic fluorine, Central Research Laboratories, June 20, 1979

2) Final Report, Acute Oral Toxicity (LD_{50}) Study in Rats, International Research and Development Corporation, Study No. 137-091, 3M Reference No. Fluorad® FC-143, Lot 340, May 5, 1978

3) Final Report, Acute Oral Toxicity Study of T-6669 in Rats, Corning Hazelton, Inc., Study No. CHW 61001760, 3M Ref. FC-143, January 10, 1997

4) Final Report, Primary Skin Irritation Study - Rabbits, Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

5) Final Report, Primary Eye Irritation Study - Rabbits (Washout Procedure), Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

6) Final Report, Primary Eye Irritation Study - Rabbits (Not Washed), Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

7) Final Report, Primary Skin Irritation Test with T-3371 in Albino Rabbits, Riker Laboratories, Study No. 0883EB0079, 3M Reference FC-26, Lot 389, July 13, 1983

8) Final Report, Acute Oral Toxicity - Rats, Biosearch, Inc., 3M Reference No. T-1585, FC-26 (perfluorooctanoic acid), September 16, 1976

9) Final Report, Primary Eye Irritation Study - Rabbits, Biosearch, Inc., 3M Reference No. T-1585, FC-26 (perfluorooctanoic acid), September 16, 1976

10) Final Report, Acute Dermal Toxicity Study of T-6342 in Rabbits, Corning Hazelton, Inc., Study No. HWI 50800374, 3M Ref. No. FC-1090, L13364, Lot 1, F11426, sodium perfluorooctanoate solution, October 24, 1995

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Acute Studies - Bibliography Only

1) Final Report, Acute Oral Toxicity - Rats, Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

2) Final Report, Primary Skin Irritation Study - Rabbits, Biosearch, Inc., 3M Reference No. T-1585, FC-26 (perfluorooctanoic acid), September 16, 1976

3) Final Report, Acute Oral Toxicity Study in Rats, Hazelton Laboratories America, Inc., 3M Reference No. T-3974, Lot 390 (FC-126, approximately 88% solid), February 6, 1987

4) Final Report, Primary Dermal Irritation Study in Rabbits - Method, Summary, Raw Data Appendix, Hazelton Laboratories America, Inc., 3M Reference No. T-3974, Lot 390 (FC-126, approximately 88% solid), December 31, 1986

5) Final Report, Primary Eye Irritation Study in Rabbits - Method, Summary, Raw Data Appendix, Hazelton Laboratories America, Inc., 3M Reference No. T-3974, Lot 390 (FC-126, approximately 88% solid), January 14, 1987

6) Final Report, Primary Eye Irritation/Corrosion Study of T-6564 in Rabbits, Corning Hazelton, Inc., Study No. CHW 60504574, 3M Ref. No. FC-1015, Fluorad® fluorochemical emulsifier, L13167, straight-chain APFO solution, September 5, 1996

7) Final Report, Primary Dermal Irritation/Corrosion Study of T-6564 in Rabbits, Corning Hazelton, Inc., Study No. CHW 60504573, 3M Ref. No. FC-1015, Fluorad® fluorochemical emulsifier, L13167, straight-chain APFO solution, August 15, 1996

8) Final Report, Acute Oral Toxicity Study of T-6564 in Rats, Corning Hazelton, Inc., Study No. CHW 60504572, 3M Ref. No. FC-1015, Fluorad® fluorochemical emulsifier, L13167, straight-chain APFO solution, November 8, 1996

9) Final Report, Acute Oral Toxicity Study of T-6342 in Rats, Hazelton Wisconsin, Inc., Study No. HWI 50800373, 3M Ref. No. FC-1090, L13364, Lot 1, F11426, sodium perfluorooctanoate solution, November 16, 1995

10) Final Report, Primary Eye Irritation/Corrosion Study of T-6342 in Rabbits, Hazelton Wisconsin, Inc., Study No. HWI 50800376, 3M Ref. No. FC-1090, L13364, Lot 1, F11426, sodium perfluorooctanoate solution, October 12, 1995

11) Final Report, Primary Dermal Irritation/Corrosion Study of T-6342 in Rabbits, Hazelton Wisconsin, Inc., Study No. HWI 50800375, 3M Ref. No. FC-1090, L13364, Lot 1, F11426, sodium perfluorooctanoate solution, September 28, 1995

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Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Genotoxicity

1) An Assay of Cell Transformation and Cytotoxicity in the C3H 10T 1/2 Clonal Cell Line for the Test Chemical T-2942 CoC, Environmental Pathology Laboratory, Stone Research Laboratories, University of Minnesota, 3M Ref. No. FC-143 Lot 340, L138679, March 5, 1981

2) Final Report, Mutagenic Evaluation of T-2015 CoC in the Ames Salmonella/Microsome Plate Test, Litton Bionetics, Inc., Study No. 20838, 3M Ref. No. FC-143, February 1978

3) Final Report, Mutagenicity Test on T-6564 in an *In Vivo* Mouse Micronucleus Assay, Corning Hazelton, Inc., Study No. 17750-0-455, 3M Ref. No. FC-1015, L13167, straight-chain APFO, November 1, 1996

4) Final Report, Mutagenicity Test on T-6564 Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: with a Confirmatory Assay with Multiple Harvests, Corning Hazelton Inc., Study No. 17750-0-437CO, 3M Ref. No. FC-1015, L13167, straight-chain APFO, September 16, 1996

5) Final Report, Mutagenicity Test with T-6564 in the *Salmonella - Escherichia Coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay, Corning Hazelton Inc., Study No. 17750-0-409R, 3M Ref. No. FC-1015, L13167, straight-chain APFO, September 13, 1996

6) Final Report, Mutagenicity Test on T-6342 Measuring Chromosome Aberrations in Human Whole Blood Lymphocytes with a Confirmatory Assay with Multiple Harvests, Corning Hazelton, Inc., Study No. 17073-0-449CO, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, November 1, 1996

7) Final Report, Mutagenicity Test on T-6342 Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: with a Confirmatory Assay with Multiple Harvests, Corning Hazelton, Inc., Study No. 17073-0-437CO, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, September 16, 1996

8) Final Report, Mutagenicity Test on T-6342 in an *In Vivo* Mouse Micronucleus Assay, Corning Hazelton, Inc., Study No. 17073-0-455, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, December 14, 1995

9) Final Report, Mutagenicity Test with T-6342 in the *Salmonella - Escherichia Coli*/Mammalian-Microsome Reverse Mutation Assay, Corning Hazelton, Inc., Study No. 1703073-0-409, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, December 14, 1995

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Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Repeated-Dose Toxicity

1) Final Report, Volumes 1-4, Two Year Oral (Diet) Toxicity / Carcinogenicity Study of Fluorochemical FC-143 in Rats, Riker Laboratories, Inc., Study No. 0281CR0012, conducted during April 1981 - May 1983, August 29, 1987, with Study Report Amendment No. 1, dated November 2, 1987

2) Ninety Day Subacute Rat Toxicity Study on Fluorad® Fluorochemical FC-143

   a) Final Report, Ninety Day Subacute Rat Toxicity Study on Fluorad® Fluorochemical FC-143, International Research and Development Corporation, Study No. 137-089, 3M Reference No. T-3141, November 6, 1978

   b) 3M Internal Correspondence re FC-143 analysis of serum samples from rats of 90-day subacute study, from Jon Belisle to JE Long, dated March 20, 1978

   c) 3M Internal Correspondence re FC-143 analysis of liver samples from rats of 90-day subacute study, from Jon Belisle to JE Long, dated March 31, 1978

3) Final Report, 28-Day Oral Toxicity Study with FC-143 in Albino Mice, Industrial Bio-Test Laboratories, Inc., Study No. 8532-10655, 3M Reference No. T-1742CoC, Lot 269, Undated [1977]

4) Final Report, 28-Day Oral Toxicity Study with FC-143 in Albino Rats, Industrial Bio-Test Laboratories, Inc., Study No. 8532-10654, 3M Reference No. T-1742CoC, Lot 269, September 29, 1977

5) Final Report, Repeat Application 28 Day Percutaneous Absorption Study with T-2618CoC in Albino Rabbits, Safety Evaluation Laboratory, Riker Laboratories, Inc., Study No. 09790AB0485, 3M Ref. No. FC-143, March 15, 1981

6) Ninety Day Subacute Rhesus Monkey Toxicity Study

   a) Final Report, Ninety Day Subacute Rhesus Monkey Toxicity Study, International Research and Development Corporation, Study No. 137-090, November 10, 1978

   b) Analytical data, FC-143 Analysis of IRDC 137-090 Samples [monkey serum and liver samples], 3M Central Research Laboratories, May 16, 1978

7) Final Report, Vol. I-II, 13-Week Dietary Toxicity Study with T-5180, Ammonium Perfluorooctanoate (CAS No. 3825-26-1) in Male Rats, Hazelton Wisconsin, Inc., Study No. HWI 6329-100, May 17, 1993

8) Final Report, 5 Daily Dose Oral Toxicity Study with T-6669 (FC-143) in Rats, Corning Hazelton, Inc., Study No. CHW 6329-197, April 30, 1997

Ongoing:

26-Week Capsule Toxicity Study with Ammonium Perfluorooctanoate (APFO) in Cynomolgus Monkeys, Covance Laboratories Inc., No. 6329-231, 3M Ref. No. T-6889.3. In progress. Protocol provided.

Note: The study is sponsored by the Association of Plastic Manufacturers of Europe, APFO Toxicology Working Group. 3M has submitted a notice under TSCA Section 8(e) regarding preliminary data from this study. 3M and other Working Group members have received draft reports on the 4-week range-finding study and the full study, but these drafts are now obsolete. Final reports are in preparation and will be provided to the docket when available. In addition, the Working Group is still awaiting the hormonal measurements report covering cholecystokinin data; serum, urine, feces and liver APFO levels; palmitoyl CoA oxidase determinations; cell proliferation evaluations; and bile acid and receptor level determinations.

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Pharmacokinetic Studies

1) Final Report, Analytical Study, Single-Dose Intravenous Pharmacokinetic Study of T-6067 in Rabbits, 3M Ref. No. L13492 (45% perfluorooctanoic acid tetrabutylammonium salt in water and isopropyl alcohol), Study No. AMDT-120694.1, November 28, 1995; report includes Final Report, Single-Dose Intravenous Pharmacokinetic Study of T-6067 in Rabbits, Hazelton Wisconsin, Inc., Study No. HWI 6329-151, February 1, 1995

2) Final Report, Analytical Study, Single-Dose Absorption/Toxicity Study of T-6067 T-6068, and T-6069 in Rabbits, 3M Environmental Technology & Services, Study No. AMDT-011095.1, November 28, 1995; report includes Final Report, Single-Dose Absorption/Toxicity Study of T-6067, T-6068, and T-6069 in Rabbits, Hazelton Wisconsin, Inc., Study No. HWI 6329-152, May 26, 1995;

   T-6067 is L13492, 45% perfluorooctanoate tetrabutyl ammonium salt in water and isopropyl alcohol;

   T-6068 is fabric treated with high level of L13492, 45% perfluorooctanoate tetrabutyl ammonium salt in water and isopropyl alcohol;

   T-6069 is fabric treated with low level of L13492, 45% perfluorooctanoate tetrabutyl ammonium salt in water and isopropyl alcohol

3) ADME studies with FC-143-^{14}C

   a) Final Report, Absorption of FC-143-^{14}C in Rats After a Single Oral Dose, Riker Laboratories, Inc., January 14, 1980

   b) Final Report, Synthesis and Characterization of FC-143-^{14}C, Commercial Chemicals Division and Riker Laboratories, Inc., January 23, 1980

   c) Final Report, Extent and Route of Excretion and Tissue Distribution of Total Carbon-14 in Male and Female Rats After a Single IV Dose of FC-143-^{14}C, Riker Laboratories, Inc., February 7, 1980

   d) Final Report, Extent and Route of Excretion of Total Carbon-14 in Pregnant Rats After a Single Oral Dose of Ammonium ^{14}C-Perfluorooctanoate, Riker Laboratories, Inc., July 1, 1983

   e) Final Report, Enhanced Elimination of FC-95-^{14}C and FC-143-^{14}C in Rats with Cholestyramine Treatment, Riker Laboratories, Inc., March 14, 1980

4) Final Report, Single-Dose Intravenous Pharmacokinetic Study of T-6564 in Rabbits, Corning Hazelton Inc., Study No. CHW 6329-186, April 18, 1997

5) Final Report, 5-Daily Dose Dermal Absorption/Toxicity Study of T-6564 in Rabbits, Corning Hazelton, Inc., Study No. CHW 6329-185, April 28, 1997

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Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Teratology

1) Teratology Study of T-2998CoC in Rats

   a) Oral Rangefinder Study of T-2998CoC in Pregnant Rats, Riker Laboratories, Inc., Study No. 0680RR0018, February 25, 1981

   b) Final Report, Oral Teratology Study of T-2998 CoC in Rats, Riker Laboratories, Inc., Study No. 0681TR0110, December 15, 1981, with Amendment to Final Report, December 22, 1981 and Protocol

2) Teratology Study of T-3141CoC in Rabbits

   a) Oral Rangefinder Study of T-3141 CoC in Pregnant Rabbits, Riker Laboratories, Inc., Study No. 0681RB0331, November 18, 1981

   b) Final Report, Oral Teratology Study of T-3141CoC in Rabbits, Riker Laboratories, Inc., Study No. 0681TB0398, February 23, 1982

   c) 3M Internal Correspondence re analytical analyses of T-3141CoC, from LD Winter to DR Ricker, dated February 5, 1982

3) Letter re further testing from E. Marshall Johnson, Jefferson Medical College to Dr. Franklin D. Griffith, dated November 19, 1982

4) 3M Memo re FC 95 and 143 Teratology, from Marv Case to Georjean Adams, dated May 26, 1998, enclosing an analysis of the eye lens defect

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Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Human Sera/Medical Surveillance/Epidemiology

1) F. A. Ubel, et al. *Health Status of Plant Workers Exposed to Fluorochemicals- A Preliminary Report*, 41 Am. Ind. Hyg. Assoc. J. 584-589 (August 1980), with Summary.

2) Leonard M. Schuman & Jack S. Mandel, *An Epidemiologic Mortality Study of Employees at the Chemolite Plant* (February 1980), with Summary of study.

3) Jack S. Mandel & Leonard M. Schuman, "*Mortality Study at the 3M Chemolite Plant*" (January 1989), with Summary of study.

4) Frank D. Gilliland & Jack S. Mandel, *Mortality Among Employees of a Perfluorooctanoic Acid Production Plant*, 35 JOM 950-954 (September 1993), with Summary of study.

5) Frank Davis Gilliland, Fluorocarbons and Human Health: Studies in an Occupational Cohort (October 1992)(unpublished Ph.D. thesis, University of Minnesota), with Summary.

6) Geary W. Olsen, et al., *An Epidemiological Investigation of Reproductive Hormones in Men with Occupational Exposure to Perfluorooctanoic Acid*, 40 JOEM 614-619 (July 1, 1998), with Summary of study.

7) Frank D. Gilliland & Jack S. Mandel, *Serum Perfluorooctanoic Acid and Hepatic Enzymes, Lipoproteins, and Cholesterol: A Study of Occupationally Exposed Men*, 29 American Journal of Industrial Medicine 560-568 (1996), with Summary of study.

8) Geary W. Olsen, et al., *An Epidemiologic Investigation of Plasma Cholecystokinin and Hepatic Function in Perfluorooctanoic Acid Production Workers*, 3M Final Report EPI-0003, (1997), with Summary of study, Protocol, and Manuscript accepted for publication in 2000, Drug & Chemical Toxicology.

9) Physician Plant Summary Reports Regarding Medical Surveillance Program at Cottage Grove (1978-1991)

   a) Summary of Program Reports

   b) Blood Levels of RF/F in Selected Employees, dated June 20, 1978

   c) 3M Internal Correspondence re 1981 Chemical Division Health Evaluations from DE Roach to PF Riehle, dated February 16, 1982

   d) 3M Internal Correspondence re 1981 Chemolite Health Evaluations, from DE Roach to PF Riehle, dated August 12, 1982

e) 3M Internal Correspondence re Inorganic Fluoride Determinations, from DE Roach to PF Riehle, dated April 9, 1984

f) 3M Internal Correspondence re Organic Fluorine Levels, from DE Roach to PF Riehle, dated August 31, 1984

g) 3M Internal Correspondence re Medical Examinations, from L Zobel to DW Dworak, dated March 20, 1987

h) 3M Internal Correspondence re Chemolite Evaluations, Fall, 1990, from Larry R Zobel to Clair Murphy, et al., dated May 10, 1991

Previously submitted with April 21, 2000 letter to Charlie Auer, Fluorochemical Exposure (Serum) Assessment of (3M) Decatur Chemical and Film Plant Employees.

Ongoing Studies

See list of planned studies submitted with letter of April 21, 2000, which will address perfluorooctanoic acid as well as perfluorooctane sulfonate.

Attachments to Letter to C. Auer Dated May 25, 2000
Published Literature in 3M's Possession

Abdellatif, A.G., V. Préat, H.S. Taper, and M. Roberfroid. The modulation of rat liver carcinogenesis by perfluorooctanoic acid, a peroxisome proliferator. *Toxicology & Applied Pharmacology* **111** (1991) 530-537.

Abdellatif, A.G., V. Préat, J. Vamecq, R. Nilsson, and M. Roberfroid. Peroxisome proliferation and modulation of rat liver carcinogenesis by 2,3-dichlorophenoxyacetic acid, 2,4,5-trichlorophenoxyacetic acid, perfluorooctanoic acid and nafenopin. *Carcinogenesis* **11** (1990) 1899-1902.

Belisle, J., and D. Hagen. A method for determination of perfluorooctanoic acid in blood and other biological samples. *Analytical Biochemistry* **101** (1980) 369-376.

Biegel, L.B., M.E. Hurtt, and J.C. Cook. Effects of ammonium perfluorooctanoate (C8) on Leydig cell function: In vivo, ex vivo, and in vitro studies. *The Toxicologist* **13[1]** (1993) 399.

Biegel, L.B., R.C.M. Liu, M.E. Hurtt, and J.C. Cook. Effects of ammonium perfluorooctanoate on Leydig cell function: In vivo, ex vivo, and in vitro studies. *Toxicology & Applied Pharmacology* **134** (1995) *18-25.*

Borjes, H.K. and R.G. Thurman. Peroxisomal proliferators inhibit Acyl CoA synthesis and stimulate protein kinase C in vivo. *Toxicology & Applied Pharmacology* **126** (1994) 233-239.

Clapperton, R.M., B.T. Ingram, R.H. Ottewill, and A.R. Rennie. NMR spectroscopic and neutron scattering studies on ammonium decanoate-ammonium perfluorooctanoate mixtures. In: *Mixed Surfactant Systems. ACS Symposium Series 501,* Eds.: P.M. Holland and D.N. Rubingh, American Chemical Society: Washington, DC, 1992, 268-277.

Clegg, E.D., J.C. Cook, R.E. Chapin, P. Foster, and G.P. Daston. Leydig cell hyperplasia and adenoma formation: Mechanisms and relevance to humans (abstract). *Reproductive Toxicology* **11(1)** (1997) 107-121.

Cook, J.C., S.M. Murray, S.R- Frame, and M.E. Hurtt. Induction of Leydig cell adenomas by ammonium perfluorooctanoate: A possible endocrine related mechanism. *Toxicology & Applied Pharmacology* **113** (1991) 209-217.

Cook, J.C., M.E. Hurtt, S.R. Frame, L.B. Biegel. Effects of Wyeth-14,643 (WY) and ammonium perfluorooctanoate (C8) in Crl:CD BR (CD) rats. *The Toxicologist* **13[1]** (1993) 399.

Cook, J.C., M.E. Hurtt, S.R. Frame, L.B. Biegel. Mechanisms of extrahepatic tumor induction by peroxisome proliferators in Crl:CD BR (CD) rats. *The Toxicologist* **14[1]** (1994) 301.

Feller, D.R. and U. Intrasuksri. Mechanism of peroxisome proliferation by perfluorinated fatty acids in primary cultures of rat hepatocytes (abstract). *Toxicologist* **13** (1993) 395.

Gilliland, F.D. Fluorocarbons and human health: Studies in an occupational cohort. Unpublished Ph.D. Dissertation, University of Minnesota, 1992.

Gilliland, F.D. and J.S. Mandel. Mortality among employees of a perfluorooctanoic acid production plant. JOM **35[9]** (September 1993) 950-954.

Gilliland, F.D. and J.S. Mandel. Serum perfluorooctanoic acid and hepatic enzymes, lipoproteins, and cholesterol: a study of occupationally exposed men. *American Journal of Industrial Medicine* **29** (1996) 560-568.

Griffith, F.D., and J.E. Long. Animal toxicity studies with ammonium perfluorooctanoate. *American Industrial Hygiene Association Journal* **41** (1980) 576-583.

Handler, J.A., C.B. Seed, B.U. Bradford, and R.G. Thurmond. Induction of peroxisomes by treatment with perfluorooctanoate does not increase rates of H_2O_2 production in intact liver. *Toxicology Letters* **60** (1990) 61-68.

Hanhijärvi, H., M. Ylinen, A. Kojo, and V.M. Kosma. Elimination and toxicity of perfluorooctanoic acid during subchronic administration in the Wistar rat. *Pharmacology & Toxicology* **61** (1987) 66-68.

Hanhijärvi, H., R.H. Ophaug, and L. Singer. The sex-related difference in perfluorooctanoate excretion in the rat. *Proceedings of the Society for Experimental Biology & Medicine* **171** (1982) 50-55.

Haughom, B., and O. Spydevold. The Mechanism Underlying the Hypolipemic Effect of Perfluorooctanoic Acid (PFOA), Perfluorooctane Sulphonic Acid (PFOSA) and Clofibric Acid. *Biochim. Biophys. Acta.* **1128[I]** (1992) 65-72.

Hosokawa, M., and T. Satoh. Differences in the induction of carboxylesterase isozymes in rat liver microsomes by perfluorinated fatty acids. *Xenobiorica* **23** (1993) 1125-1133.

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PFOA and Associated Salts

Synonyms: FC-26, FX-1001, PFO, FC-143, 78.03, FC-126, N-2803-3, FX-1003, FC-118, FC-1015, FC-1015-X

Physical/Chemical Properties

Title	Laboratory or Author	Date Completed	Type
Water, acetone and toluene solubilitiy estimates - FC-143	3M Env. Lab	11/17/81	Robust summary, copy of data sheet

Environmental Fate and Transport

Title	Laboratory or Author	Completion Date	Type
Ready biodegradation of FC-143 (BOD/COD/TOC)	3M Env. Lab	7/14/77	Robust summary, copy of laboratory data summary
Technical Report Summary - Adsorption of FC 95 and FC 143 on Soil, and a critique from Dr. S. Boyd, Michigan State University	3M Env. Lab	2/27/78, 5/19/93	Robust summary, technical report, critique by S. Boyd (MSU)
Technical Report Summary - Biodegradation Studies of Fluorocarbons - III (FC-143)	3M Env. Lab	7/19/78	Robust summary, technical report
Technical Report Summary - FC-143 Photolysis Study Using Simulated Sunlight	3M Agrichemical Lab	2/2/79	Robust summary, technical report.
Technical Report Summary - Analysis for Fluorochemicals in Bluegill Fish, and a critique by J. W. Gillett of Cornell University	3M Env. Lab	5/1/1979, 3/8/93	Robust summary, technical report, critique by J. Gillett (Cornell)
Ready biodegradation of FC-143 (BOD/COD)	3M Env. Lab	6/5/80	Robust summary, copies of data sheets.
Calculated octanol water partition coefficient - FC-143	3M Env. Lab	12/7/81	Robust summary, copy of calculations
Ready biodegradation of FX-1001 (BOD/COD)	3M Env. Lab	2/7/85	Robust summary, computer-generated final report, copies of raw data sheets.
Ready biodegradation of FC-126 (BOD/COD)	Pace Analytical, Minneapolis, MN	5/20/87	Robust summary, computer-generated final report, copy of final report

PFOA and Associated Salts

Environmental Fate and Transport

Title	Laboratory or Author	Completion Date	Type
Technical Report Summary - Assessment of the Bioaccumulative Properties of Ammonium Perfluorooctanate: Static (fish test)	3M Env. Lab	5/31/95	Robust summary, technical report, critique by J. Giesy (MSU)

Ecotoxicity Elements

Title	Laboratory or Author	Completion Date	Type
96-hour acute static toxicity to fathead minnow - FC-143	3M Env. Lab	6/29/74	Robust summary, copy of data sheet
96-hour acute static toxicity to fathead minnow - FC-26	3M Env. Lab	11/10/74	Robust summary, copy of data sheet.
96-hour acute static toxicity to bluegill sunfish - FC-143	3M Env. Lab	4/8/78	Robust summary, copy of data sheet
96-hour acute static toxicity to bluegill sunfish - FC-143	3M Env. Lab	5/27/78	Robust summary, copy of data sheet
Two reports : "The Effects of Continuous Aqueous Exposure to 78.03 on Hatchability of Eggs and Growth and survival of Fry of Fathead Minnow (Pimephales promelas)" and "Summary of Histopathological Examinations of Fathead Minnow (Pimephales promelas) Exposed to 78.03 for 30 Days".	EG&G Bionomics, Wareham, MA	June 1978 and Sept. 1978	Robust summary, copies of two final reports.
Technical Report Summary - Aquatic Toxicity Testing: FC-143 (Lot-37) L.R. 5625 S	3M Env. Lab	5/8/80	Robust summary, technical report
Toxicity to activated sludge - FC-143	3M Env. Lab	6/4/80	Robust summary, copies of data sheets
Technical Report Summary - Multi-Phase Exposure/Recovery Algal Assay Test method (FC-143)	3M Env. Lab	11/16/81	Robust summary, technical report
48-hour acute static toxicity to *Daphnia magna* - FC-143 (3 studies on diet)	3M Env. Lab	5/5/82, 5/6/82, 6/2/82	Robust summary, copies of data sheets
Chronic Toxicity of Fluorochemicals to Daphnia magna (Water Flea) - FC-143, and statistical analysis of data provided by AScI Corp., Duluth, MN	3M Env. Lab	8/31/1984, 8/10/98	Robust summary, summary report, letter report
96-hour acute static toxicity to fathead minnow - FX-1001	3M Env. Lab	2/2/85	Robust summary, copy of data sheet.

PFOA and Associated Salts

Ecotoxicity Elements

Title	Laboratory or Author	Completion Date	Type
Activated sludge respiration inhibition (OECD 209) - FC-126	3M Env. Lab	4/20/87	Robust summary, copy of data sheets.
Microtox test - FC-126	3M Env. Lab	4/29/87	Robust summary, copy of data sheets.
48-hour acute static toxicity to *Daphnia magna* - FC-126	3M Env. Lab	4/30/87	Robust summary, copy of data sheets.
96-hour acute static toxicity to fathead minnow - FC-126	3M Env. Lab	5/1/87	Robust summary, copy of data sheets.
Activated sludge respiration inhibition (OECD 209) - FX-1003	3M Env. Lab	2/16/90	Robust summary, copies of data sheets
Microtox test - FX-1003	3M Env. Lab	3/7/90	Robust summary, copies of data sheets
Static Acute Toxicity of FX-1003 to the Fathead Minnow, *Pimephales promelas*	EnviroSystems, Hampton, New Hampshire	3/15/90	Robust summary, final report, protocol
Static Acute Toxicity of FX-1003 to the Daphnid, *Daphnia magna*	EnviroSystems, Hampton, New Hampshire	4/9/90	Robust summary, final report, protocol
Growth and Reproduction Toxicity Test with N2803-3 and the Freshwater Alga, *Selenastrum capricornutum*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	1/24/96	Robust summary, final report
Acute Toxicity of N2803-3 to the Fathead Minnow, *Pimephales promelas*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	1/24/96	Robust summary, final report
Acute Toxicity of N2803-3 to the Daphnid, *Daphnia magna*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	3/7/96	Robust summary, final report
Microtox test - FC-143	3M Env. Lab	4/24/96	Robust summary, copies of data sheets
Microtox test - FC-118	3M Env. Lab	4/24/96	Robust summary, copies of data sheets
Microtox test - FC-1015-X	3M Env. Lab	4/24/96	Robust summary, copies of data sheets

PFOA and Associated Salts

Ecotoxicity Elements

Title	Laboratory or Author	Completion Date	Type
Activated Sludge Respiration Inhibition Test - FC-1015-X	3M Env. Lab	4/25/96	Robust summary, copies of data sheets
Acute Toxicity of FC-1015 to the Fathead Minnow, *Pimephales promelas*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	5/15/96	Robust summary, final report
Growth and Reproduction Toxicity Test with FC-1015 and the Freshwater Alga, *Selenastrum capricornutum*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	5/15/96	Robust summary, final report
Acute Toxicity of FC-1015 to the Daphnd, *Daphnia magna*	T.R. Wilbury Laboratories, Inc, Marblehead, MA	5/15/96	Robust summary, final report
Summary Reports			
Title	**Laboratory or Author**	**Completion Date**	**Type**
Technical Report Summary - Final Comprehensive Report: FC 143	3M Env. Lab	3/23/79	Robust summary, technical report

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Update to Submission of May 18th

13. PFOS	**Perfluorooctane Sulfonate**

1) Letter from E. Marshall Johnson to William C. McCormick, III, re Hazleton teratology studies, dated December 7, 1983.

2) Letter from E. Marshall Johnson to William C. McCormick, III re Riker teratology studies on PFOS and ethyl FOSE, dated November 12, 1982.

8. N-EtFOSE alcohol	**N-ethyl perfluorooctane sulfonamidoethanol**

1) Letter from E. Marshall Johnson to William C. McCormick, III re Riker teratology studies on PFOS and ethyl FOSE, dated November 12, 1982.

2) Final Report, Biological Phase, Metabolism of N-Ethyl Perfluorooctane Sulfanomido Ethanol (Net-Fose; T-6316) In Cynomolgus Monkeys Following Administration of a Single Capsule Dose, Covance, Study No. 6329-226, June 9, 1999
Note: Analytical work associated with this study is ongoing.

PFOS didecyldimethylammonium salt

Synonyms: P3025, L-14394

Physical/Chemical Properties

Title	Laboratory or Author	Date Completed	Type
None			

Environmental Fate and Transport

Title	Laboratory or Author	Completion Date	Type
Determination of the 28-day Carbonaceous Biochemical Oxygen Demand (CBOD) for P3025	3M Env. Lab	5/20/97	Robust summary, final report

Ecotoxicity Elements

Title	Laboratory or Author	Completion Date	Type
Acute Toxicity of P3025 Developmental Material to Fathead Minnow (*Pimphales promelas*)	AScI Corporation, Duluth, MN	1/2/97	Robust summary, final report
Acute Toxicity of P3025 Developmental Material to *Daphnia magna*	AScI Corporation, Duluth, MN	1/10/97	Robust summary, final report
Growth Inhibition of P3025 Green Alga (*Selenastrum capricornutum*)	AScI Corporation, Duluth, MN	1/29/97	Robust summary, final report
Growth Inhibition of P3025 to Green Alga (*Selenastrum capricornutum*)	AScI Corporation, Duluth, MN	2/21/97	Robust summary, final report
Inhibitory Effects of P3025 on Microtox	3M Env. Lab	5/12/97	Robust summary, final report
Inhibitory Effects of P3025 on Activated Sludge Respiration	3M Env. Lab	5/12/97	Robust summary, final report

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

PFOA	

Acute Toxicity

1) Inhalation Toxicity Study of T-2305 CoC - Rat

   a) Final Report, An Acute Inhalation Toxicity Study of T-2305 CoC in the Rat, Bio/dynamics, Inc., Study No. 78-7184, May 3, 1979

   b) Technical Report Summary, Analysis of rat serum of FC-143, reported in terms of organic and inorganic fluorine, Central Research Laboratories, June 20, 1979

2) Final Report, Acute Oral Toxicity (LD_{50}) Study in Rats, International Research and Development Corporation, Study No. 137-091, 3M Reference No. Fluorad® FC-143, Lot 340, May 5, 1978

3) Final Report, Acute Oral Toxicity Study of T-6669 in Rats, Corning Hazelton, Inc., Study No. CHW 61001760, 3M Ref. FC-143, January 10, 1997

4) Final Report, Primary Skin Irritation Study - Rabbits, Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

5) Final Report, Primary Eye Irritation Study - Rabbits (Washout Procedure), Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

6) Final Report, Primary Eye Irritation Study - Rabbits (Not Washed), Biosearch, Inc., 3M Reference No. T-1395, FC-143, March 4, 1976

7) Final Report, Primary Skin Irritation Test with T-3371 in Albino Rabbits, Riker Laboratories, Study No. 0883EB0079, 3M Reference FC-26, Lot 389, July 13, 1983

8) Final Report, Acute Oral Toxicity - Rats, Biosearch, Inc., 3M Reference No. T-1585, FC-26 (perfluorooctanoic acid), September 16, 1976

9) Final Report, Primary Eye Irritation Study - Rabbits, Biosearch, Inc., 3M Reference No. T-1585, FC-26 (perfluorooctanoic acid), September 16, 1976

10) Final Report, Acute Dermal Toxicity Study of T-6342 in Rabbits, Corning Hazelton, Inc., Study No. HWI 50800374, 3M Ref. No. FC-1090, L13364, Lot 1, F11426, sodium perfluorooctanoate solution, October 24, 1995

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Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 78-7184

AN ACUTE INHALATION TOXICITY STUDY OF T-2305 CoC IN THE RAT

Submitted to: 3M Company
St. Paul, Minnesota 55101

Attention: Frank Griffith, Ph.D.

Date: May 3, 1979

I. GENERAL

An experiment was performed to investigate the acute inhalation toxicity of a dust of T-2305CoC in rats. The test material, received from 3M Company, was labeled "3M Company; T-2305CoC" and was in the form of a fine white powder.

II. EXPERIMENTAL

The test material was sieved through a 60-mesh sieve and hand packed into the large diameter cylinder of a Wright dust-feed mechanism (gear ratio 1:6). Dry air, at a flow rate of 16.0 liters per minute, was passed through the dust-feed mechanism to generate the desired concentration. The resultant dust-laden air was passed, undiluted, into the 32.2-liter glass exposure chamber housing the test animals. The exposure lasted for 1.0 hour.

The packed cylinder, cutting blade, and nozzle were weighed before and after the exposure. The weight loss was equal to the amount of material consumed during the exposure. The nominal concentration was determined by dividing this weight loss by the total air flow through the chamber during the exposure.

The test animals consisted of five male and five female Sprague-Dawley rats obtained from Charles River Breeding Laboratories, Wilmington, Massachusetts. On the day of exposure (Day 0-January 23, 1979) the pre-exposure weights ranged from 211 to 264 grams. The animals were observed prior to exposure to insure that they were free from abnormalities. Observations for abnormal signs were made at 15-minute intervals during the exposure, upon removal from the chamber, hourly for four hours post-exposure, and daily thereafter for 14 days.

II. EXPERIMENTAL (cont.)

Individual body weights were recorded on Day 0 (prior to exposure), Day 1, Day 2, Day 4, Day 7, and Day 14 (terminus). On Day 14, all animals were sacrificed (ethly ether) and blood samples were drawn from the dorsal aorta of all animals. These samples were spun for serum, pooled according to sex, and sent to the sponsor packed in dry ice for analysis. Gross necropsy examinations were also performed at this time.

III. RESULTS AND DISCUSSION

During the exposure, a total of 17.90 grams of test material was delivered in a total volume of 960 liters of dry air, yielding a nominal exposure concentration of 18.6 milligrams per liter. The chamber atmosphere appeared cloudy for the duration of the exposure and the chamber walls became coated with the test material. A second exit tube was added to the exposure chamber after the first half-hour of the exposure, when the first tube became obstructed with the test material.

Five minutes after the exposure was initiated, all the rats that could be observed through the dust cloud exhibited excessive lacrimation and salivation, decreased activity, labored breathing, and gasping. At ten minutes into the exposure, most of the rats also had their eyes closed. At 20 minutes, some rats exhibited mucoid nasal discharge and at 30 minutes, some rats exhibited irregular breathing in addition to all the abnormalities previously mentioned. Upon removal from the chamber, red nasal discharge (ten of ten), yellow staining of the ano-genital fur (nine of ten), dry rales (six of ten), red material around the eyes (five of ten), excessive salivation (four of ten), excessive lacrimation (one of ten), and body tremors (one of ten) were observed in the rats. Excessive salivation and lacrimation and body tremors had abated by the

III. RESULTS AND DISCUSSION (cont.)

one hour post-exposure observation and the rats did not exhibit red material around the eyes after the two hour post-exposure observation. Red nasal discharge (ten of ten), yellow staining of the ano-genital fur (six of ten), and dry rales (five of ten) were still seen at the four hour post-exposure observation.

During the 14-day observation period, excessive lacrimation (six of ten, one observation each), excessive salivation (three of ten), mucoid nasal discharge (ten of ten), yellow staining of the ano-genital fur (four of ten), dry rales (eight of ten), dry red material around the nose (two of ten), and moist rales (one of ten) were observed in the rats. These observations were generally scattered in appearance.

Individual body weights and necropsy observations are presented in Table 1. Weight gains appeared normal. Necropsy examinations revealed lung discoloration in eight of ten rats, which is a higher than normal incidence than that which is normally observed in Sprague-Dawley rats in this type of exposure.

IV. CONCLUSION

A one-hour inhalation exposure to a dust of T-2305CoC, at a nominal exposure concentration of 18.6 milligrams per liter, did not produce mortality in Sprague-Dawley rats. Immediate effects of the test material were excessive lacrimation and salivation, decreased activity, labored breathing, gasping, closing of the eyes, mucoid nasal discharge, irregular breathing, yellow staining of the ano-genital fur, and dry rales. The incidence of the lung discoloration at necropsy indicated a possible residual effect of the material at 14 days post-exposure.

George M. Rusch, Ph.D.
Director, Inhalation Technology

William E. Rinehart, Sc.D.
Vice President, Science

Report Preparation: Sandra J. Duckworth, B.A.

Table 1
An Acute Inhalation Toxicity Study
of T-2305 CoC in the Rat

78-7184

Individual Body Weights and Necropsy Observations

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
10	M	234	210	201	208	222	264	B. lungs mottled red and pink with red and white foci on all lobes.
11	M	246	215	205	229	254	303	B. lungs mottled pink and tan with dark red foci on all lobes.
12	M	248	224	212	233	253	306	B. lungs mottled orange and white.
13	M	241	205	196	207	236	315	B. lungs mottled orange and tan.
14	M	264	242	234	244	281	328	B. lungs mottled tan and dark pink with light tan and brown foci on all lobes.
20	F	232	201	199	233	242	257	B. lungs mottled pink and tan.
21	F	216	204	208	217	229	255	N.O.A.
22	F	234	205	199	223	240	240	B. lungs mottled orange and tan.
23	F	216	201	206	210	223	234	B. lungs mottled brown, dark pink, and tan.
24	F	211	192	196	212	226	237	N.O.A.

* N.O.A. - no observed abnormalities

Key: R = right; L = left; B = bilateral.

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Form 0747-11A

TECHNICAL REPORT SUMMARY

Date: June 20, 1979

TO: TECHNICAL COMMUNICATIONS CENTER – 201-2CN

(Important – If report is printed on both sides of paper, send two copies to TCC.)

Division: CENTRAL RESEARCH LABORATORIES, Analytical and Properties Research Laboratory	Dept. Number: 0502
Project: Trace Fluorochemicals in the Environment	Project Number: A000007
Report Title: AR No. 7166 - FC-143 Inhalation Study - Analysis For F^- and RF	Report Number: 166
To: W. C. McCORMICK - 220-2E	
Author(s): JON BELISLE, VICKI BUNNELLE	Employee Number(s): 088240, 013817
Notebook Reference:	No. of Pages Including Coversheet: 2

SECURITY ▶ ☐ Open (Company Confidential) ☒ Closed (Special Authorization)

3M CHEMICAL REGISTRY ▶ New Chemicals Reported ☐ Yes ☒ No

KEYWORDS: (Select terms from 3M Thesaurus. Suggest other applicable terms.)

Central Research
Analytical Report
Chemical Analysis

CURRENT OBJECTIVE:

Request No. A71423
Requestor - Bill McCormick
Project No. 91721100

REPORT ABSTRACT: (200-250 words) This abstract information is distributed by the Technical Communications Center to alert 3M'ers to Company R&D. It is Company confidential material.

The analysis of serum from the Bio/Dynamics rat inhalation study of FC-143 is reported in terms of organic and inorganic fluoride.

ABSTRACT CLOSED

Information Liaison Initials: _____

000036

CENTRAL ANALYTICAL LABORATORY

Report No. 7166

Date June 20, 1979

Subject: FC-143 Inhalation Study - Analysis For F^- and RF

Requestor: Bill McCormick Dept. Name Toxicology Proj. No. 91721100

Request No. A71423 Dated February 15, 1979

Report:

Serum from Bio/Dynamics study 78-7184 (3M designation T-2305 CoC) was received for analysis of organic and inorganic fluoride. The 2 submitted samples were from Group I, one being the male rats (animals 10-14) and the other female rats (animals 20-24). Therefore, only one exposure concentration was analyzed.

Rat	F^- (Inorganic)	RF (Organic)
female	0.01 ppm	2 ppm
male	0.02	42

It is most interesting to once again see the difference in RF levels between male and female. You will recall that the 28 day IBT and the 90 day IRDC feeding study (both reported on Request A67821, Report 6925) found the male serum FC-143 levels approximately 100x greater than the female serum levels. The difference was confirmed by analysis of the IRDC livers.

Therefore, 3 separate studies (IBT, IRDC, Bio/Dynamics) using 2 approaches (feeding, inhalation) indicate that the male rat accumulates more perfluorooctanoic acid/salt than the female. A similar study on monkeys (A68616, Report 6919) indicated no or very little difference between male and female.

Jon Belisle

Jon Belisle

Vicki Bunnelle

Vicki Bunnelle

JB/VB/rs

International Research and Development Corporation

SPONSOR: 3M Company

TEST MATERIAL: Fluorad® Fluorochemical FC-143

SUBJECT: Acute Oral Toxicity (LD_{50}) Study in Rats.

Wilson P. Dean, B.A.
Director of Acute Toxicology
and Special Studies
(Study Director)

D. Clifford Jessup, Ph.D.
Associate Director of Research

Collaborators:

Gary Thompson, B.S.
Group Technical Supervisor
Greg Romig, B.S.
Unit Technical Supervisor
David Powell, B.A.
Unit Supervisor,
Report Preparation,
Acute and Special Studies
Department

Date: May 5, 1978

137-091

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Table No.

1. Pharmacotoxic Signs 5- 6

I. SYNOPSIS

Based upon the data obtained, the acute oral LD_{50} values and 95% confidence limits were calculated to be as follows:

Male Rats: 680 (399 - 1157) mg/kg.
Female Rats: 430 (295 - 626) mg/kg.
Combined Male and Female Rats: 540 (389 - 749) mg/kg.

II. TEST MATERIAL

The test material was received from the 3M Company, St. Paul, Minnesota on October 24, 1977. It was identified as "Fluorad® Fluorochemical FC-143, 3M Stock No. 98-0211-0008-0, Lot 340" and was received as a white powder.

III. METHOD

Twenty-five male and 25 female rats of the Charles River CD strain (obtained from Charles River Breeding Laboratories, Inc., Portage, Michigan), weighing from 180 to 221 grams, were used for this study. The rats were housed by sex in groups of 5 rats per cage, in hanging wire-mesh cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals". Water and Purina Laboratory Chow were available ad libitum, except for an overnight period immediately preceding oral administration during which food, but not water, was withheld.

The test material was administered orally by gavage as an emulsion in 40% acetone/60% corn oil at the following dosage levels to male and female rats: 100, 215, 464, 1000 and 2150 mg/kg.

Five rats of each sex were used at each dosage level. Volumes of 10 ml/kg of body weight were administered at all dosage levels.

All rats were observed for mortality and pharmacotoxic signs during the first four hours after dosing, at 24 hours and daily thereafter for a total of 14 days. Body weights were recorded immediately prior to dosing (control weight) and at 7 and 14 days. All rats which died on study were subjected to gross necropsy examination as were all survivors at the end of the 14 day observation period.

IV. RESULTS

A. MORTALITY AND LD_{50} VALUES:

Dose - Mortality Data

Dosage Level mg/kg	Number of Deaths														Total Mortalities		
	Hrs 0-4		Days 1		2		3		4		5		6		7-14				
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female	Total
100															1		1/5	0/5	1/10
215																	0/5	0/5	0/10
464					2	2				1							2/5	3/5	5/10
1000				2	2	2		1	1								3/5	5/5	8/10
2150	1	3	4	2													5/5	5/5	10/10

The Acute Oral LD_{50} Values and 95% Confidence Limits

Male Rats: 680 (399 - 1157) mg/kg.
Female Rats: 430 (295 - 626) mg/kg.
Combined Male and Female Rats: 540 (389 - 749) mg/kg.

Slope

Male Rats: 1.00.
Female Rats: 1.00.
Combined Male and Female Rats: 1.00.

Statistical References

[1]Weil, C. S. 1952. Tables for Convenient Calculation of Median Effective Dose and Instruction in Their Use. Biometrics, 8: 249-263.

[2]Thompson, W. R. and Weil, C. S. 1952. On the Construction of Tables for Moving Average Interpolation. Biometrics, 8: 51-54.

[3]Eby, R. 1957. Statistical Tables for Dose Evaluation, Report No. 5711. Miles-Ames Research Laboratory, Elkhart, Indiana.

B. PHARMACOTOXIC SIGNS:

The following pharmacotoxic signs were observed during the 14 day observation period: (see Table 1).

NUMBER OF RATS SHOWING PHARMACOTOXIC SIGNS AND TIME [HOUR] (DAY) OBSERVED

TABLE - 1.

COMPOUND - FC-143:

MALES

OBSERVATION	100 mg/kg	215 mg/kg	464 mg/kg	1000 mg/kg	2150 mg/kg
Normal	3 (2 - 12), 4 (13 - 14)	4 (2 - 5), 5 (6 - 14)	2 (2 - 5), 3 (6 - 14)	2 (6 - 14)	
Ptosis	2 (1)	2 (1)	3 (1)	1 [1], 3 (1)	
Piloerection				1 (1)	
Hypoactivity	5 [1, 2 1/2, 4], 5 (1)	5 [1, 2 1/2, 4], 5 (1), 1 (2 - 3)	5 [1, 2 1/2, 4], 5 (1), 1 (2 - 3)	5 [1, 2 1/2, 4], 5 (1), 3 (2 - 3),, 2 (4 - 5)	5 [1, 2 1/2], 4 [4]
Decreased Limb Tone	3 [1], 4 [2 1/2, 4], 3 (1)	4 [1, 2 1/2], 3 [4], 3 (1)	2 [1], 3 [2 1/2], 5 [4], 5 (1)	2 [1, 2 1/2], 4 [4], 5 (1), 1 (2 - 3)	5 [2 1/2], 4 [4]
Ataxia	4 [1], 5 [2 1/2], 2 [4]	4 [1], 3 [2 1/2, 4]	3 [1], 2 [2 1/2, 4], 1 (1)	2 [1], 3 [2 1/2,4], 5 (1), 1 (2 - 3)	3 [1], 5 [2 1/2], 4 [4]
Corneal Opacity	2 (1 - 6), 1 (7 - 12)	2 (1), 1 (2 - 5)	2 (1), 1 (2 - 5)	4 (1)	
Death	1 (7)		2 (2)	2 (2), 1 (4)	1 [4], 4 (1)

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NUMBER OF RATS SHOWING PHARMACOTOXIC SIGNS AND TIME [HOUR] (DAY) OBSERVED

TABLE - 1.(Cont.)

COMPOUND - FC-143:

FEMALES

OBSERVATION	100 mg/kg	215 mg/kg	464 mg/kg	1000 mg/kg	2150 mg/kg
Normal	5 (2 - 14)	5 (2 - 14)	2 (4 - 14)		
Ptosis			3 (1)	2 (1)	
Piloerection				3 (1), 1 (2)	
Hypothermic to Touch			1 (2 - 3)		
Hypoactivity	5 [1, 2 1/2, 4], 5 (1)	5 [1, 2 1/2, 4], 5 (1)	5 [1, 2 1/2, 4], 5 (1), 3 (2 - 3)	5 [1, 2 1/2, 4], 3 (1), 1 (2)	5 [1, 2 1/2], 2 [4]
Decreased Limb Tone	4 [1, 2 1/2], 3 [4], 3 (1)	1 [1], 2 [2 1/2], 3 [4], 3 (1)	1 [1], 2 [2 1/2], 5 [4], 5 (1), 2 (2 - 3)	2 [1], 4 [2 1/2], 5 [4], 3 (1), 1 (2)	5 [2 1/2], 2 [4]
Ataxia	4 [1], 5 [2 1/2], 3 [4]	4 [1, 2 1/2,4]	2 [1, 2 1/2], 3 [4], 3 (1), 2 (2 - 3)	4 [1, 2 1/2], 5 [4], 3 (1), 1 (2)	1 [1], 5 [2 1/2], 2 [4]
Corneal Opacity				1 (1)	
Death			2 (2), 1 (4)	2 (1), 2 (2), 1 (3)	3 [4], 2 (1)

Study No.: 137-091

C00004

C. BODY WEIGHTS:

The following body weights were obtained during the 14 day observation period:

Dosage Level (mg/kg)	Individual Rat Number	Sex	Control Weight (grams)	7 Day Weight (grams)	14 day Weight (grams)
100	76888	Male	194	242	296
	76889	Male	189	228	275
	76890	Male	210	Died	Died
	76891	Male	190	240	285
	76892	Male	198	246	304
	76908	Female	198	217	240
	76909	Female	192	212	226
	76910	Female	186	208	227
	76911	Female	204	225	244
	76912	Female	188	191	212
215	76893	Male	214	266	318
	76894	Male	213	267	330
	76895	Male	212	254	312
	76896	Male	210	252	290
	76897	Male	203	234	298
	76913	Female	195	218	243
	76914	Female	182	203	232
	76915	Female	190	209	230
	76916	Female	185	205	222
	76917	Female	182	203	236
464	76898	Male	215	Died	Died
	76899	Male	202	249	330
	76900	Male	216	239	296
	76901	Male	218	Died	Died
	76902	Male	200	245	302
	76918	Female	180	200	227
	76919	Female	180	Died	Died
	76920	Female	182	204	223
	76921	Female	192	Died	Died
	76922	Female	194	Died	Died
1000	76903	Male	188	208	270
	76904	Male	194	Died	Died
	76905	Male	192	Died	Died
	76906	Male	186	Died	Died
	76907	Male	192	223	290

Dosage Level (mg/kg)	Individual Rat Number	Sex	Control Weight (grams)	7 Day Weight (grams)	14 Day Weight (grams)
1000	76923	Female	202	Died	Died
	76924	Female	180	Died	Died
	76925	Female	184	Died	Died
	76926	Female	198	Died	Died
	76927	Female	196	Died	Died
2150	77208	Male	206	Died	Died
	77209	Male	213	Died	Died
	77210	Male	208	Died	Died
	77211	Male	211	Died	Died
	77212	Male	213	Died	Died
	77213	Female	221	Died	Died
	77214	Female	213	Died	Died
	77215	Female	217	Died	Died
	77216	Female	219	Died	Died
	77217	Female	206	Died	Died

D. NECROPSY FINDINGS:

Gross necropsy observations were noted as indicated on pages 9, 10 and 11.

1. Rats which died during the study period:

Dosage Level (mg/kg)
Number Exhibiting Sign/Number Necropsied

Gross Necropsy Observations:	100		215		464		1000		2150	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Yellow stained urogenital region								2/5	3/5	2/5
Lungs, congestion	1/1				2/2	1/3	2/3	4/5	4/5	5/5
Lungs, pitted									2/5	
Lungs, red foci										1/5
Stomach, distension						1/3	2/3	4/5	5/5	3/5
Stomach, fluid filled						1/3			5/5	4/5
Stomach, mucosa, hyperemia						3/3	1/3	1/5	4/5	1/5
Stomach, mucosa, thickened						2/3	2/3			
Stomach, contains dark red fluid						1/3				
Stomach, glandular mucosa, erosion						1/3				
Stomach, contains dark red particulate material									1/5	
Stomach, red fluid filled										1/5

Gross Necropsy Observations:	Dosage Level (mg/kg) Number Exhibiting Sign/Number Necropsied									
	100		215		464		1000		2150	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Intestines, red fluid filled									2/5	1/5
Liver, pale coloration									1/5	
Partially, cannibalized	1/1									
Red stain around nose/ mouth									3/5	4/5

2. Rats which were sacrificed following 14 days of observation:

Gross Necropsy Observations:	Dosage Level (mg/kg) Number Exhibiting Sign/Number Necropsied							
	100		215		464		1000	
	Male	Female	Male	Female	Male	Female	Male	Female
No gross lesions					1/3	1/2	1/2	
Lungs, foci				1/5				
Stomach, mucosa, thickened	4/4	5/5	5/5	4/5	2/3	1/2	1/2	
Stomach, glandular mucosa, hyperemia	1/4	2/5	1/5	1/5			1/2	
Uterus, hydrometra		1/5		2/5				
Kidneys, mottled coloration	2/4	2/5	3/5	4/5	1/3		1/2	

ning Hazleton Inc.
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608.241.4471 608.241.7227 Fax

CORNING Hazleton

Sponsor:

3M
St. Paul, Minnesota

FINAL REPORT

Study Title:

Acute Oral Toxicity Study of T-6669 in Rats
(OECD Guidelines)

Author:

Steven M. Glaza

Study Completion Date:

January 10, 1997

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

CHW 61001760

RECEIVED
JAN 13 1997

COMPLIANCE STATEMENT

Acute Oral Toxicity Study of T-6669 in Rats
(OECD Guidelines)

This study was conducted in accordance with the Organisation for Economic Cooperation and Development and Principles of Good Laboratory Practice, C(81)30(Final) with the exception that analysis of the test material mixtures for concentration, homogeneity/solubility and stability was not conducted.

Steven M. Glaza
Study Director
Acute Studies
Corning Hazleton Inc.

1-10-97
Date

QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Corning Hazleton Inc., in accordance with the Organisation for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice, C(81)30(Final). The following inspections were conducted and findings reported to the Study Director and management.

Inspection Dates From	To	Phase	Date Reported to Study Director	Date to Management
10/24/96	10/24/96	Necropsy	10/24/96	10/24/96
12/29/96	12/30/96	Data/Report Review	12/30/96	12/30/96

Susan K. Swatch
Representative, Quality Assurance Unit

1-10-97
Date

STUDY IDENTIFICATION

Acute Oral Toxicity Study of T-6669 in Rats
(OECD Guidelines)

Test Material	T-6669
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	Roger G. Perkins, PhD, DABT 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-3222
Study Director	Steven M. Glaza Corning Hazleton Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Corning Hazleton Inc. 3301 Kinsman Boulevard Madison, WI 53704
Study Timetable	
Study Initiation Date	October 9, 1996
Experimental (In-life) Start Date	October 10, 1996
In-life End Date	November 14, 1996
Experimental Termination Date	January 10, 1997
Study Completion Date	January 10, 1997

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KEY PERSONNEL

Acute Studies

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Jeffrey B. Hicks
In-life Supervisor

Rose M. Bridge
Administrative Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

Quality Assurance

Sherry R. W. Petsel
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Cindy J. Cary, DVM
Diplomate, ACLAM
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Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

Deborah L. Pirkel/
Jack Serfort
Supervisors
Necropsy

Anne Mosher
Supervisor
Pathology Data

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OBJECTIVE

The objective of this study was to assess the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats.[1]

All procedural times presented in this report fall within the acceptable ranges as specified in the Wisconsin facility of Corning Hazleton (CHW) Inc. Standard Operating Procedure (SOP).

TEST MATERIAL

Identification

The test material was identified as T-6669 and described as a white powder.

Purity and Stability

The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Analysis of the test material mixture for concentration, homogeneity/solubility and stability was not conducted

Storage and Retention

The test material was stored at room temperature. Any unused test material will be returned to the sponsor after issuance of the final report according to CHW SOP.

Safety Precautions

The test material handling procedures were according to CHW SOPs and policies.

TEST SYSTEM

Test Animal

Young adult albino rats of the Crl:CD (SD)BR strain were procured from Charles River Laboratories, Inc. on September 23, October 7, October 21, 1996 (Portage, Michigan facility) and on October 1 and October 15, 1996 (Kingston, New York facility).

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were separated by sex and group housed in screen-bottom stainless steel cages. Environmental controls for the animal room were set to maintain a temperature of 19° to 25°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark lighting cycle. In cases where variations from these conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Animal Diet

The animals were provided continuous access to Laboratory Rodent Diet #5001, PMI Feeds, Inc., and water except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by CHW. There were no known contaminants in the feed or water at levels that could be expected to interfere with or affect the results of the study.

Animal Selection and Grouping

Ten male and 10 female healthy, acclimated rats, weighing from 208 to 269 g and approximately 8 to 12 weeks of age, were assigned to two treatment groups of 250 and 500 mg/kg of body weight. Each dose level consisted of 5 male and 5 female rats. The animals were identified by animal number and corresponding ear tag throughout the study.

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Justification for Species Selection

Historically, rats have been used as a representative of a rodent species and are preferred by various regulatory agencies.

PROCEDURES

Preparation and Administration of Test Material

The test material was mixed with distilled water to a concentration of 0.025 g/mL for the 250 mg/kg dose level and 0.050 g/mL for the 500 mg/kg dose level. The prepared test material mixtures appeared to be solutions. An individual dose of the respective test mixture was calculated for each animal based on its fasted body weight and administered by gavage at a volume of 10 mL/kg of body weight. The test material mixtures were stored at room temperature until administered.

Reason for Route of Administration

Historically, the oral route has been the route of choice for administering a known amount of test material.

Observations

Clinical observations and mortality checks were conducted at 1, 2.5, and 4 hours after test material administration and daily thereafter for 14 days. Mortality checks were conducted twice a day (morning and afternoon) for 13 days after test material administration and again the morning of Day 14.

Body weights were determined before test material administration (Day 0). Additional body weights were determined at Day 7, at termination of the in-life phase (Day 14), or at death when survival exceeded 1 day.

Pathology

At termination of the respective in-life phase for each dose level, all surviving animals were euthanized. All animals, whether found dead during the study or euthanized, were

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subjected to an abbreviated gross necropsy examination and any abnormalities were recorded. After necropsy, the animals were discarded and no tissues were saved.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and an original signed copy of the final report will be retained in the archives of CHW in accordance with CHW SOP.

RESULTS

Mortality

A summary of the observed mortality is in Table 1. No mortality was observed at the 250 mg/kg dose level. Two males and all five females treated at 500 mg/kg were found dead within 4 days of test material administration. No other mortality was observed. Based on the observed mortality, the estimated oral LD_{50} values were determined to be greater than 500 mg/kg for males and between 250 and 500 mg/kg for females.

Body Weights

Individual and mean body weights and body weight gains are in Table 2. All surviving animals exhibited body weight gain throughout the study.

Clinical Signs

Individual clinical signs are in Table 3. All animals treated at 250 mg/kg appeared normal during the study with the exception of two females which exhibited red-stained face and/or wet urogenital area within 24 hours of test material administration. Clinical signs of toxicity observed in the animals treated at 500 mg/kg included red-stained face, yellow-stained or wet urogenital area, hypoactivity, hunched posture, staggered gait, excessive

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salivation, and death. The surviving animals treated at 500 mg/kg returned to a normal appearance by Day 7.

Pathology

Individual gross necropsy pathology findings are in Table 4. A summary report by the study pathologist is on Page 14. There were no test material related lesions observed at necropsy.

DISCUSSION

The acute oral toxicity of T-6669 was evaluated in male and female rats when administered as a single gavage dose at levels of 250 and 500 mg/kg of body weight. Based on the observed mortality, the estimated oral LD_{50} values for male rats was determined to be greater than 500 mg/kg and between 250 and 500 mg/kg for females. All mortality occurred at the 500 mg/kg dose level within 4 days of test material administration. All animals treated at 250 mg/kg appeared normal during the study with the exception of two females which exhibited red-stained face and/or wet urogenital area within 24 hours of treatment. Clinical signs of toxicity observed in the animals treated at 500 mg/kg included red-stained face, yellow-stained or wet urogenital area, hypoactivity, hunched posture, staggered gait, and excessive salivation. Animals surviving to the end of the observation period exhibited body weight gain during the study. The gross necropsy examinations did not reveal any test material related lesions.

SIGNATURE

Steven M. Glaza
Study Director
Acute Studies

1-10-97
Date

REFERENCE

1. "Acute Oral Toxicity," *Organisation for Economic Cooperation and Development Guidelines for Testing of Chemicals*, Section 4, Health Effects, Number 401, Paris Cedex (February 24, 1987).

PATHOLOGY REPORT

There were 10 rats (five male, five female) each from dose levels of 250 and 500 mg/kg necropsied. All animals given 500 mg/kg, except for three males, died on test. The surviving animals were euthanized and necropsied at the termination of the study. The dose level, day of death, and gross observations recorded for each animal are in the Individual Pathology Comments that follow this report.

At necropsy, there were few findings and all of these were considered incidental and unrelated to the test material. In the animals that died on test, one male was partially cannibalized, one female had multiple, dark brown areas of variable size in the glandular mucosa of the stomach, and both horns of the uterus in another female were filled with clear fluid. The pelvis of both kidneys in one female given 250 mg/kg was observed to be large. There were no visible lesions in the remaining animals.

Thomas E. Palmer, PhD
Pathologist

1-10-97
Date

(61001760.fin)
121696

Table 1

Mortality Summary

Dose Level (mg/kg)	Sex	Mortality Results No. Died/ No. Dosed*
250	M	0/5
250	F	0/5
500	M	2/5, Days 3^1, 4^1
500	F	5/5, Days 0^1, 1^1, 3^1, 4^2

* Superscript number indicates number of animals found dead on the indicated day.

Table 2

Individual and Mean Body Weights/ Body Weight Gains (g)

Animal Number	Day 0 Weight	Day 7		Day 14	
		Weight	Gain*	Weight	Gain*
		Males (250 mg/kg)			
C12551	269	330	61	383	114
C12550	269	325	56	339	70
C12611	248	307	59	375	127
C12612	259	296	37	354	95
C12613	253	296	43	375	122
Mean	260	311	51	365	106
		Females (250 mg/kg)			
C12371	261	294	33	315	54
C12367	248	285	37	294	46
C12368	235	280	45	285	50
C12369	259	303	44	309	50
C12370	252	287	35	288	36
Mean	251	290	39	298	47

* Gain from Day 0 body weight.

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Table 2 (Continued)

Individual and Mean Body Weights/ Body Weight Gains (g)

Animal Number	Day 0 Weight	Day 7		Day 14	
		Weight	Gain*	Weight	Gain*
		Males (500 mg/kg)			
C12231	213	249	36	302	89
C12227	221	$(167)^4$	-	-	-
C12228	208	$(168)^3$	-	-	-
C12229	217	271	54	320	103
C12230	215	274	59	334	119
Mean	215	265	50	319	104
		Females (500 mg/kg)			
C12276	248	$(231)^3$	-	-	-
C12277	223	$(175)^4$	-	-	-
C12278	224	†	-	-	-
C12279	246	$(234)^1$	-	-	-
C12280	236	$(193)^4$	-	-	-
Mean	235	-	-	-	-

* Gain from Day 0 body weight.

† Animal was found dead on the day of dosing. No body weight required.

( ) Value in parentheses is a dead body weight and was not considered in calculating the mean. Superscript number indicates the day the animal was found dead.

\- Not applicable.

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Table 3

Individual Clinical Signs

Animal Number	Observation	Hour			Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Males (250 mg/kg)																		
C12551	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12550	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12611	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12612	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12613	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Females (250 mg/kg)																		
C12371	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12367	Appeared normal	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Red-stained face	-	-	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
C12368	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
C12369	Appeared normal	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Red-stained face	-	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Wet urogenital area	-	-	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C12370	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ Condition existed.
- Condition not evident.

Table 3 (Continued)

Individual Clinical Signs

Animal Number	Observation	Hour			Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
								Males (500 mg/kg)										
C12231	Appeared normal	✓	✓	✓	-	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓
	Red-stained face	-	-	-	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-
	Yellow-stained urogenital area	-	-	-	-	-	-	-	✓	✓	-	-	-	-	-	-	-	-
C12227	Appeared normal	✓	✓	✓	-	-	-											
	Red-stained face	-	-	-	✓	✓	✓											
	Hypoactivity	-	-	-	-	✓	✓											
	Hunched posture	-	-	-	-	-	✓											
	Staggered gait	-	-	-	-	-	✓											
	Found dead	-	-	-	-	-	-	✓										
C12228	Appeared normal	✓	✓	✓	-	-												
	Red-stained face	-	-	-	✓	✓												
	Hypoactivity	-	-	-	-	✓												
	Yellow-stained urogenital area	-	-	-	-	✓												
	Found dead	-	-	-	-	-	✓											
C12229	Appeared normal	✓	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Red-stained face	-	-	-	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-
C12230	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ Condition existed.
- Condition not evident.

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Table 3 (Continued)

Individual Clinical Signs

Animal Number	Observation	Hour 1.0	2.5	4.0	Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Females (500 mg/kg)													
C12276	Appeared normal	✓	✓	✓	-	-												
	Red-stained face	-	-	-	✓	✓												
	Wet urogenital area	-	-	-	✓	✓												
	Hypoactivity	-	-	-	-	✓												
	Hunched posture	-	-	-	-	✓												
	Found dead	-	-	-	-	-	✓											
C12277	Appeared normal	✓	✓	✓	-	-	-											
	Red-stained face	-	-	-	✓	✓	✓											
	Wet urogenital area	-	-	-	✓	✓	✓											
	Hypoactivity	-	-	-	-	✓	✓											
	Hunched posture	-	-	-	-	✓	✓											
	Found dead	-	-	-	-	-	-	✓										
C12278	Appeared normal	✓	✓															
	Excessive salivation	✓	✓															
	Found dead	-	-	✓														
C12279	Appeared normal	✓	✓	✓	-													
	Red-stained face	-	-	-	✓													
	Wet urogenital area	-	-	-	✓													
	Hypoactivity	-	-	-	✓													
	Staggered gait	-	-	-	✓													
	Found dead (after clinical observation)	-	-	-	✓													
C12280	Appeared normal	✓	✓	✓	-	-	-											
	Red-stained face	-	-	-	✓	✓	✓											
	Wet urogenital area	-	-	-	✓	✓	✓											
	Hypoactivity	-	-	-	-	-	✓											
	Hunched posture	-	-	-	-	-	✓											
	Staggered gait	-	-	-	-	-	✓											
	Found dead	-	-	-	-	-	-	✓										

✓ Condition existed.
- Condition not evident.

Table 4

Individual Pathology Comments

Dose Level: 250 mg/kg of Body Weight

Animal Number	Sex	Test Day		Necropsy Observation
		Died	Sacrificed	
C12551	M	-	14	No visible lesions.
C12550	M	-	14	No visible lesions.
C12611	M	-	14	No visible lesions.
C12612	M	-	14	No visible lesions.
C12613	M	-	14	No visible lesions.
C12371	F	-	14	Both of the kidneys have a large pelvis.
C12367	F	-	14	No visible lesions.
C12368	F	-	14	No visible lesions.
C12369	F	-	14	No visible lesions.
C12370	F	-	14	No visible lesions.

- Not applicable.

Table 4 (Continued)

Individual Pathology Comments

Dose Level: 500 mg/kg of Body Weight

Animal Number	Sex	Test Day		Necropsy Observation
		Died	Sacrificed	
C12231	M	-	14	No visible lesions.
C12227	M	4	-	The right flank was cannibalized.
C12228	M	3	-	No visible lesions.
C12229	M	-	14	No visible lesions.
C12230	M	-	14	No visible lesions.
C12276	F	3	-	The glandular mucosa of the stomach has multiple dark brown areas, up to 2 x 1 mm.
C12277	F	4	-	No visible lesions.
C12278	F	0	-	No visible lesions.
C12279	F	1	-	The lumen in the bilateral horns of the uterus is filled with clear fluid.
C12280	F	4	-	No visible lesions.

- Not applicable.

APPENDIX

Protocol TP2069
Protocol Amendment No. 1
Protocol Amendment No. 2
Protocol Amendment No. 3

10/ 00/ 96 12:42 MEDICAL ZE 02 008

Sample Submittal Form

This form is to be used when submitting samples for routine acute testing. Special testing needs can be easily arranged by contacting the Acute Studies Department at (608) 241-7292.

CHW Study No. 61001760
Enclose with samples and send to:
Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Submitted by: ROGER G. PERKINS
Company: 3M
Date Sample Sent: (PAPER ONLY) 10/8/96
Number of Reports Required: 3

Full GLP Compliance: ✓ Yes ___ No
___ FDA (21 CFR 58)
___ EPA (TSCA—40 CFR 792)
___ EPA (FIFRA—40 CFR 160)
X OECD
___ MAFF
___ MOHW

Sample Name: T-6669
Physical Description: WHITE SOLID
Special Handling Precautions: SEE MSDS 10-3803-2
Test material purity and stability information (including under test conditions) on file with Sponsor: X Yes ___ No
Test mixture analysis for concentration/homogeneity/stability to be conducted: ___ Yes* X by Sponsor ___ by CHW
X No
Sample Disposal: ✓ Return to Sponsor at following address:

L.J. PICKETT
3M SCD
BLDG 53-3S-02 3M CENTER
ST. PAUL, MN 55144-1000

___ Dispose of according to CHW SOPs

Sample Storage Requirements:
X Room temperature
___ Refrigerated
___ Other

* At additional cost to Sponsor (CHW will contact Sponsor as to these additional charges).

Tests

Acute Oral Toxicity in Rats

___TP8084 Up and down LD50 procedure
___TP3206 FHSA screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
___TP3013 EPA screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
X TP2069 OECD screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg

Special Instructions: ___

Acute Dermal Toxicity in Rabbits

___TP3207 FHSA screen; 5M-5F at 2.0 g/kg
___TP3016 EPA screen; 5M-5F at 2.0 g/kg
___ Conduct defined study if death occurs at 2.0 g/kg
___TP2070 OECD screen; 5M-5F at 2.0 g/kg
___ Conduct defined study if death occurs at 2.0 g/kg

Special Instructions: ___

Primary Skin Irritation

___TP3208 FHSA; 6 rabbits-1 abraded, 1 intact site/rabbit
___TP3014 EPA; 6 rabbits-1 intact site/rabbit
___TP2071 OECD; 3 rabbits-1 intact site/rabbit
___TP4206 DOT corrosivity; 6 rabbits-1 intact site/rabbit
___TP7145 Phototoxicity; 6 rabbits-2 intact sites/rabbit (one site with UVA exposure)

Special Instructions: ___

Primary Eye Irritation

___TP6360 Low-volume procedure; 6 rabbits unwashed
___TP3209 FHSA; 6 rabbits unwashed
___TP2012 1978 EPA; 6 rabbits unwashed, 3 washed
___TP3015 1982 EPA; 6 rabbits unwashed
___TP2072 OECD; 3 rabbits unwashed
___ 3 rabbits washed at 4 seconds
___ 3 rabbits washed at 30 seconds

Special Instructions: ___

Guinea Pig Sensitization

___TP2017 EPA Magnusson-Kligman maximization
___TP6164.EC OECD/EC Magnusson-Kligman maximization
___TP2008 Buehler sensitization
___TP6289 Photoallergenic contact dermatitis (Armstrong)

Special Instructions: ___

For CHW Use Only

Protocol Issue Date: 10-9-96
Study Director: Steven M. Olga

White copy—CHW Yellow copy—Submitter

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HAZLETON
WISCONSIN
POST OFFICE BOX 7545
MADISON, WISCONSIN 53707-7545

a CORNING Laboratory Services Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP2069

Study Title:

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

Date:

June 1, 1993

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 61001760

STUDY IDENTIFICATION

Acute Oral Toxicity Study in Rats
(OECD Guidelines)

HWI No.	61001760
Test Material	(See sample submittal form)
Sponsor	3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. Building No. 3 3802 Packers Avenue Madison, WI 53704
Proposed Study Timetable	
Experimental Start Date	Week of 10-7-96
Experimental Termination Date	Week of 12-9-96
Final Report Date	Week of 12-9-96

1. Study
Acute Oral Toxicity Study in Rats (OECD Guidelines)

2. Purpose
To assess the acute oral toxicity produced when the test material is administered by the oral route (gavage) to rats

3. Regulatory Compliance
This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines:

[ ] Conduct as a Nonregulated Study
[ ] 21 CFR 58 (FDA)
[ ] 40 CFR 160 (EPA-FIFRA)
[ ] 40 CFR 792 (EPA-TSCA)
[X] C(81)30 (Final) (OECD)
[ ] Notification No. 3850, August 10, 1984 (Japanese MAFF)
[ ] Notification No. 313, March 31, 1982, and as amended by Notification No. 870, October 5, 1988 (Japanese MOHW)

All procedures in this protocol are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study does not unnecessarily duplicate any previous work.

4. Quality Assurance
For regulated studies, the protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with Hazleton Wisconsin (HWI) Standard Operating Procedures (SOPs) and policies.

5. Test Material

A. Identification
(See sample submittal form)

B. Physical Description
(See sample submittal form)

C. Purity and Stability
The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Samples of test material/vehicle mixture(s) (if applicable) for concentration, solubility, homogeneity, and stability analyses will be taken before administration if requested by the Sponsor. These samples (if taken) will be sent to the Sponsor after experimental termination for possible analysis.

D. Storage
(See sample submittal form)

E. Reserve Samples
Studies of less than 4 weeks in experimental duration will not have reserve samples retained.

Reserve sample(s) of each batch/lot of test material will be taken if this study is more than 4 weeks in experimental duration.

The test material reserve sample will be stored at HWI in a freezer set to maintain a temperature of below 0°C for 10 years per HWI SOP. The Sponsor will be contacted after 10 years for disposition in accordance with the appropriate regulatory Good Laboratory Practices.

F. Retention
Any unused test material will be discarded after issuance of the final report, unless directed otherwise by the Sponsor.

G. Safety Precautions
As required by HWI SOPs and policies

6. Experimental Design

A. Animals

(1) Species
Rat

(2) Strain/Source
[X] Crl:CD®BR/Charles River Laboratories, Inc.
[ ] Hsd:Sprague Dawley SD®/Harlan Sprague Dawley, Inc.

(3) Age at Initiation
Young adult

(4) Weight at Initiation
200 to 300 g

(5) Number and Sex
5 males and 5 females for the initial dose level
5 males and/or 5 females for any additional dose levels (if required)

(6) Identification
Individual numbered ear tag

(7) Husbandry

(a) Housing
Separated by sex and group housed in screen-bottom stainless steel cages (heavy gauge)

(b) Food
Rodent Chow® #5001 (Purina Mills, Inc.) *ad libitum* except for overnight before test material administration. The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.

(c) Water
Ad libitum from an automatic system. Samples of the water are analyzed by HWI for total dissolved solids, hardness, and specified microbiological content and for selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons.

(d) Contaminants
There are no known contaminants in the food or water that would interfere with this study.

(e) Environment
Environmental controls for the animal room will be set to maintain a temperature of 19 to 25°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark cycle.

(f) Acclimation
At least 7 days

(8) Selection of Test Animals
Based on health and body weight according to HWI SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test.

(9) Justification for Species Selection
Historically, rats have been used as representative of a rodent species and are preferred by various regulatory agencies.

B. Dose Administration

(1) Dose Level
A single dose of 5,000 mg/kg of body weight will be administered to five males and five females. If no test material-related mortality is produced at this level, no

further testing will be required. If any mortality occurs at the 5,000 mg/kg dose level, additional dose levels may be added at the direction of the study director in order to meet the objectives of the study.

(2) Dose Preparation and Administration
All animals will receive the same concentration of test mixture per dose level. If a solid, the test material will be suspended in an appropriate vehicle. If a liquid, the test material will be dosed undiluted, using the bulk density to determine the dose volume. If the material is an aerosol, it will be discharged into a beaker and administered as a liquid. Individual doses will be based upon the animal's body weight taken just before test material administration, and administered by gavage. The animals will have food withheld for 17 to 20 hours before test material administration. The prepared test mixtures will be stored at room temperature until administration. After administration, any remaining test mixtures will be discarded.

(3) Reason for Route of Administration
Historically, the oral route has been the route of choice for administering a known amount of test material.

C. Observation of Animals

(1) Clinical Observations
At approximately 1, 2.5, and 4 hours after test material administration and daily thereafter for at least 14 days for clinical signs and twice daily (a.m. and p.m.) for mortality. Observations may be extended when directed by the study director.

(2) Body Weights
Before experimental initiation, at 7 and 14 days after test material administration, and at death (when survival exceeds 1 day)

D. Pathology
At termination of the experimental phase, surviving animals will be euthanized. All animals, whether dying during the study or euthanized, will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. After necropsy, the animals will be discarded and no tissues will be saved.

E. Statistical Analyses
Other than LD_{50} calculations (when applicable) no statistical analyses are required.

7. Report
A final report including those items listed below will be submitted.

Description of the test material
Description of the test system
Procedures
Dates of experimental initiation and termination
Tabulation of mortality data by sex and dose level
Description of any toxic effects
Tabulation of mean body weights by sex and dose level
LD_{50} calculations for each sex with 95% confidence intervals (when applicable)
Gross pathology findings/gross pathology report (when applicable)

8. Location of Raw Data, Records, and Final Report
Original data, or copies thereof, will be available at HWI to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those items listed below will be retained in the archives of HWI according to HWI SOP.

Protocol and protocol amendments
Dose preparation records
In-life records
  Body weights
  Dose administration
  Observations
Anatomical pathology records
Study correspondence
Final report (original signed copy)

The following supporting records will be retained at HWI but will not be archived with the study data.

Animal receipt/acclimation records
Water analysis records
Animal room temperature and humidity records
Refrigerator and freezer temperature records
Instrument calibration and maintenance records

PROTOCOL APPROVAL

John L. Butenhoff, PhD
Sponsor's Representative
3M

July 22, 1993
Date

Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

6-1-93
Date

Rebecca S. Nelson
Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

6/1/93
Date

(TP2069.3M)

CHW No. 61001760

PROTOCOL AMENDMENTS

Amendment No. 1

Effective October 9, 1996

Portion of Protocol Being Modified: Applicable sections of the protocol.

Reason for Modification: To identify the location where the study will be conducted and to reflect a company name change from Hazleton Wisconsin, Inc. (HWI) to Corning Hazleton Inc. (CHW), replace wherever applicable the following changes

Modification: Corning Hazleton Inc. (CHW)
3301 Kinsman Boulevard.
Madison, WI 53704

Study Director Approval: Steven M. Yoh 10-9-96

(G21/01-07-91)

CHW No. 61001760

PROTOCOL AMENDMENTS

Amendment No. 2

Effective October 9, 1996

Portion of Protocol Being Modified: Page 4, 6. Experimental Design; A. Animals (2) Strain/Source

Reason for Modification: To correctly identify the nomenclature used for animals received from Charles River Laboratories, Inc.

Modification: Replace this section with the following change:

(2) Strain/Source

☒ Crl:CD®(SD)BR/Charles River Laboratories, Inc.
☐ Hsd:Sprague Dawley SD®/Harlan Sprague Dawley, Inc.

Study Director Approval: [signature] 10-9-96

(G21/01-07-91)

CHW No. 61001760

PROTOCOL AMENDMENTS

Amendment No. 3

Effective October 9, 1996

Portion of Protocol Being Modified: Page 5, 6. Experimental Design; B. Dose Administration; (1) Dose Level.

Reason for Modification: The Sponsor requested that a level of 500 mg/kg be treated initially.

Modification: Replace 5,000 mg/kg with 500 mg/kg wherever listed in this section.

Study Director Approval: Steven M. Glaza 10-9-96

(G21/01-07-91)

BIOSEARCH, INC. p.o. box 8598 philadelphia, pennsylvania 19101
telephone: (215) 848-4499

Submitted to: 3M Company
3M Center
St. Paul, Minnesota
55101

Material: 3M Company - T-1395

Sample Received: December 6, 1975

Date of Report: March 4, 1976

Test: Primary Skin Irritation Study - Rabbits

Object of Test: To determine the degree of irritation, if any, which the subject material may produce when applied to the intact and abraded skin of albino rabbits. The test was performed in order to classify this material under the Federal Hazardous Substances Labeling Act.

Method of Test: The method employed in the testing, evaluation and the scoring of the results was similar to that described in Section 1500.41 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973.

In carrying out the study the experimental sample was used as supplied. A group of six albino rabbits were clipped over a wide area. One side of the animals' backs was abraded at one site with a lancet sufficiently deep to penetrate the stratum corneum but not enter the derma to produce bleeding. The skin of the other side was allowed to remain intact. A 0.5 gm portion of material was applied to an abraded and an intact skin site on the same rabbit. Gauze patches were then placed over the treated areas and an impervious material was wrapped snugly around the trunks of the animals to hold the patches in place.

The wrapping was removed at the end of the twenty-four hour period and the treated areas were examined. Readings were also made after seventy-two hours. The Draize method of scoring was employed. Both sites (intact and abraded) were examined dry as well as after treatment with water.

3M Company - T-1395, Primary Skin Irritation Study.

Results: See Table 1.

Conclusion: Based on the accompanying table, the subject material would not be classified as a primary irritant to albino rabbits within the definition of the Act-Reference: Section 1500.3 (c) (4) and requires no cautionary labeling with respect to that section.

Karl L. Gabriel

Karl L. Gabriel, V.M.D., Ph.D.
Director

TABLE 1

Primary Skin Irritation

WET

Material: 3M Company - T-1395, as supplied.

Erythema and Eschar Formation	Reading (Hours)	Rabbit Number 1	2	3	4	5	6	Average
Intact Skin	24	0	0	0	0	0	0	0.00
Intact Skin	72	0	0	0	0	0	0	0.00
Abraded Skin	24	0	0	0	0	0	0	0.00
Abraded Skin	72	0	0	0	0	0	0	0.00
				Subtotal				0.00
Edema Formation								
Intact Skin	24	0	0	0	0	0	0	0.00
Intact Skin	72	0	0	0	0	0	0	0.00
Abraded Skin	24	0	0	0	0	0	0	0.00
Abraded Skin	72	0	0	0	0	0	0	0.00
				Subtotal				0.00
				Total				0.00

Primary Irritation Score: 0

TABLE 1

Primary Skin Irritation

DRY

Material: 3M Company - T-1395, as supplied.

Erythema and Eschar Formation	Reading (Hours)	Rabbit Number 1	2	3	4	5	6	Average
Intact Skin	24	0	0	0	0	0	0	0.00
Intact Skin	72	0	0	0	0	0	0	0.00
Abraded Skin	24	0	0	0	0	0	0	0.00
Abraded Skin	72	0	0	0	0	0	0	0.00
				Subtotal				0.00
Edema Formation								
Intact Skin	24	0	0	0	0	0	0	0.00
Intact Skin	72	0	0	0	0	0	0	0.00
Abraded Skin	24	0	0	0	0	0	0	0.00
Abraded Skin	72	0	0	0	0	0	0	0.00
				Subtotal				0.00
				Total				0.00

Primary Irritation Score: 0

BIOSEARCH, INC. p.o. box 8598 philadelphia, pennsylvania 19101
telephone: (215) 848-4499

Submitted to: 3M Company
3M Center
St. Paul, Minnesota
55101

Material: 3M Company - T-1395

Sample Received: December 6, 1975

Date of Report: March 4, 1976

Test: Primary Eye Irritation Study - Rabbits

Object of Test: To determine the degree of irritation, if any, which the subject material may produce when instilled into the eyes of albino rabbits. This test was performed in order to classify this material under the Federal Hazardous Substances Labeling Act.

Method of Test: The methods employed in the testing, evaluation and in the grading of the test material are those described in Section 1500.42 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973.

The sample was used as supplied.

Six healthy young adult albino rabbits were used in this study. 0.1 gm of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to serve as controls. The test material was washed from the eyes in 3 animals after 5 sec. with 200 cc of water and after 30 sec. in 3 animals with 200 cc of water. The treated eyes were examined at 1,24,48 & 72 hrs. & 5 & 7 days following instillation of the test material into the eyes. Interpretation of the results was made in accordance with the grading system outlined in the "Illustrated Guide for Grading Eye Irritation By Hazardous Substances".

Results: The results of the tests are shown in the accompanying Table which covers each of the animals treated with the test material.

3M Company - T-1395, Primary Eye Irritation Study.

Conclusion: Based on the accompanying table, the subject material is not an ocular irritant within the definition of the Act-Reference: Section 1500.42 (b) (1) (2) P. 27019 and requires no cautionary labeling with respect to that section.

Karl L. Gabriel

Karl L. Gabriel, V.M.D., Ph.D.
Director

TABLE 1

Grades for Ocular Lesions

Material: 3M Company - T-1395, as supplied and washed after 5 seconds with 200 cc of water.

Rabbit Number	Hours After Application											
	1			24			48			72		
	Co	I	C	Co	I	C	Co	I	C	Co	I	C
1	0	0	4	0	0	4	0	0	4	0	0	4
2	0	0	4	0	0	4	0	0	4	0	0	4
3	0	0	2	0	0	4	0	0	2	0	0	2

	5 Days			7 Days		
	Co	I	C	Co	I	C
	0	0	4	0	0	4
	0	0	4	0	0	4
	0	0	2	0	0	2

Co = Cornea
I = Iris
C = Conjunctivae

000092

TABLE 1

Grades for Ocular Lesions

Material: 3M Company - T-1395, as supplied and washed after 30 seconds with 200 cc of water.

Rabbit Number	Hours After Application											
	1			24			48			72		
	Co	I	C	Co	I	C	Co	I	C	Co	I	C
1	0	0	6	0	0	6	0	0	6	0	0	6
2	0	0	4	0	0	4	0	0	4	0	0	6
3	0	0	4	0	0	4	0	0	4	0	0	4

5 Days			7 Days		
Co	I	C	Co	I	C
0	0	6	0	0	6
0	0	6	0	0	6
0	0	4	0	0	4

Co = Cornea
I = Iris
C = Conjunctivae

000093

BIOSEARCH, INC. p.o. box 8598 philadelphia, pennsylvania 19101
telephone: (215) 848-4499

Submitted to: 3M Company
3M Center
St. Paul, Minnesota
55101

Material: 3M Company - T-1395

Sample Received: December 6, 1975

Date of Report: March 4, 1976

Test: Primary Eye Irritation Study - Rabbits

Object of Test: To determine the degree of irritation, if any, which the subject material may produce when instilled into the eyes of albino rabbits. This test was performed in order to classify this material under the Federal Hazardous Substances Labeling Act.

Method of Test: The methods employed in the testing, evaluation and in the grading of the test material are those described in Section 1500.42 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973.

The sample was used as supplied.

Six healthy young adult albino rabbits were used in this study. 0.1 gm of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to serve as controls. The test material was not washed from the eyes.

The treated eyes were examined at 1,24,48 & 72 hrs. & 5 & 7 days following instillation of the test material into the eyes. Interpretation of the results was made in accordance with the grading system outlined in the "Illustrated Guide for Grading Eye Irritation By Hazardous Substances".

Results: The results of the tests are shown in the accompanying Table which covers each of the animals treated with the test material.

3M Company - T-1395, Primary Eye Irritation Study.

Conclusion: Based on the accompanying table, the subject material is a primary ocular irritant within the definition of the Act-Reference: Section 1500.42 (b) (1) (2) P. 27019 and requires cautionary labeling with respect to that section.

Karl L. Gabriel

Karl L. Gabriel, V.M.D., Ph.D.
Director

TABLE 1

Grades for Ocular Lesions

Material: 3M Company - T-1395, as supplied.

Rabbit Number	Hours After Application											
	1			24			48			72		
	Co	I	C	Co	I	C	Co	I	C	Co	I	C
1	0	5	10	0	5	6	0	5	6	0	5	6
2	0	5	10	0	5	4	0	5	2	0	5	2
3	0	5	6	0	5	4	0	5	2	0	0	0
4	0	5	10	0	5	6	0	5	4	0	5	2
5	0	5	10	0	5	6	0	5	4	0	0	2
6	0	5	8	0	5	8	0	5	2	0	5	0

	5 Days			7 Days		
	Co	I	C	Co	I	C
	0	5	4	0	5	2
	0	0	0	0	0	0
	0	0	0	0	0	0
	0	5	2	0	5	0
	0	0	0	0	0	0
	0	0	0	0	0	0

Co = Cornea
I = Iris
C = Conjunctivae

960003

Primary Skin Irritation Test

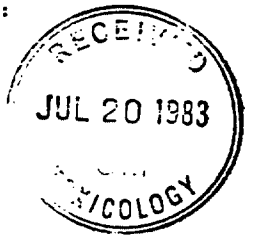
with T-3371

in Albino Rabbits

Experiment No.: 0883EB0079

Conducted At: Safety Evaluation Laboratory
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted: March 1, 1983 to March 17, 1983



Conducted By: D. M. Markoe, Jr. 6/30/83
D. M. Markoe, Jr., BS — Date
Toxicologist
Study Director

Reviewed By: Karen D O'Malley 7/13/83
K. D. O'Malley, BS — Date
Senior Toxicologist
Acute Toxicology

dc: M. T. Case
K. L. Ebbens
F. D. Griffith
W. C. McCormick

Summary

The results of the ICAO skin irritation test conducted from March 1, 1983 to March 17,1983 at Riker Laboratories, Inc., St. Paul, Minnesota indicate that T-3371 produced irreversible tissue damage to the skin of female albino rabbits following a four hour, a one hour, and a three minute contact period. Moderate erythema and edema, as well as, chemical burn, eschar and necrosis were produced following all three contact periods. An endpoint, as required by ICAO, was not achieved due to the extreme irritation following each contact period.

Introduction

The objective of this study was to determine the ICAO skin irritation potential of T-3371 to the skin of female albino rabbits. This study is not regulated by the Food and Drug Administration's Good Laboratory Practice Regulation of 1978, although the standard operating procedures of this laboratory adhere to the general principles of this regulation. The raw data generated by the Study Director and the final report are stored in the conducting laboratory's archives.

Method and Results

Young albino rabbits of the New Zealand breed[a] were used in the evaluation of the primary skin irritating properties of the test article. The test procedure was modeled after that of Draize et al[b].

One day prior to the application of the test article, the hair was clipped from the back and flanks of each rabbit and two test sites selected lateral to the midline of the back approximately ten centimeters apart.

The test article (0.5 g) was applied to each of the test sites on each rabbit and immediately covered with two-inch square gauze patches. The patches, which were placed directly over the test sites, were secured with gauze wrap. The trunk of each animal was then wrapped with impervious plastic sheeting[c] which held the patches in position during either a four hour, one hour or three minute[d] exposure period.

At the end of the exposure period, the plastic wrappings, patches, and all residual test article were removed[e]. One, 24 and 48 hours after removal of the test article, the test sites were examined for irreversible damage and scored separately for erythema and edema on a graded scale of 0 - 4 (Table 1).

The length of the exposure period is reduced until an endpoint of no irreversible damage is reached, if possible.

The results are presented in Tables 2-4. The protocol, principal personnel involved in the study, composition characteristics and Quality Assurance statement are contained in Appendices I - IV.

[a] Hazleton Dutchland, Inc., Denver, PA
[b] Draize: Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1965).
[c] 10 x 12 x .002 Extra Clear polyethylene sleeves, PPC Industries, Inc., Wheeling, Illinois.
[d] Three animals per exposure group.
[e] The test article was removed with water.

Table 1

Scoring Criteria for Skin Reactions

Reaction	Description	Score
Erythema	Barely perceptible (Edges of area not defined	1
	Pale red in color and area definable	2
	Definite red in color and area well defined.	3
	Beet or crimson red in color	4
Edema	Barely perceptible (Edges of area not defined)	1
	Area definable but not raised more than 1 mm.	2
	Area well defined and raised approximately 1 mm.	3
	Area raised more than 1 mm.	4
	Maximum Primary Irritation Score =	8

Table 2

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (four hour contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B358	2 E	4	2 EC	3	2 EN	2
3B350	2 E	4	2 EC	3	2 EN	2
3B353	2	4	2 EC	3	2 ENX	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B358	2 E	4	2 EC	3	2 EN	3
3B350	2 E	4	2 EC	3	2 EN	2
3B353	2	4	2 EC	3	2 ENX	3

Key: C = Chemical burn
E = Eschar
N = Necrosis
X = Epithelial sloughing
ED = Edema
ER = Erythema

Table 3

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (one hour contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B349	1	2	2 C	3	2 EN	3
3B384	1	1	2 C	2	2 EN	2
3B355	1	2	2 C	2	2 EN	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	Immediately ED	24 Hours ER	24 Hours ED	48 Hours ER	48 Hours ED
3B349	1	2	2 C	3	2 EN	2
3B384	1	1	2 C	2	2 XE	2
3B355	1	2	2 C	2	2 NXE	2

Key: C = Chemical burn
E = Eschar
N = Necrosis
X = Epithelial sloughing
ED = Edema
ER = Erythema

Table 4

Primary Skin Irritation Test - Albino Rabbits

with T-3371 (three minute contact)

Irritation Scores for Right Intact Skin Sites After Removal

Animal Number	Immediately ER	ED	24 Hours ER	ED	48 Hours ER	ED
3B397	2 B	1	2 NOX	2	2 NOX	2
3B395	2 B	1	2 NO	2	2 NO	2
3B394	2 B	1	2 NOX	2	2 NOX	2

Irritation Scores for Left Intact Skin Sites After Removal

Animal Number	Immediately ER	ED	24 Hours ER	ED	48 Hours ER	ED
3B397	2 B	1	2 NOX	2	2 NOX	2
3B395	2 B	1	2 NO	2	2 NO	2
3B394	2 B	1	2 NO	2	2 NO	2

Key: B = Blancing
X = Epithelial sloughing
O = Eschar
N = Necrosis
ED = Edema
ER = Erythema

0883AB0079

APPENDIX I Riker Experiment No.: _____

PROTOCOL

7.

TEST: Acute Primary Skin Irritation Test

SPONSOR: 3M Commercial Chemicals Division

CONDUCTED BY: Safety Evaluation Laboratory, Riker Laboratories, Inc., St. Paul, Minnesota

TEST ARTICLE: T-3371

CONTROL ARTICLE: None

PROPOSED STARTING/COMPLETION DATE OF TEST: 2/83 - 6/83

TEST SYSTEM: Female New Zealand White Albino Rabbits

SOURCE: DUTCHLAND LABS, DENVER, PA

OBJECTIVE: To determine the irritation potential of the test article to the skin of 6 animals. Rabbits were selected as the test system due to their historical use, sensitivity to irritants, ease of handling and general availability.

METHOD: The animals will be housed in standard wire-mesh cages in temperature and humidity controlled rooms with food[a] and water offered *ad libitum*. Each animal will be assigned a numbered ear tag, which will correspond to a card affixed to the outside of the cage. Prior to the application of the test article, the hair will be clipped from the back and flanks of each animal and 2 test sites selected lateral to the midline of the back approximately ten centimeters apart. 0 of the 2 sites will be abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site(s) will remain intact. The test article (0.5 g) will be applied to 0 abraded and [illegible] intact site(s) on each animal, covered with gauze and secured with ~~tape~~ [illegible]. The trunk of each animal will then be wrapped with impervious plastic sheeting which will occlude the test article during the 1 day exposure period.* ~~One hour and 48 hours~~** after removal of the test article, the intact and abraded test sites will be examined and scored separately for erythema and edema on a graded scale of 0 to 4[b]. The average irritation produced will be evaluated by adding the mean scores for erythema and edema of the intact test sites ~~one and 48 hours post removal~~ of the test article. ~~Similarly, the mean scores for erythema and edema of the abraded test sites will be added~~. These ~~two~~ values will be totaled and divided by ~~four~~ six to obtain the mean primary irritation index and then assigned a descriptive primary skin irritation rating as follows:

2 1 hour contact on three rabbits
4 hour contact on remaining three rabbits

Mean Primary Irritation Score	Descriptive Rating
0	Non-irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

RECEIVED
FEB 21 1983
SAFETY EVALUATION

The rating for a test article may be increased if the reaction caused is beyond erythema and edema and are deemed to be of importance in the interpretation of the results. All raw data generated by the study director and the final report will be stored in the Riker Laboratories' Archive, St. Paul, Minnesota.

* one sight: one hr. application, 2nd sight 4 hr. application.

a Purina Rabbit Chow, Ralston Purina Co., St. Louis, Missouri

b Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965) Published by the Editorial Committee of the Association of Food and Drug Officials of the United States

** Read each site upon removal of test substance and 1 and 3 days.

[signature] 2/16/83 [signature] 2/22/83

Sponsor Date Study Director Date

Form 19171-12-B-PWO

Riker Experiment No.: 0883EB0079

APPENDIX I (concluded)
Deviations and/or Amendments to Protocol

1. In addition to the four hour and one hour contact applications an additional application of three minute contact with three animals will be dosed.

D. M. Markowitz 3/3/83
Study Director Date

2. Due to a delay in report processing the proposed completion date should be amended to 6/83.

D. M. Markowitz 6/30/83
Study Director Date

3. _____

Study Director Date

4. _____

Study Director Date

5. _____

Study Director Date

APPENDIX II

Principal Participating Personnel Involved in the Study

Name	Function
D. M. Markoe, Jr., BS	Toxicologist Study Director
K. L. Ebbens, BS	Supervisor Toxicology Testing
K. D. O'Malley, BS	Senior Toxicologist Acute Toxicology
G. C. Pecore	Supervisor Animal Laboratory

APPENDIX III

Composition Characteristics

This study is not regulated by the Good Laboratory Practice Act of 1978 and therefore information pertaining to composition characteristics is not applicable for inclusion in this study.

APPENDIX IV

Quality Assurance Statement

This study is not officially regulated by the Good Laboratory Practice Regulation of 1978, and therefore a statement signed and prepared by the Compliance Audit department is not applicable.

The standard operating procedures of this laboratory does adhere to the general principles of this regulation. The Compliance Audit department does inspect different significant phases for studies underway in the Acute Toxicology Laboratory on a recurring cycle, and the facilities are examined on a three month schedule. In addition a select number of Research & Development studies are routinely picked at random from the Archives by the Compliance Audit department for review.

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telephone: (215) 848-4499

Submitted to: 3M Company
3M Center
St. Paul, Minnesota
55101

Material: 3M Company - T-1585

Sample Received: August 25, 1976

Date of Report: September 16, 1976

Test: Acute Oral Toxicity - Rats

Object of Test: To study the acute oral toxicity in rats of the subject material.

Procedure: One group of 5 male & 5 female albino rats of the Sherman-Wistar Strain weighting between 200 and 300 gm were employed in this study. The rats were deprived of food but not water for 24 hours prior to dosing. Each animal was weighed and dosed by direct administration of the experimental material into the stomach by means of a syringe and dosing needle.

The sample was dosed as a 50% w/v suspension in water.

The following dosage level was administered:

1,000 mg/kg.

Following administration the animals were allowed food and water ad libitum for the 14 day observation period during which time the rats were observed for signs of toxicity and mortalities.

Results: See Table 1.

Conclusion: The subject material when studied in male and female albino rats has an acute oral LD_{50} of less than 1,000 mg/kg.

Karl L. Gabriel

Karl L. Gabriel, V.M.D., Ph.D.
Director

TABLE 1

Acute Oral Toxicity

Material: 3M Company - T-1585, as a 50% w/v suspension in water.

Dosage Level mg/kg	Number of Animals Dosed	Mortalities Days 1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total Dead 14 Days	Total Survived 14 Days
1,000	5 males	2	1	0	0	0	0	0	0	0	0	0	0	0	0	3	2
1,000	5 females	4	0	0	0	0	0	0	0	0	0	0	0	0	0	4	1

The LD_{50} is less than 1,000 mg/kg.

The gastric mucosa was eroded.

The animals exhibited signs of writhing at times.

	Initial Weight gm	Final Weight gm
Males	240	250
Females	220	220

000110

BIOSEARCH, INC. p.o. box 8598 philadelphia, pennsylvania 19101
telephone: (215) 848-4499

Submitted to: 3M Company
3M Center
St. Paul, Minnesota
55101

Material: 3M Company - T-1585

Sample Received: August 25, 1976

Date of Report: September 16, 1976

Test: Primary Eye Irritation Study - Rabbits

Object of Test: To determine the degree of irritation, if any, which the subject material may produce when instilled into the eyes of albino rabbits. This test was performed in order to classify this material under the Federal Hazardous Substances Labeling Act.

Method of Test: The methods employed in the testing, evaluation and in the grading of the test material are those described in Section 1500.42 - Hazardous Substances and Articles, Administration and Enforcement Regulations, Federal Register, Vol. 38, No. 187, P. 27019, 27 September 1973.

The sample was used as supplied.

Six healthy young adult albino rabbits were used in this study. 0.1 gm of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to serve as controls. The test material was not washed from the eyes.

The treated eyes were examined at 1, 24, 48 & 72 hrs. & 5 & 7 days following instillation of the test material into the eyes. Interpretation of the results was made in accordance with the grading system outlined in the "Illustrated Guide for Grading Eye Irritation By Hazardous Substances".

Results: The results of the tests are shown in the accompanying Table which covers each of the animals treated with the test material.

3M Company - T-1585, Primary Eye Irritation Study.

Conclusion: Based on the accompanying table, the subject material is a primary ocular irritant within the definition of the Act-Reference: Section 1500.42 (b) (1) (2) P. 27019 and requires cautionary labeling with respect to that section.

Karl L. Gabriel

Karl L. Gabriel, V.M.D., Ph.D.
Director

TABLE 1

Grades for Ocular Lesions

Material: 3M Company - T-1585, as supplied.

	Rabbit No.	Cornea		Iris	Conjunctivae		
		Opacity	Area		Redness	Chemosis	Discharge
1 hour	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3
24 hours	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3
48 hours	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3
72 hours	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3
5 days	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3
7 days	1	4	4	2	2	4	3
	2	4	4	2	2	4	3
	3	4	4	2	2	4	3
	4	4	4	2	2	4	3
	5	4	4	2	2	4	3
	6	4	4	2	2	4	3

Corning Hazleton Inc.
P.O. Box 7545
Madison, WI 53707-7545
Deliveries: 3301 Kinsman Blvd., Madison, WI 53704
608.241.4471 608.241.7227 Fax

CORNING Hazleton

Sponsor:

3M
St. Paul, Minnesota

FINAL REPORT

Study Title:

Acute Dermal Toxicity Study of T-6342 in Rabbits (OECD Guidelines)

Author:

Steven M. Glaza

Study Completion Date:

October 24, 1995

Performing Laboratory:

Corning Hazleton Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 50800374

000114

COMPLIANCE STATEMENT

Acute Dermal Toxicity Study of T-6342 in Rabbits
(OECD Guidelines)

This study was conducted in accordance with the Organization for Economic Cooperation and Development's Principles of Good Laboratory Practice, C(81)30(Final).

Steven M. Glaza
Study Director
Acute Studies
Corning Hazleton Inc.

10-24-95
Date

HWI 50800374

QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Hazleton Wisconsin, Inc., in accordance with the Organisation for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice, C(81)30(Final). The following inspections were conducted and findings reported to the Study Director and management. Written status reports of inspections and findings are issued to Hazleton management monthly according to standard operating procedures.

Inspection Dates From	To	Phase	Date Reported to Study Director	Date to Management
08/31/95	08/31/95	Dose Administration	08/31/95	09/10/95
10/13/95	10/16/95	Data/Report Review	10/16/95	11/10/95

Representative, Quality Assurance Unit

10.24.95
Date

STUDY IDENTIFICATION

Acute Dermal Toxicity Study of T-6342 in Rabbits
(OECD Guidelines)

Test Material	T-6342
Sponsor	3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220
Sponsor's Representative	Roger G. Perkins, PhD 3M Toxicology Service Medical Department 3M Center, Bldg. 220-2E-02 P.O. Box 33220 St. Paul, MN 55133-3220 (612) 733-3222
Study Director	Steven M. Glaza Corning Hazleton Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Corning Hazleton Inc. 3301 Kinsman Boulevard Madison, WI 53704
Study Timetable	
Study Initiation Date	August 25, 1995
Experimental (In-life) Start Date	August 31, 1995
In-life End Date	September 14, 1995
Experimental Termination Date	October 24, 1995
Study Completion Date	October 24, 1995

KEY PERSONNEL

Acute Studies

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Toxicology Support

Kathy Myers
Manager

Calvin L. Horton
Supervisor

Quality Assurance

Sherry R. W. Petsel
Manager

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

Deborah L. Pirkel/
Jack Serfort
Supervisors
Necropsy

Anne Mosher
Supervisor
Pathology Data

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SUMMARY

The test material, T-6342, was evaluated for its acute dermal toxicity potential in male and female rabbits when administered as a single topical application at a level of 2,000 mg/kg of body weight. The estimated dermal LD_{50} for male and female rabbits was determined to be greater than 2,000 mg/kg. All animals appeared normal throughout the study. All animals exhibited body weight gain during the study with the exception of one male which exhibited a weight loss of 29 g during the first week. The test material produced slight to moderate dermal irritation. The gross necropsy at termination revealed no visible lesions.

OBJECTIVE

The objective of this study was to assess the systemic toxicity and relative skin irritancy of a test material when applied to the skin of rabbits.[1]

All procedures used in this study were in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study did not unnecessarily duplicate any previous work.

TEST MATERIAL

Identification

The test material was identified as T-6342 and described as a clear, colorless liquid.

Purity and Stability

The Sponsor assumes responsibility for purity and stability determinations (including under test conditions).

Storage and Retention

The test material was stored at room temperature. Any unused test material will be returned to the Sponsor after issuance of the final report according to Corning Hazleton (CHW) Standard Operating Procedure (SOP).

Safety Precautions

The test material handling procedures were according to CHW SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were procured from HRP, Inc., Kalamazoo, Michigan on August 9, 1995.

Housing

After receipt, the animals were acclimated for a period of at least 7 days. During acclimation and throughout the study, the animals were individually housed in screen-bottom stainless steel cages. Environmental controls for the animal room were set to maintain a temperature of 19° to 23°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark lighting cycle. In cases where variations from these conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Animal Diet

The animals were provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF #5326, PMI Feeds, Inc. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by CHW. There were no known contaminants in the feed or water at levels that would have interfered with or affected the results of the study.

Animal Selection and Preparation of Exposure Area

Five male and five female healthy, acclimated rabbits, weighing from 2,386 to 2,675 g, were used for a single dose level of 2,000 mg/kg of body weight. The animals were identified by animal number and corresponding ear tag throughout the study. On the day before test material application, each rabbit's back was clipped free of hair with an electric clipper. The clipped area made up not less than 10% of the total body surface. The animals were clipped as needed throughout the study.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

PROCEDURES

Preparation of Test Material

The test material was administered as received. An individual dose was calculated and weighed out based on each animal's body weight on the day of test administration.

Treatment

The test material was applied to the intact skin on each animal's back at a dose level of 2,000 mg/kg of body weight. The test material was applied to the test site at a rate of approximately 0.03 g/cm^2 in a thin and uniform layer. The area of application (approximately 200 cm^2)was covered with a 9.5-cm x 21.0-cm, 4-ply gauze patch secured with paper tape and overwrapped with Saran Wrap® and Elastoplast® tape to provide an occlusive dressing. Collars were used to restrain the test animals during the 24-hour exposure period.

At the end of the 24-hour exposure period, the restraining collars and bandages were removed and the test sites were washed using tap water and disposable paper towels.

Reason for Route of Administration

Historically, the dermal route has been the route of choice based on the method of Draize.[2]

Observations

Clinical observations and mortality checks were conducted at approximately 1, 2.5, and 4 hours after test material administration. Additional clinical observations and twice a day mortality checks (morning and afternoon) were conducted daily thereafter for 14 days.

Body weights were determined before test material application (Day 0), at Day 7, and at termination of the in-life phase (Day 14).

The initial dermal irritation reading was made approximately 30 minutes after removal of the test material according to the Draize technique (recorded as the Day 1 score). Subsequent readings of dermal irritation were made on Days 3, 7, 10, and 14.

Pathology

At termination of the in-life phase, all animals were euthanized, subjected to an abbreviated gross necropsy examination, and any abnormalities were recorded. After necropsy, the animals were discarded and no tissues were saved.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and an original signed copy of the final report will be retained in the archives of CHW in accordance with CHW SOP.

RESULTS

Mortality

A summary of the survival rate is in Table 1. No mortality was observed during the study. The estimated dermal LD_{50} for male and female rabbits was determined to be greater than 2,000 mg/kg of body weight.

Body Weights

Individual and mean body weights and body weight gains are in Table 2. All animals exhibited body weight gain throughout the study with the exception of one male which exhibited a weight loss of 29 g during the first week.

Clinical Signs

Individual clinical signs are in Table 3. All animals appeared normal throughout the study.

Dermal Reactions

Individual dermal irritation observations are in Table 4. Dermal irritation (based on the most severe score for each animal at any time point) consisted of slight to moderate erythema, edema, and atonia, and slight desquamation, coriaceousness, and fissuring. No other dermal irritation was observed.

Pathology

Individual gross necropsy pathology findings are in Table 5. A summary report by the study pathologist is on Page 12. There were no visible lesions observed at necropsy.

DISCUSSION

The acute dermal toxicity of T-6342 was evaluated in male and female rabbits when administered as a single topical application at a level of 2,000 mg/kg of body weight. The estimated dermal LD_{50} for male and female rabbits was determined to be greater than 2,000 mg/kg. All animals appeared normal throughout the study. All animals exhibited body weight gain during the study with the exception of one male which exhibited a weight loss of 29 g during the first week. The test material produced slight to moderate dermal irritation. The gross necropsy at termination revealed no visible lesions.

SIGNATURE

Steven M. Glaza
Study Director
Acute Studies

10-24-95
Date

REFERENCES

1. "Acute Dermal Toxicity," *Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals*, Section 402 (adopted May 12, 1981).

2. Draize, J. H., "Acute Dermal Toxicity (Single Exposure)," In: *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity*, Association of Food and Drug Officials of the U.S., pp. 54-56 (1959).

HWI 50800374

PATHOLOGY REPORT

There were 10 rabbits (five males and five females) euthanized and necropsied at the termination of the study. The dose level, day of death, and gross observations recorded for each animal are in the Individual Pathology Comments that follow this report. There were no visible lesions in any of the animals.

Thomas E. Palmer, PhD
Pathologist

10-24-95
Date

(50800374.rpt)
092695

Table 1

Mortality Summary

Dose Level (mg/kg)	Sex	Mortality Result No. Died/ No. Dosed
2,000	M	0/5
2,000	F	0/5

Table 2

Individual and Mean Body Weights/Body Weight Gains (g)

Animal Number	Day 0 Weight	Day 7		Day 14	
		Weight	Gain*	Weight	Gain*
		Males (2,000 mg/kg)			
F56261	2,553	2,524	-29	2,642	89
F56271	2,481	2,562	81	2,582	101
F56265	2,391	2,393	2	2,480	89
F56266	2,526	2,577	51	2,707	181
F56267	2,529	2,613	84	2,714	185
Mean	2,496	2,534	38	2,625	129
		Females (2,000 mg/kg)			
F56268	2,534	2,685	151	2,770	236
F56269	2,448	2,484	36	2,555	107
F56264	2,386	2,512	126	2,536	150
F56270	2,675	2,679	4	2,684	9
F56274	2,487	2,521	34	2,582	95
Mean	2,506	2,576	70	2,625	119

* Gain from the Day 0 body weight.

Table 3

Individual Clinical Signs

Animal Number	Observation	Hour			Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
					Males (2,000 mg/kg)													
F56261	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56271	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56265	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56266	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56267	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
					Females (2,000 mg/kg)													
F56268	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56269	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56264	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56270	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
F56274	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

✓ Condition existed.

Table 4

Individual Dermal Irritation Observations

Animal Number	Observation	Observation Period (Day) 1	3	7*	10	14*
		Males				
F56261	Erythema	1	1	1	1	1
	Edema	1	0	0	0	0
	Atonia	1	0	0	0	0
	Desquamation	0	0	0	1	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	1	0	0
F56271	Erythema	1	0	0	0	0
	Edema	1	0	0	0	0
	Atonia	0	0	0	0	0
	Desquamation	0	0	0	0	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	0	0	0
F56265	Erythema	1	1	0	0	0
	Edema	1	0	0	0	0
	Atonia	1	0	0	0	0
	Desquamation	0	0	0	0	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	0	0	0
F56266	Erythema	1	1	2	1	1
	Edema	1	0	0	0	0
	Atonia	1	0	0	0	0
	Desquamation	0	0	0	1	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	0	0	0
F56267	Erythema	1	0	0	0	0
	Edema	0	0	0	0	0
	Atonia	1	0	0	0	0
	Desquamation	0	0	0	0	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	0	0	0

* Animals shaved before dermal observation.

Table 4 (Continued)

Individual Dermal Irritation Observations

Animal Number	Observation	Observation Period (Day) 1	3	7*	10	14*
		Females				
F56268	Erythema	1	1	2	2	1
	Edema	1	1	1	1	0
	Atonia	1	0	0	0	0
	Desquamation	0	0	0	1	1
	Coriaceousness	0	0	1	0	0
	Fissuring	0	0	1	1	0
F56269	Erythema	1	2	2	2	2
	Edema	1	2	2	2	1
	Atonia	2	1	0	0	0
	Desquamation	0	0	0	1	1
	Coriaceousness	0	0	1	0	0
	Fissuring	0	0	0	1	0
F56264	Erythema	1	1	1	0	0
	Edema	1	0	0	0	0
	Atonia	0	0	0	0	0
	Desquamation	0	0	0	0	0
	Coriaceousness	0	0	0	0	0
	Fissuring	0	0	0	0	0
F56270	Erythema	1	2	2	2	1
	Edema	1	2	2	1	1
	Atonia	0	0	0	0	0
	Desquamation	0	0	0	1	1
	Coriaceousness	0	0	1	0	0
	Fissuring	0	0	0	1	0
F56274	Erythema	1	1	2	1	0
	Edema	0	1	1	1	0
	Atonia	0	0	0	0	0
	Desquamation	0	0	0	1	0
	Coriaceousness	0	0	1	0	0
	Fissuring	0	0	0	0	0

* Animals shaved before dermal observation.

Table 5

Individual Pathology Comments

Dose Level: 2,000 mg/kg of Body Weight

Animal Number	Sex	Test Day Died	Test Day Sacrificed	Necropsy Observation
F56261	M	-	14	No visible lesions.
F56271	M	-	14	No visible lesions.
F56265	M	-	14	No visible lesions.
F56266	M	-	14	No visible lesions.
F56267	M	-	14	No visible lesions.
F56268	F	-	14	No visible lesions.
F56269	F	-	14	No visible lesions.
F56264	F	-	14	No visible lesions.
F56270	F	-	14	No visible lesions.
F56274	F	-	14	No visible lesions.

- Not applicable.

APPENDIX A

Protocol
Protocol Amendment No. 1
Protocol Amendment No. 2

Sample Submittal Form

This form is to be used when submitting samples for routine acute testing. Special testing needs can be easily arranged by contacting the Acute Toxicology Department at (608) 241-4471, Ext. 7292, or the Client Service Center at (608) 241-7210.

HWI Study No. 50800374

Enclose with samples and send to:
Hazleton Wisconsin
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Submitted by: ROGER G. PERKINS
Company: 3M
P.O. Number: _____

Date Sample Sent: 6/7/95
Invoice to: _____
Number of Reports Required: 3

Full GLP Compliance: X Yes ___ No
___ FDA (21 CFR 58)
___ EPA (TSCA—40 CFR 792)
___ EPA (FIFRA)—40 CFR 160)
X OECD

Sample Name: T-6342
Physical Description: liquid 07-1405-5 light colored
Special Handling Precautions: SEE MSDS ↑

Storage Requirements: X Room Temperature
___ Refrigerated
___ Other _____

Disposal: X Return to submitter
___ Dispose of according to Hazleton SOPs

Tests

Acute Oral Toxicity in Rats

___TP8084 Up and down LD50 procedure
___TP3206 FHSA screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
___TP3013 EPA screen; 5M-5F at 5.0 g/kg
X ___ Conduct defined study if death occurs at 5.0 g/kg
X TP2069 OECD screen; 5M-5F at 5.0 g/kg
___ Conduct defined study if death occurs at 5.0 g/kg
Special instructions: _____

Acute Dermal Toxicity in Rabbits

___TP3207 FHSA screen; 5M-5F at 2.0 g/kg
___TP3016 EPA screen; 5M-5F at 2.0 g/kg
X ___ Conduct defined study if death occurs at 2.0 g/kg
X TP2070 OECD screen; 5M-5F at 2.0 g/kg
___ Conduct defined study if death occurs at 2.0 g/kg
Special instructions: _____

For Hazleton Use Only
Protocol Issue Date: 8-25-95
Study Director: Steven M. Hoya

White copy—Hazleton Yellow copy—Submitter

Primary Skin Irritation

___TP3208 FHSA; 6 rabbits-1 abraded, 1 intact site/rabbit
___TP3014 EPA; 6 rabbits-1 intact site/rabbit
X TP2071 OECD; 3 rabbits-1 intact site/rabbit
___TP4206 DOT corrosivity; 6 rabbits-1 intact site/rabbit
___TP7145 Phototoxicity; 6 rabbits-2 intact sites/rabbit (one site with UVA exposure)
Special instructions: _____

Primary Eye Irritation

___TP6360 Low-volume procedure; 6 rabbits unwashed
___TP3209 FHSA; 6 rabbits unwashed
___TP2012 1978 EPA; 6 rabbits unwashed, 3 washed
___TP3015 1982 EPA; 6 rabbits unwashed
X TP2072 OECD; 3 rabbits unwashed
___ 3 rabbits washed at 4 seconds
___ 3 rabbits washed at 30 seconds
Special instructions: _____

Guinea Pig Sensitization

___TP2017 EPA Magnusson-Kligman maximization
___TP6164 OECD Magnussun-Kligman maximization
___TP2008 Buehler sensitization
___TP6289 Photoallergenic contact dermatitis (Armstrong)
Special instructions: _____

HAZLETON
WISCONSIN
POST OFFICE BOX 7545
MADISON WISCONSIN 53707-7545

a CORNING Laboratory Services Company

Sponsor:

3M
St. Paul, Minnesota

PROTOCOL TP2070

Study Title:

Acute Dermal Toxicity Study in Rabbits
(OECD Guidelines)

Date:

June 1, 1993

Performing Laboratory:

Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification:

HWI 50800374

Phone 608 241 4471
FOR EXPRESS MAIL DELIVERY 3301 KINSMAN BOULEVARD MADISON WISCONSIN 53704
Fax 608 241 7227

STUDY IDENTIFICATION

Acute Dermal Toxicity Study in Rabbits
(OECD Guidelines)

HWI No.	50800374
Test Material	(See sample submittal form)
Sponsor	3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144
Sponsor's Representative	John L. Butenhoff, PhD 3M Toxicology Services 220-2E-02 3M Center St. Paul, MN 55144 (612) 733-1962
Study Director	Steven M. Glaza Hazleton Wisconsin, Inc. P.O. Box 7545 Madison, WI 53707-7545 (608) 241-7292
Study Location	Hazleton Wisconsin, Inc. Building No. 3 3802 Packers Avenue Madison, WI 53704
Proposed Study Timetable	
Experimental Start Date	Week of 8-28-95
Experimental Termination Date	Week of 9-11-95
Final Report Date	Week of 10-23-95

1. Study
   Acute Dermal Toxicity Study in Rabbits (OECD Guidelines)

2. Purpose
   To assess the systemic toxicity and relative skin irritancy of a test material when applied to the skin of rabbits

3. Regulatory Compliance
   This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines:

   [ ] Conduct as a Nonregulated Study
   [ ] 21 CFR 58 (FDA)
   [ ] 40 CFR 160 (EPA-FIFRA)
   [ ] 40 CFR 792 (EPA-TSCA)
   [X] C(81)30 (Final) (OECD)
   [ ] Notification No. 3850, August 10, 1984 (Japanese MAFF)
   [ ] Notification No. 313, March 31, 1982, and as amended by Notification No. 870, October 5, 1988 (Japanese MOHW)

   All procedures in this protocol are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study does not unnecessarily duplicate any previous work.

4. Quality Assurance
   For regulated studies, the protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with Hazleton Wisconsin (HWI) Standard Operating Procedures (SOPs) and policies.

5. Test Material

   A. Identification
      (See sample submittal form)

   B. Physical Description
      (See sample submittal form)

   C. Purity and Stability
      The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Samples of test material/vehicle mixture(s) (if applicable) for concentration, solubility, homogeneity, and stability analyses will be taken before administration if requested by the Sponsor. These samples (if taken) will be sent to the Sponsor after experimental termination for possible analysis.

D. Storage
(See sample submittal form)

E. Reserve Samples
Studies of less than 4 weeks in experimental duration will not have reserve samples retained.

Reserve sample(s) of each batch/lot of test material will be taken if this study is more than 4 weeks in experimental duration.

The test material reserve sample will be stored at HWI in a freezer set to maintain a temperature of below 0°C for 10 years per HWI SOP. The Sponsor will be contacted after 10 years for disposition in accordance with the appropriate regulatory Good Laboratory Practices.

F. Retention
Any unused test material will be discarded after issuance of the final report, unless directed otherwise by the Sponsor.

G. Safety Precautions
As required by HWI SOPs and policies

6. Experimental Design

A. Animals

(1) Species
Rabbit

(2) Strain/Source
Hra:(NZW)SPF/Hazleton Research Products, Inc.

(3) Age at Initiation
Adult

(4) Weight at Initiation
2.0 to 3.0 kg

(5) Number and Sex
5 males and 5 females for the initial dose level
5 males and/or 5 females for any additional dose levels (if required)

(6) Identification
Individual numbered ear tag

(7) Husbandry

(a) Housing
Individually, in screen-bottom stainless steel cages (heavy gauge)

(b) Food
A measured amount of High Fiber Rabbit Chow® #5326 (Purina Mills, Inc.). The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.

(c) Water
Ad libitum from an automatic system. Samples of the water are analyzed by HWI for total dissolved solids, hardness, and specified microbiological content and for selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons.

(d) Contaminants
There are no known contaminants in the food or water that would interfere with this study.

(e) Environment
Environmental controls for the animal room will be set to maintain a temperature of 19 to 23°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark cycle.

(f) Acclimation
At least 7 days

(8) Selection of Test Animals
Based on health and body weight according to HWI SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test.

(9) Justification for Species Selection
Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

B. Dose Administration

(1) Dose Level
A single dose of 2,000 mg/kg of body weight will be administered to the intact skin of five males and five females. If no test material-related mortality is produced at this level, no further testing will be required. If any mortality occurs at the 2,000 mg/kg

level, additional dose levels may be added at the direction of the study director in order to meet the objectives of the study.

(2) Preparation of Exposure Area
On the day before test material application, the back of each rabbit will be clipped free of hair with an electric clipper. Not less than 10% of the total body surface area will be clipped. The animals will be clipped as needed throughout the study.

(3) Dose Administration
All animals will receive a single administration of test material. The dose will be based upon the animal's body weight just before administration of the test material. The area of application will be covered with as thin and uniform a layer as possible. If a liquid, the test material will be applied undiluted. If a solid, the test material will be moistened with 0.9% saline. Aerosol materials will be discharged into a beaker and administered as a liquid. The area of application will be wrapped with a 10.0-cm x 10.0-cm gauze bandage secured with paper tape around all edges, overwrapped with Saran Wrap®, and secured with Elastoplast® tape to provide an occlusive dressing. The rabbits will be collared during the 24-hour application period.

(4) Reason for Route of Administration
Historically, the dermal route has been the route of choice based on the method of Draize.

(5) Removal of Test Material
Approximately 24 hours after test material application, the bandages and collars will be removed, and the residual test material will be removed using water or an appropriate solvent, if necessary.

C. Observation of Animals

(1) Clinical Observations
At approximately 1, 2.5, and 4 hours after test material administration for clinical signs and mortality, daily thereafter for clinical signs, and twice daily (a.m. and p.m.) for mortality for at least 14 days. Observations may be extended when directed by the study director.

(2) Reading of Dermal Irritation
Approximately 30 minutes after bandage removal, the initial dermal irritation reading will be made and

recorded as the Day 1 reading (Attachment 1). Additional dermal irritation readings will be made on Study Days 3, 7, 10, and 14. Individual dermal irritation records will be maintained for each animal.

(3) Body Weights
Just before test material application, on Days 7 and 14, and at death (when survival exceeds 1 day)

D. Pathology
At termination of the experimental phase, surviving animals will be euthanized. All animals, whether dying during the study or euthanized, will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. After necropsy, the animals will be discarded and no tissues will be saved.

E. Statistical Analyses
Other than LD_{50} calculations (when applicable) no statistical analyses are required.

7. Report
A final report including those items listed below will be submitted:

Description of the test material
Description of the test system
Procedures
Dates of experimental initiation and termination
Tabulation of mortality data by sex and dose level
Description of any toxic effects/dermal irritation
Tabulation of mean body weights by sex and dose level
LD_{50} values by sex with 95% confidence intervals (when applicable)
Gross pathology findings/gross pathology report (when applicable)

8. Location of Raw Data, Records, and Final Report
Original data, or copies thereof, will be available at HWI to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those items listed below will be retained in the archives of HWI according to HWI SOP.

Protocol and protocol amendments
Dose preparation records
In-life records
  Body weights
  Dose administration
  Observations
Anatomical pathology records
Study correspondence
Final report (original signed copy)

The following supporting records will be retained at HWI but will not be archived with the study data.

Animal receipt/acclimation records
Water analysis records
Animal room temperature and humidity records
Refrigerator and freezer temperature records
Instrument calibration and maintenance records

PROTOCOL APPROVAL

John L. Butenhoff

July 28, 1993

John L. Butenhoff, PhD
Sponsor's Representative
3M

Date

Steven M. Glaza

6-1-93

Steven M. Glaza
Study Director
Acute Toxicology
Hazleton Wisconsin, Inc.

Date

Rebecca S. Nelson

6/1/93

Representative
Quality Assurance Unit
Hazleton Wisconsin, Inc.

Date

(TP2070.3M)

Attachment 1

Scoring Scale for Acute Dermal Reactions

Erythema

0 - None
1 - Slight
2 - Moderate
3 - Severe

Edema

0 - None
1 - Slight (barely perceptible to well defined by definite raising)
2 - Moderate (raised approximately 1 mm)
3 - Severe (raised more than 1 mm)

Atonia

0 - None
1 - Slight (slight impairment of elasticity)
2 - Moderate (slow return to normal)
3 - Marked (no elasticity)

Desquamation

0 - None
1 - Slight (slight scaling)
2 - Moderate (scales and flakes)
3 - Marked (pronounced flaking with denuded areas)

Coriaceousness

0 - None
1 - Slight (decrease in pliability)
2 - Moderate (leathery texture)
3 - Marked (tough and brittle)

Fissuring

0 - None
1 - Slight (definite cracks in epidermis)
2 - Moderate (cracks in dermis)
3 - Marked (cracks with bleeding)

HWI No. 50800374

PROTOCOL AMENDMENTS

Amendment No. 1

Effective August 25, 1995

Portion of Protocol Being Modified: Page 2, Study Location

Reason for Modification: To identify the location where the study will be conducted, replace this section with the following change:

Modification: Study Location — Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard.
Madison, WI 53704

Study Director Approval: Steven M. Olga 8-25-95

(G21/01-07-91)

HWI No. 50800374

PROTOCOL AMENDMENTS

Amendment No. 2

Effective August 28, 1995

Portion of Protocol Being Modified: Page 6, 6. Experimental Design; B. Dose Administration; (3) Dose Administration.

Reason for Modification: To correctly identifiy the size of the gauze bandage used to wrap the area of application.

Modification: Replace the seventh sentence of this section with the following change: The area of application will be wrapped with a 4-ply gauze bandage (approximately 9.5-cm x 21-cm) secured with paper tape around all edges, overwrapped with Saran Wrap®, and secured with Elastoplast® tape to provide an occlusive dressing.

Study Director Approval: Steven M. Klaas 10-9-95

(G21/01-07-91)

Attachments to Letter to C. Auer dated May 25, 2000
Toxicology Studies and Other Information on PFOA

Genotoxicity

1) An Assay of Cell Transformation and Cytotoxicity in the C3H 10T 1/2 Clonal Cell Line for the Test Chemical T-2942 CoC, Environmental Pathology Laboratory, Stone Research Laboratories, University of Minnesota, 3M Ref. No. FC-143 Lot 340, L138679, March 5, 1981

2) Final Report, Mutagenic Evaluation of T-2015 CoC in the Ames Salmonella/Microsome Plate Test, Litton Bionetics, Inc., Study No. 20838, 3M Ref. No. FC-143, February 1978

3) Final Report, Mutagenicity Test on T-6564 in an *In Vivo* Mouse Micronucleus Assay, Corning Hazelton, Inc., Study No. 17750-0-455, 3M Ref. No. FC-1015, L13167, straight-chain APFO, November 1, 1996

4) Final Report, Mutagenicity Test on T-6564 Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: with a Confirmatory Assay with Multiple Harvests, Corning Hazelton Inc., Study No. 17750-0-437CO, 3M Ref. No. FC-1015, L13167, straight-chain APFO, September 16, 1996

5) Final Report, Mutagenicity Test with T-6564 in the *Salmonella - Escherichia Coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay, Corning Hazelton Inc., Study No. 17750-0-409R, 3M Ref. No. FC-1015, L13167, straight-chain APFO, September 13, 1996

6) Final Report, Mutagenicity Test on T-6342 Measuring Chromosome Aberrations in Human Whole Blood Lymphocytes with a Confirmatory Assay with Multiple Harvests, Corning Hazelton, Inc., Study No. 17073-0-449CO, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, November 1, 1996

7) Final Report, Mutagenicity Test on T-6342 Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: with a Confirmatory Assay with Multiple Harvests, Corning Hazelton, Inc., Study No. 17073-0-437CO, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, September 16, 1996

8) Final Report, Mutagenicity Test on T-6342 in an *In Vivo* Mouse Micronucleus Assay, Corning Hazelton, Inc., Study No. 17073-0-455, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, December 14, 1995

9) Final Report, Mutagenicity Test with T-6342 in the *Salmonella - Escherichia Coli*/Mammalian-Microsome Reverse Mutation Assay, Corning Hazelton, Inc., Study No. 1703073-0-409, 3M Ref. No. FC-1090, L13364, F11426, Lot 1, sodium perfluorooctanoate, December 14, 1995

AN ASSAY OF CELL TRANSFORMATION AND CYTOTOXICITY IN C3H 10T 1/2 CLONAL CELL LINE FOR THE TEST CHEMICAL T-2942 CoC

Submitted to the 3M Corporation

3M Center
St. Paul, Minnesota 55133

By the Environmental Pathology Laboratory
Department of Laboratory Medicine and Pathology
Stone Research Laboratories
Room 110
421 S.E. 29th Avenue
Minneapolis, Minnesota 55414

March 4, 1981

Report Submitted By:

Vincent F. Garry, M.D. — Date 3/5/81
Study Director

Richard L. Nelson — Date 3/5/81
Associate Scientist

TEST ARTICLE SPECIFICATIONS

STUDY NUMBER: 1

TEST ARTICLE I.D.: T-2942 CoC

TEST ARTICLE LOT NUMBER: -

DATE RECEIVED: 8/20/80

DATE STUDY BEGINS: 8/27/80

DATE STUDY COMPLETED: 10/5/80

TEST ARTICLE STORAGE CONDITIONS: Room Temperature

DILUENT(S)USED: DMSO

TEST ARTICLE FORM: GAS ____ LIQUID ____ SOLID X

TEST ARTICLE QUANTITY RECIEVED: 10 grams

SPECIAL HANDLING PRECAUTIONS: None

HAZARD RATING:

____ CHEMICAL 1 4

____ EXPLOSIVE 1 4

____ BIOLOGICAL 1 4

LD_{50} ORAL ACUTE: 540 mg/kg

SOLUBILITY OF TEST MATERIAL: (H_2O; CH_3OH; Lipid, etc.) H_2O; CH_3OH; Acetone

Quality Assurance Statement

The C3H 10T-1/2 cell transformation assay is a highly reproducible method requiring several internal controls. Cells, media and serum are routinely screened for growth potential and contaminants prior to incorporation into the test system. This function has been carried out by Mr. Nelson and reviewed by Dr. Garry in this initial study. The raw data and the final report has been reviewed by our Quality Control Officer, Mr. Robert Kreiger.

Vincent F. Garry, M.D.
Study Director

Robert Kreiger, M.S.
Quality Control Officer

Executive Summary

Assays for both cytotoxicity and cell transformation have been completed for test article T-2942 CoC, using C3H 10T-1/2 cell cultures *in vitro*. Cytotoxicity was measured by a reduction of cloning efficiency for treated cells. The data showed an LD_{50} of approximately 50 ug/ml. A dose range extending from 0 to 200 ug/ml was tested for cytotoxic effect. Comparison to a wide range of chemicals reported in the literature indicates that the chemical studied (T-2942 CoC) exhibits a low order of cytotoxicity, utilizing C3H 10T-1/2 cells.

Transformation assays were conducted using the previously derived LD_{50} as the median dose, with a dose range spread of four log units. Both the 14 day colony assay for transformation and a longer term foci transformation regimen (38 day) were completed for the test article T-2942 CoC. No evidence of transformation was observed for either the colony or foci assay methods using C3H 10T-1/2 cell cultures.

Introduction

This study was conducted for 3M by V. F. Garry, M.D., M.S., R. Nelson, B.A., R. Krieger, M.S. and M. Sinn, B.A., from 8/27/80 to 10/5/80 at the Environmental Pathology Laboratory of the University of Minnesota, Minneapolis, Minnesota. The experimental procedures employed are the test methods described by Reznikoff, Brankow and Heidelberger for the determination of transformation and cytotoxicity in the C3H 10T-1/2 cell line. Aside from this classical methodology, we have provided 3M an early reporting feature to give a preliminary evaluation of results. All procedures are described in detail in the protocol included in the appendix of the report.

Materials and Methods

Cell Source

Cryopreserved cells of the C3H 10T-1/2 clone 8 (Lot Number 3C1-1-4) utilized in these studies were derived from passage 11. The original cell stock was obtained from Dr. C. Heidelberger, Director for Basic Research of the University of Southern California. The cryopreserved lots were prepared from subcultures of the original cell line obtained at the 5th passage.

Cell Culture Conditions

Stock cultures for these studies were grown in Eagle Basal Medium (BME) containing 10% heat inactivated fetal bovine serum (Reheis Chem. Co., Lot Number T-48609). Prior to the study, the serum lot was tested for cloning efficiency and transformation efficiency in the presence of direct and indirect acting carcinogens. In addition, the entire cell system was tested for possible bacterial or mycoplasma contamination to insure the adequacy of the procedures.

Test Chemicals

The test chemical, T-2942 CoC was received on 8/20/80 from W. McCormick, an employee of 3M Corporation. Contained in a coded glass vial was approximately 10gm of white powder. The material was accompanied by a letter of authorization and information regarding *in vivo* toxicity. The test chemical was stored at room temperature. Immediately before use, the test material was dissolved in spectral grade DMSO (Fisher Chemical Co. Lot Number 702398) and diluted to appropriate concentrations. Within 20 minutes the diluted chemical was added to the cultures under subdued yellow light to avoid photo-inactivation. No more than 20 microliters of the diluted chemical was added to the cultures to avoid solvent effects. The chemicals, Benzo(a)pyrene (Eastman Kodak Lot Number 4941) and di-epoxybutane (Aldrich Chem. Co. Lot Number 082297) were used as positive controls.

Initial Cytotoxicity Determination

Prior to performance of the transformation assay, dose range data was obtained in the form of cytotoxicity measurements as expressed by plating (cloning) efficiency. The test chemical T-2942 CoC was added to cultures seeded the day before at 300 cells per 60mm culture dish. After 24-hour exposure to the test chemicals in 5ml BME media supplemented with 10% fetal calf serum; T-2942 CoC was removed with a complete change of media. The test chemical was applied through a 4 log scale dilutions ranging from 200 to 0.1 ug/ml. Six replicate cultures per dose point were employed and a total of six dose points were studied. The cultures were refed with fresh media every three days. After 7 days in culture, the plates were washed in PBS, fixed with absolute methanol and stained with giemsa stain. Positive controls, solvent controls and serum baseline controls were included in this study. The number of colonies per plate were counted and the plating efficiency was determined by the formula:

$$PE = \frac{\text{Average No. Colonies/plate}}{\text{No. of Cells seeded/plate}} \times 100$$

Transformation Assay

The approximate *in vitro* LD_{50} cytotoxicity dose was chosen as the median dose for the study of the transformation potential of the test chemical (T-2942 CoC). The test was conducted in two phases. In the first phase, cell transformation in the colony mode was assessed. In the second part, foci transformation potential was determined.

Phase 1 - Colony Transformation Potential

Six replicate plates seeded with 300 cells per plate were treated with 200, 100, 50, 10, 1.0 and 0.1 ug/ml to give appropriate two-fold and logarithmic dose relationships for the test chemical T-2942 CoC. The positive control, benzo(a)pyrene (BP) was tested at 10, 5, 2.5, 1.0, and 0.1 ug/ml. A solvent control (DMSO) was included (10ug/ml). After removal of the chemical after 24 hours exposure, the cultures were refed fresh media and thereafter every 3 days for 14 to 17 days. At 14 days after removal of the test chemical, the plates were washed, fixed and stained as described before. Each colony was

carefully examined macroscopically and microscopically and scored for transformation according to criteria of Reznikoff, et al.

Phase 2 - Foci Transformation Potential

Remaining replicates at 6 replicates per dose were allowed to continue in culture for 38 days. Three dose increments were studied; 100, 10 and 1.0 ug/ml respectively. A positive control (butadiene epoxide) in dose increments of 0.01, 0.001, 0.005 and 0.0001 ug/ml was included along with a DMSO solvent control. The cultures were refed according to the schedule mentioned above for the first fourteen days. For the remainder of time in culture, the cells were refed once weekly with BME supplemented with 10% fetal calf serum. At 38 days after removal of the test chemical, the culture plates were processed as mentioned above.

Scoring for Transformation

Focal areas of transformation are classified according to the criteria of Reznikoff as follows:

Type I. Foci composed of monolayer cells are more densely packed than the background cells. This type is not considered malignant and is not scored.

Type II. Foci show massive piling up into virtually opaque multilayers. The cells are only moderately polar, thus criss-crossing is not pronounced. Fifty percent of Type II foci have been shown to be malignantly transformed.

Type III. Foci are composed of highly polar, fibroblastic, multilayerd, criss-crossed arrays of densely stained cells. Eighty-five percent of Type III foci have been shown to be malignantly transformed.

Selected Type III foci will be retained from living cultures and subcultured twice, after which the cells will be cryopreserved for one year. If, during that time, confirmatory in vivo tumorogenesis studies are requested, these cells will be made available for injection into a suitable host.

Materials and Methods, Continued

Special C3H 10T-1/2 Early Reporting (Phase I)

Although the classic methodology for the C3H 10T-1/2 prescribed a 6-week course of study, recent data obtained by our Laboratory shows that the assay time may be foreshortened to 15 to 20 days. Detailed microscopic study of the colonies allows for quantitation in this somewhat shorter frame using the classic morphologic criteria previously described. This early reporting capability is available as preliminary information and is included in our report.

Recording of Data and Reports

All data from the cytotoxicity screening, transformation assay and early reporting information are recorded in tabular form (see enclosure). A coded access number will be provided to allow retrieval of cryopreserved material, and the fixed and stained cultures. All reports will remain confidential, subject to disclosure by the Corporation. Although there are no specific FDA guidelines for *in vitro* carcinogenesis testing, we will in future, adhere more closely to the Good Laboratory Practices protocol by formal establishment of a quality control unit in our laboratory.

References

1. Reznikoff, C., Brankow, D., Heidelberger, C. Cancer Research, 33:3231-3238, Dec. 1973.
2. Renzikoff, C., Brankow, D., Heidelberger, C. Cancer Research, 33:3239-3249, Dec. 1973.
3. Modal, S., Brankow, D., Heidelberger, C. Cancer Research, 36:7, Part I, 2254-2260, July, 1976.
4. Bertram, J. S. Cancer Research, 17:51, 1976.
5. Bertram, J. S. Cancer Research, 37:2, 514-523, 1977.
6. Haber, D. A., Fox, D. A., Dynan, W. S., Thilly, W. G., Cancer Research, 37:6, 1644-1648, June 1977.
7. Bertram, J. S., Cancer Letters 7:5, 288-298, September, 1979.

Results

In the dose ranging cytotoxicity test, the chemical T-2942 CoC showed a plating efficiency of 21.9% of control at 100 ug/ml (Table 1). To provide an efficient description of the transformation potential of the chemical, both colony and foci were studied based on the initial cytotoxicity screening. In the colony mode, eight dose points enclosing the in vitro LD_{50} were assessed in log scale and two-fold dilutions. There was no morphologic evidence of transformation in the fourteen day colonies treated with the test chemical (Table 2)

Longer term foci (38 days in culture) were studied in dose increments of 100, 10, and 1.0 ug/ml. No evidence of morphologic transformation were observed at any of the concentrations studied (Table 3).

The positive control, benzo(a)pyrene showed a dose related transformation frequency in the colony forming mode. In the foci mode, the positive control (butadiene epoxide) transformants were again observed in the dose increments studied. The combined number of type two and type three foci varied from 43.0 to 21.3/plate. No abnormalities were detected in the solvent controls.

Conclusions

The test chemical T-2942 CoC was studied in C3H 10T-1/2 cells for morphologic evidence of transformation in vitro. At the dose levels employed, no evidence of transformation was observed. The positive controls, benzo(a)pyrene and diepoxybutane showed development of either Type II and Type III colonies or Type II or Type III foci. The solvent control showed normal morphology.

Table 1

TOXICITY AND PLATING EFFICIENCY
IN CLONED C3H 10T 1/2 CL 8 CELLS
AFTER EXPOSURE TO CHEMICAL T-2942 CoC

3M Corporation	V. F. Garry, M.D.	T-2942 CoC
Client	Investigator	Test Compound I.D. No.
1	DMSO	200 ug/ml - 0.1 ug/ml
Study Number	Solvent	Dose Range

7 DAY COLONIES

DOSE ug/ml	Av. No. Col 300 Cells/Dish 6 Dishes/Dose	P.E.**** Percent of Controls	Transformed Colonies/ Cell***	Transformed Colonies (Total Colonies Percent)**
T-2942 CoC				
200	0	0		
100	9.0	21.96		
50	22.0	53.66		
10	33.66	81.99		
1.0	37.16	90.04	NONE	NONE
0.1	40.00	97.58		
CONTROL	41.0	-		
S. CONTROL*	40.8	99.27		

*10 ug/ml Solvent Control (DMSO)

**Percent Transformation (T/Col.%) = $\frac{\text{Average No. T/Plate}}{\text{Average No. Col./Plate}}$

***Transformation = $\frac{\text{Average No. T/Plate}}{\text{No. Cells Plated/Dish}}$

****P.E. Percent of Control = $\frac{\text{P.E. of Dose}}{\text{P.E. (Control)}} \times 100$

Table II

COLONY TRANSFORMATION AND CLONING EFFICIENCY
IN CLONED C3H 10T-1/2 CL 8 CELLS
AFTER EXPOSURE TO CHEMICAL T-2942 CoC

3M Corporation	V. F. Garry, M.D.	T-2942 CoC
Client	Investigator	Test Compound I.D. Number
1	DMSO	200 ug/ml - 1 ug/ml
Study Number	Solvent	Dose Range

Dose ug/ml	Av. No. Col. 300 Cells/Dish 5 Dishes/ Dose	P.E.(d) Percent	P.E.(e) Percent of Controls	Combined Type II and Type II Colonies	
				Transformed Colonies/Cell(c)	Transformed Colonies(b) (Total Colonies Percent)
T-2942 CoC					
200	0	0	0		
100	27.61	9.05	63.15		
50	32.67	10.89	79.99		
20	35.0	11.67	81.44		
10	37.5	12.5	87.23		
5	38.67	12.89	89.95	NONE	NONE
2.5	40.5	13.5	94.21		
1.0	41.0	13.67	95.39		
CONTROL (a)	43.0	14.33	-		
S. CONTROL	41.33	13.77	96.09		
10	26.0	8.67	56.78	11.1×10^{-3}	12.81
5	29.3	9.7	63.52	8.86×10^{-3}	9.08
2.5	37.83	12.6	82.51	7.7×10^{-3}	6.16
1.0	40.5	13.5	88.41	7.2×10^{-3}	5.32
0.1	44.33	14.78	96.79	4.43×10^{-3}	3.0
CONTROL	45.8	15.27	-	-	-
S. CONTROL	43.0	14.3	93.65	-	-

(14 Day Colonies)

(a) 10 ug/ml Solvent Control (DMSO)

(b) Percent Transformation (T/Col.Percent) = $\frac{\text{Average No. T/Plate}}{\text{Average No. Col./Plate}}$

(c) Transformation (T/Cell) = $\frac{\text{Average No. T/Plate}}{\text{No. Cells Plated/Dish}}$

(d) P. E. Percent = $\frac{\text{Average No. of Col./Dish}}{\text{No. Cells Plated/Dish}} \times 100$

(e) P. E. Percent of Control = $\frac{\text{P. E. of Dose}}{\text{P. E. (Control)}} \times 100$

Table III

C3H 10T-1/2 CELLS
TRANSFORMED FOCI FORMATION ASSAY
AFTER EXPOSURE TO CHEMICAL T-2942 CoC

3M Corporation	V. F. Garry M.D.	T-2942 CoC
Client	Investigator	Test Compound I.D. No.
1	DMSO	100 ug/ml - 1.0 ug/ml
Study Number	Solvent	Dose Range

Dose	Number of Days	Combined Type II and Type III Foci		Transformation Per Cell Plated Percent
		Total No. Foci	Av. No. Foci per plate	
T-2942 CoC				
100	38	0/6		
10	38	0/6		
1.0	38	0/6	NONE	NONE
CONTROL	38	0/6		
S. CONTROL	38	0/3		
+ Control Butadiene Diepoxide				
0.01	36	0	0	0
0.001	36	129/3	43.0	14.33
0.0005	36	84/3	28.0	9.33
0.0001	36	64/3	21.3	7.1

$$\frac{\text{Average No. of Type II and Type III Foci per Dish}}{\text{No. of Cells Plated per Dish}} \times 100$$

C3H 10T 1/2 CLONE 8 TRANSFORMATION ASSAY

The C3H 10T 1/2 cell line is derived from mouse embryonic cells. In the early 1970's Reznikoff, Bankow and Heidelberger[1,2] utilized clonal cells from the initial isolate to establish an *in vitro* measure of carcinogenesis, the transformation assay. In brief, the assay consists of exposure of mammalian cells to a potential carcinogen *in vitro* for a precise period of time; followed by a cultivation of newly seeded cells for a period of 30 to 35 days. During this time, cytotoxicity and morphologic evidence of neoplastic transformation is obtained. Because the cells are morphologically homogenous and sensitive to post confluence inhibition, abnormal cellular foci can easily be detected. The number of foci detected are proportional to the dose of the carcinogen applied. Similarly, the number of colonies of cells detected within the first 7-10 days of culture provide a quantitative basis for the determination of cytotoxicity. To confirm the carcinogenic potential of the transformed foci, the abnormal cells are injected into a susceptible host. The development of macroscopic tumors within 90 days constitutes confirmation of the neoplastic character of injected, morphologically abnormal cells.

The assay has good reproducibility in our hands as well as in those of our colleagues in the field. Each assay to be performed includes a positive control, solvent control and five dose points for the test chemical. Six separate cultures are used to establish each dose point.

1. Procedures

   A. Cell Source

      Low passage cryopreserved cells of the C3H 10T 1/2 clone 8 were obtained from Dr. Heidelberger. From the initial culture, a low passage stock of cells has been established. For long-term storage, the cells are first suspended in 8 percent DMSO plus media and are preserved in liquid nitrogen. For short-term storage, we routinely maintain cells in a -80° centigrade freezer. Periodically, sample cultures are tested for mycoplasma contamination, cloning efficiency and postconfluence inhibition. In the past sixteen months, cloning efficiency has varied from 12 to 16 percent. There is no evidence of "spontaneous transformation" in any of our cultures tested to date.

   B. Cell Culture Conditions

      Routinely, stock cultures are grown in Eagle Basal Medium (BME) containing 10 percent heat-inactivated fetal bovine serum without the use of antibiotics. The media is made from powdered form in high purity water obtained from certified commercial sources. Fetal calf serum lots are periodically tested for their effect on cloning efficiency and selected on this basis. To insure continuity of testing sufficient quantities of serum are held on reserve.

C. Test Chemicals

Chemicals to be tested should be identified as precisely as possible. Information regarding the physical characteristics (eg) solubility, in vivo toxicity (LD50), and source are important considerations. Each chemical received is coded and duplicate records of the test procedure are maintained by the Laboratory.

Chemicals to be studied will be tested on a ug/ml basis in an appropriate solvent (eg) DMSO. Addition of the chemicals to culture is accomplished by media dilutions under photographic safety light. Subsequent media changes are carried out under gold fluorescent light.

2. Cytotoxicity

Prior to performance of the transformation assay, dose range data is obtained in the form of cytotoxicity measurements. In accordance with the protocol established by Reznikoff, Bertram, Brankow, and Heidelberger[1], cytotoxicity is measured in terms of plating efficiency. A fixed number of cells (approximately 300/dish) are placed in culture and allowed to grow for 7 to 10 days. The percentage of surviving colonies divided by the number of cells initially plated is then determined (ie) the cloning efficiency. Routinely, chemicals to be tested are added to the cultures 24 hours after plating. After a standard 24-hour exposure period, the chemicals are removed with a change of media. The cells are refed fresh media every three days. The test chemicals are applied through a 4-log dose scale using 10 dose points. Three replicate cultures per point are employed. Positive control, solvent control and serum baseline controls are included with each study. All chemical or solvent additions to the media are not allowed to exceed 0.5% of the total media volume. At the end of 7 to 10 days, the cultures are fixed, stained and the number of colonies are counted macroscopically and microscopically.

3. Transformation Assay

The transformation assay is performed in accord with the methodology developed by Reznikoff, et al,[2] and modified by Bertram, et al[4]. In line with this classical approach, approximately 300 cells are plated in each of six separate culture dishes to achieve six replicates per dose point, once the desired concentration range has been determined by measurements of cloning efficiency. Routinely, a minimum of four dose points are studied in increasing dilutions from a dose which causes 50 to 75 percent decrease in cloning efficiency. Dilutions will be made two-fold or more, depending on the slope of the cytotoxicity curve. The procedures for chemical additions to the cultures are identical to that employed for cytotoxicity.

All cultures are refed with Basal Eagles media with 10 percent fetal calf serum. Routinely, re-feeding is done every three days until a confluent monolayer of cells is acheived; usually 15 to 20 days. Thereafter, the cultures are refed weekly.

-----Transformation Assay Continued

At 35 days after removal of the compound, all culture dishes are fixed, stained, and examined macroscopically and microscopically, and scored for transformation. All of the fixed and stained cultures are retained for one year as a semi-permanent record of the study. Scoring of morphological transformation is in accordance with the types described by Reznikoff, et al[1].

A. Scoring of Transformation

Focal areas of transformation are classified according to the criteria of Reznikoff[1] as follows:

Type I. Foci composed of monolayer cells are more densely packed than the background cells. This type is not considered malignant and is not scored.

Type II. Foci show massive piling up into virtually opaque multilayers. The cells are only moderately polar, thus criss-crossing is not pronounced. Fifty percent of Type II foci have been shown to be malignantly transformed.

Type III. Foci are composed of highly polar, fibroblastic, multilayered, criss-crossed arrays of densely stained cells. Eighty-five percent of Type III foci have been shown to be malignantly transformed.

Selected Type III foci will be retained from living cultures and sub-cultured twice, after which the cells will be cryopreserved for one year. If, during that time, confirmatory in vivo tumorogenesis studies are requested, these cells will be made available for injection into a suitable host.

4. Special C3H 10T 1/2 Early Reporting

Although the classic methodology for the C3H 10T 1/2 prescribes a 6-week course of study, recent data obtained by our Laboratory shows that the assay time may be foreshortened to 15 to 20 days. Detailed microscopic study of the colonies allows for quantitation in this somewhat shorter frame using the classic morphologic criteria previously described. This early reporting capability is available as preliminary information and is included in our report.

5. Recording of Data and Reports

All data from the cytotoxicity screening, transformation assay and early reporting information are recorded in tabular form (see enclosure). A coded access number will be provided to allow retreival of cryopreserved material, and the fixed and stained cultures. All reports will remain confidential,

-----Recording of Data and Reports, Continued

subject to disclosure by the Corporation. Although there are no specific FDA guidelines for in vitro carcinogenesis testing, we adhere to the Good Laboratory Practices Protocol put forward by this Federal Agency.

6. References

1. Reznikoff, C., Brankow, D., Heidelberger, C. Cancer Research, 33:3231-3238, Dec. 1973.

2. Reznikoff, C., Brankow, D., Heidelberger, C. Cancer Research, 33:3239-3249, Dec. 1973.

3. Mondal, S., Brankow, D., Heidelberger, C. Cancer Research, 36:7, Part I, 2254-2260, July, 1976.

4. Bertram, J.S. Cancer Research, 17:51, 1976.

5. Bertram, J.S. Cancer Research, 37:2, 514-523, 1977.

6. Haber, D.A., Fox, D.A., Dynan, W.S., Thilly, W.G., Cancer Research, 37:6, 1644-1648, June 1977.

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MUTAGENICITY EVALUATION OF

T-2015 CoC

IN THE
AMES SALMONELLA/MICROSOME
PLATE TEST

FINAL REPORT

SUBMITTED TO:

3M COMPANY
3M CENTER
SAINT PAUL, MINNESOTA 55101

SUBMITTED BY:

LITTON BIONETICS, INC.
5516 NICHOLSON LANE
KENSINGTON, MARYLAND 20795

LBI PROJECT NO. 20838

FEBRUARY 1978

Litton BIONETICS

000165

I. SPONSOR: 3M Company

II. MATERIAL*

A. Identification: T-2015 CoC

B. Date Received: December 20, 1977

C. Physical Description: White powder

III. TYPE OF ASSAY: Ames Salmonella/Microsome Assay

IV. PROTOCOL NO.: DMT-100

V. RESULTS

The results of this assay are presented in Table 1.

VI. INTERPRETATION OF RESULTS AND CONCLUSIONS

The test compound was examined for mutagenic activity in a series of in vitro microbial assays employing Salmonella and Saccharomyces indicator organisms. The compound was tested directly and in the presence of liver microsomal enzyme preparations from Aroclor-induced rats.

The compound was tested over a series of concentrations such that there was either quantitative or qualitative evidence of some chemically-induced physiological effects at the high dose level. The low dose in all cases was below a concentration that demonstrated any toxic effect. The dose range employed for the evaluation of this compound was from 0.1 µg to 500 µg per plate.

The results of the tests conducted on the compound in the absence of a metabolic activation system were all negative.

The results of the tests conducted on the compound in the presence of a rat liver activation system were all negative.

*Information was supplied by the sponsor. If information was not indicated by the sponsor, N.I. was entered.

VI. INTERPRETATION OF RESULTS AND CONCLUSIONS (Continued)

The test compound, T-2015 CoC did not demonstrate genetic activity in any of the assays conducted in this evaluation and was considered not mutagenic under these test conditions.

Submitted by:

Study Director

D. R. Jagannath 2·20·78

D. R. Jagannath, Ph.D. Date
Section Chief
Submammalian Genetics
Department of Genetics
and Cell Biology

Reviewed by:

for David Brusick, Ph.D. 2/21/78 Date
Director
Department of Genetics
and Cell Biology

Litton BIONETICS

V. RESULTS — TABLE 1

A. NAME OR CODE DESIGNATION OF THE TEST COMPOUND: T-2015 COC
B. SOLVENT: DMSO
C. TEST INITIATION DATE: DEC. 28, 1977
NOTE: CONCENTRATIONS ARE GIVEN IN MICROLITERS (UL) OR MICROGRAMS (UG) PER PLATE.

TEST	SPECIES	TISSUE	REVERTANTS PER PLATE											
			TA-1535		TA-1537		TA-1538		TA-98		TA-100		D4*	
			1	2	1	2	1	2	1	2	1	2	1	2
NONACTIVATION														
SOLVENT CONTROL	---	---	12		10		19		45		180		87	
POSITIVE CONTROL**	---	---	410		524		1555		1198		1258		840	
TEST COMPOUND														
0.100000 UG	---	---	19		12		23		54		183		50	
1.000000 UG	---	---	18		11		19		36		171		83	
10.000000 UG	---	---	18		5		29		43		193		80	
100.000000 UG	---	---	17		13		28		32		143		86	
500.000000 UG	---	---	13		6		23		39		211		86	
ACTIVATION														
SOLVENT CONTROL	RAT	LIVER	20		23		24		46		277		138	
POSITIVE CONTROL***	RAT	LIVER	262		233		963		872		1426		189	
TEST COMPOUND														
0.100000 UG	RAT	LIVER	29		6		23		38		234		173	
1.000000 UG	RAT	LIVER	24		11		29		36		232		128	
10.000000 UG	RAT	LIVER	13		16		24		34		247		170	
100.000000 UG	RAT	LIVER	19		21		28		39		231		134	
500.000000 UG	RAT	LIVER	19		9		29		30		276		150	

* TRY. CONVERTANTS PER PLATE

**	TA-1535	EMS	10 UL/PLATE
	TA-1537	QM	10 UG/PLATE
	TA-1538	NF	10 UG/PLATE
	TA-98	NF	10 UG/PLATE
	TA-100	EMS	10 UL/PLATE
	D4	EMS	10 UL/PLATE
	SOLVENT	DMSO	50 UL/PLATE

***	TA-1535	ANTH	2.5 UG/PLATE
	TA-1537	ANTH	2.5 UG/PLATE
	TA-1538	ANTH	2.5 UG/PLATE
	TA-98	ANTH	2.5 UG/PLATE
	TA-100	ANTH	2.5 UG/PLATE
	D4	DMNA	100 MICROMOLES/PLATE
	SOLVENT	DMSO	50 UL/PLATE

000168

PROTOCOL

1. PURPOSE

The purpose of this study was to evaluate the test material for genetic activity in a microbial assay with and without the addition of mammalian metabolic activation preparations.

2. MATERIALS

A. Indicator Microorganisms

A description of strain verification is given in Standard Operating Procedure on page 10.

Salmonella typhimurium	TA-1535
	TA-1537
	TA-1538
	TA-98
	TA-100
Saccharomyces cerevisiae	D4

B. Activation System

1. Reaction mixture

Component	Final Concentration/ml
TPN (sodium salt)	4 µmol
Glucose-6-phosphate	5 µmol
Sodium phosphate (dibasic)	100 µmol
$MgCl_2$	8 µmol
KCl	33 µmol
Homogenate S9 fraction	0.1 ± .05 ml

2. S9 homogenate

A 9,000 x g supernatant was prepared from Sprague-Dawley adult male rat liver induced by Aroclor 1254 five days prior to kill according to the procedure of Ames et al. (1975). S9 samples were coded by lot number and assayed for milligrams protein per milliliter and relative P448/P450 activity by methods described in LBI Technical Data on Rat Liver S9 Product.

2. MATERIALS (Continued)

C. Positive Control Chemicals

The chemicals used for positive controls in the nonactivation and activation assays are given in Table 1 of Section V. Results.

D. Solvent

Either deionized water or dimethylsulfoxide (DMSO) was used to prepare stock solutions of solid materials. All dilutions of test materials were made in either deionized water or DMSO. The solvent employed and its concentration are recorded in Table 1 of Section V. Results.

3. EXPERIMENTAL DESIGN

A. Plate Test (Agar Incorporation)*

Approximately 10^8 cells from an overnight culture of each indicator strain were added to separate test tubes containing 2.0 ml molten agar supplemented with biotin and a trace of histidine. For nonactivation tests, at least 4 dose levels of the test compound were added to the contents of the appropriate tubes and poured over the surfaces of selective agar plates. In activation tests, at least 4 dose levels of the test chemical were added to the appropriate tubes with cells. Just prior to pouring, an aliquot of reaction mixture (0.5 ml containing the 9,000 x g liver homogenate) was added to each of the activation overlay tubes, which were then mixed, and the contents poured over the surface of a minimal agar plate and allowed to solidify. The plates were incubated for 48 hr at 37°C and scored for the number of colonies growing on each plate. D4 yeast plates were incubated at 30°C (nonactivation) and 37°C (activation) for 3-5 days and then scored. The concentrations of all chemicals are given in Table 1 of Section V. Results. Positive and solvent controls using both directly active positive chemicals and those that require metabolic activation were run with each assay.

---

* Certain classes of chemicals known to be mutagens and carcinogens do not produce detectable responses using the standard Ames agar incorporation method. Some dialkyl nitrosamines and certain substituted hydrazines are mutagenic in suspension assays, but not in the plate assay. Chemicals of these classes should be screened in a suspension assay.

3. EXPERIMENTAL DESIGN (Continued)

B. Recording and Presenting Data

The numbers of colonies on each plate were counted and recorded on printed forms. These raw data were analyzed in a computer program and reported on a printout. The results are presented as revertants (or convertants for D4) per plate for each indicator strain employed in the assay. The positive and solvent controls are provided as reference points. Other relevant data are provided on the computer printout.

4. EVALUATION CRITERIA

Plate test data consist of direct revertant colony counts obtained from a set of selective agar plates seeded with populations of mutant cells suspended in a semisolid overlay. Because the test chemical and the cells are incubated in the overlay for 2 days, and a few cell divisions occur during the incubation period, the test is semiquantitative in nature. Although these features of the assay reduce the quantitation of results, they provide certain advantages not contained in a quantitative suspension test:

- The small number of cell divisions permits potential mutagens to act on replicating DNA, which is often more sensitive than nonreplicating DNA.
- The combined incubation of the compound and the cells in the overlay permits constant exposure of the indicator cells for 2 days.

A. Surviving Populations

Plate test procedures do not permit exact quantitation of the number of cells surviving chemical treatment. At low concentrations of the test chemical, the surviving population on the treatment plates is essentially the same as that on the negative control plate. At high concentrations, the surviving population is usually reduced by some fraction. Our protocol normally employs several doses ranging over 2 or 3 log concentrations, the highest of these doses being selected to show slight toxicity as determined by subjective criteria.

B. Dose-Response Phenomena

The demonstration of dose-related increases in mutant counts is an important criterion in establishing mutagenicity. A factor that might modify dose-response results for a mutagen would be the

4. EVALUATION CRITERIA (Continued)

B. Dose-Response Phenomena

selection of doses that are too low (usually mutagenicity and toxicity are related). If the highest dose is far lower than a toxic concentration, no increases may be observed over the dose range selected. Conversely, if the lowest dose employed is highly cytotoxic, the test chemical may kill any mutants that are induced, and the compound will not appear to be mutagenic.

C. Control Tests

Positive and negative control assays are conducted with each experiment and consist of direct-acting mutagens for nonactivation assays and mutagens that require metabolic biotransformation in activation assays. Negative controls consist of the test compound solvent in the overlay agar together with the other essential components. The negative control plate for each strain gives a reference point to which the test data are compared. The positive control assay is conducted to demonstrate that the test systems are functional with known mutagens.

D. Evaluation Criteria for Ames Assay

Because the procedures used to evaluate the mutagenicity of the test chemical are semiquantitative, the criteria used to determine positive effects are inherently subjective and are based primarily on a historical data base. Most data sets are evaluated using the following criteria:

1. Strains TA-1535, TA-1537, and TA-1538

   If the solvent control value is within the normal range, a chemical that produces a positive dose response over three concentrations with the lowest increase equal to twice the solvent control value is considered to be mutagenic.

2. Strains TA-98, TA-100, and D4

   If the solvent control value is within the normal range, a chemical that produces a positive dose response over three concentrations with the highest increase equal to twice the solvent control value for TA-100 and 2-3 times the solvent control value for strains TA-98 and D4 is considered to be mutagenic. For these strains, the dose-response increase should start at approximately the solvent control value.

4. EVALUATION CRITERIA (Continued)

D. Evaluation Criteria for Ames Assay

3. Pattern

Because TA-1535 and TA-100 are both derived from the same parental strain (G-46) and because TA-1538 and TA-98 are both derived from the same parental strain (D3052), there is a built-in redundancy in the microbial assay. In general the two strains of a set respond to the same mutagen and such a pattern is sought. It is also anticipated that if a given strain, e.g., TA-1537, responds to a mutagen in nonactivation tests, it will generally do so in activation tests (The converse of this relationship is not expected.). While similar response patterns are not required for all mutagens, they can be used to enhance the reliability of an evaluation decision.

4. Reproducibility

If a chemical produces a response in a single test that cannot be reproduced in one or more additional runs, the initial positive test data lose significance.

The preceding criteria are not absolute, and other extenuating factors may enter into a final evaluation decision. However, these criteria are applied to the majority of situations and are presented to aid those individuals not familiar with this procedure. As the data base is increased, the criteria for evaluation can be more firmly established.

E. Relationship between Mutagenicity and Carcinogenicity

It must be emphasized that the Ames Salmonella/Microsome Plate Test is not a definitive test for chemical carcinogens. It is recognized, however, that correlative and functional relationships have been demonstrated between these two endpoints. The results of comparative tests on 300 chemicals by McCann et al. (1975) show an extremely good correlation between results of microbial mutagenesis tests and in vivo rodent carcinogenesis assays.

All evaluations and interpretation of the data presented in this report are based only on the demonstration, or lack, of mutagenic activity.

REFERENCES

Ames, B.N., McCann, J. and Yamasaki, E. (1975). Methods for detecting carcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test. Mutation Res. 31, 347-364.

McCann, J., Choi, E., Yamasaki, E. and Ames, B.N. (1975). Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. Proc. Nat. Acad. Sci. 72, 5135-5139.

5. STANDARD OPERATING PROCEDURE

All data will be entered in ink (no pencil).

All changes or corrections in entries will be made with a single line through the change, and an explanation for the change must be written.

All calculations (weights, dilutions, dose calculations, etc.) will be shown on data records.

All data entries will be dated and initialed.

All laboratory operations will be written out in standard protocol manuals. These manuals will be present in each laboratory area.

Deviations from any established protocol will be described and justified.

Data will be stored in bound form (notebooks or binders). These bound data books will be reviewed by the appropriate Section Heads.

Chemicals submitted for testing will have date of receipt and initials of entering person.

Lot numbers for all reference mutagens, solvent, or other materials used in assays will be recorded.

Animal orders, receipts, and identification will be recorded and maintained such that each animal can be traced to the supplier and shipment. All animals on study will be properly identified.

A copy of the final report plus all raw data and support documents will be permanently stored in the archival system of Litton Bionetics, Inc.

Current curricula vitae and job descriptions will be maintained on all personnel involved in the study.

Salmonella strains will be routinely checked for the his, uvrB, rfa, and pKM 101 phenotypes. Only appropriately screened stock cultures will be used in chemical evaluations.

CORNING Hazleton

MUTAGENICITY TEST ON

T-6564

IN AN *IN VIVO* MOUSE MICRONUCLEUS ASSAY

FINAL REPORT

AUTHOR

Hemalatha Murli, Ph.D.

PERFORMING LABORATORY

Corning Hazleton Inc. (CHV)
9200 Leesburg Pike
Vienna, Virginia 22182

LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17750-0-455

SUBMITTED TO

3M Corporation
Building 220-2E-02, 3M Center
St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

November 1, 1996

000176

QUALITY ASSURANCE STATEMENT

Project Title: *In Vivo* Mouse Micronucleus Assay

Project No.: 20996 Assay No.: 17750

Protocol No.: 455 Edition No.: 17, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Dosing/07/30/1996	07/30/1996	C. Orantes
Harvest/08/1/1996	08/1/1996	C. Smith
Draft Report Review/09/17,18/1996	09/18/1996	C. Orantes/C. Smith
Final Report Review/11/01/1996	11/01/1996	C. Smith

Quality Assurance Unit 11/1/96 Date Released

000177

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Food and Drug Administration (FDA) Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

Hemalatha Murli

Hemalatha Murli, Ph.D.
Mammalian Cytogenetics
Department of Genetic and Cellular Toxicology

11/1/96
Study Completion Date

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SUMMARY

Mutagenicity Test on T-6564 in an *In Vivo* Mouse Micronucleus Assay

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-6564, to induce micronuclei in bone marrow polychromatic erythrocytes of Crl:CD-1®(ICR) BR mice.

In the dose selection study, the test article was solubilized in deionized water and dosed by oral gavage at 1000, 1510, 2010, 2540 and 3010 mg/kg in a first trial and then dosed at 1010, 1520, 2020, and 2530 mg/kg in a second trial. Six animals (three males and three females) were assigned to each dose group. Animals were observed for four days after dosing for toxic signs and/or mortality.

Based on the results of the dose selection study, the maximum tolerated dose was estimated as about 2000 mg/kg. In the micronucleus assay, the test article was solubilized in deionized water and dosed by oral gavage at 498, 995, and 1990 mg/kg. Ten animals (five males and five females) were randomly assigned to each dose/harvest time group. Vehicle and positive control groups, euthanized approximately 24 hours after dosing, were included in the assay. The animals dosed with the test article were euthanized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow.

The test material, T-6564, did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes under the conditions of this assay and is considered negative in the mouse bone marrow micronucleus test.

Mutagenicity Test on T-6564 in an *In Vivo* Mouse Micronucleus Assay

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (Test Article)

2.1 Client's Identification: T-6564 L-13167 FC1015-X

2.2 Date Received: May 30, 1996

2.3 Physical Description: Clear colorless liquid

2.4 Genetics Assay No.: 17750

3.0 TYPE OF ASSAY: *In Vivo* Mouse Micronucleus Assay

4.0 PROTOCOL NO.: 455, Edition 17, Modified for 3M Corporation

5.0 STUDY DATES

5.1 Initiation Date: June 4, 1996

5.2 Experimental Start Date: July 11, 1996

5.3 Experimental Termination Date: August 22, 1996

6.0 SUPERVISORY PERSONNEL

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Monica Vegarra, B.S.

7.0 OBJECTIVE

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-6564, to induce micronuclei in bone marrow polychromatic erythrocytes of Crl:CD-1®(ICR) BR mice. This study was conducted using modifications of the procedures suggested by Heddle et al. (1983).

8.0 MATERIALS

Adult male and female mice, strain Crl:CD-1®(ICR) BR, were purchased from Charles River Laboratories, Portage, MI. This healthy, random bred strain was selected to maximize genetic heterogeneity and at the same time assure access to a common source. The protocol for this study was approved by the CHV-IACUC prior to the initiation of dosing.

Animals were housed five per cage during quarantine, and housed five per cage at randomization. The temperature and relative humidity were maintained at 72 ± 6 °F and 55 ± 15%, respectively, except on July 31, 1996, for the definitive study, when the humidity was recorded as 75.1%. A 12-hour light/12-hour dark cycle was maintained. A commercial diet (Purina® Certified Laboratory Pellets ® # 5002) and water were available ad libitum for the duration of the study. The feed was analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, organophosphates, and specified nutrients. The water was analyzed on a retrospective basis for specified microorganisms, pesticides, alkalinity, heavy metals, and halogens. Sanitized caging was used for housing the animals. Personnel handling animals or working within the animal facilities were required to wear suitable protective garments and equipment.

Animals were quarantined for seven days before being placed on study. Animals were randomly assigned to study groups and were individually weighed prior to dosing. All animals were dosed based upon the individual body weights. Animals were uniquely identified by ear tag. Dose or treatment groups were identified by cage card/label.

At the termination of the study all surviving animals were euthanized by CO_2/O_2 inhalation, followed by CO_2 inhalation and penetration of the thorax. Any extra animals not used for the study were saved for training.

9.0 SOLUBILITY AND STABILITY

The test article, T-6564, was supplied as a clear colorless liquid. The specific gravity of the test article was calculated in the testing laboratory as 1.22 g/ml. This specific gravity was used to prepare dosing stocks for the assay. Deionized water was used as the vehicle in this assay. The determination of the test article stability under the dosing conditions of this assay and the test article characteristics as defined in the GLP regulations of FDA (21 CFR 58.105), EPA-TSCA (40 CFR 792.105), and EPA-FIFRA (40 CFR 160.105) is the responsibility of the sponsor.

10.0 DOSE SELECTION STUDY I

10.1 Dose Selection

Dose levels of 1000, 1510, 2010, 2540 and 3010 mg/kg were administered by oral gavage for the first dose selection study.

10.2 Dosing Information

The animals used in the first dose selection assay were dosed on July 11, 1996. The weight range of the animals used in the dose range finding assay was 30.9-35.1 and 22.2-27.6 grams, for the males and females, respectively. Dosing solutions were prepared just prior to dosing and were prepared by making a 301 mg/ml stock for the high dose (3010 mg/kg). This was prepared by adding deionized water (CHV, Lot # 19) up to a volume of 15.0 ml to 3.7 ml of T-6564, resulting in a clear colorless solution. Dilutions of this stock were prepared for the 2540, 2010, 1510 and 1000 mg/kg dose levels.

Dosing was achieved using a 10 ml/kg dosing volume. All animals were eight weeks and three days old at the time of dosing. An outline of the dosing scheme is found in the following table.

Dosing Scheme for Dose Selection Assay I

Treatment	Male	Female
T-6564		
1000 mg/kg	3	3
1510 mg/kg	3	3
2010 mg/kg	3	3
2540 mg/kg	3	3
3010 mg/kg	3	3

A total of 30 animals was used in this assay. All doses given were on an acute (one-time only) basis.

10.3 Results and Interpretation

All animals were examined after dosing and daily throughout the duration of the study (four days) for toxic effects and/or mortalities. The animal observations for this assay are summarized in the following table:

Animal Observations for Toxicity for Dose Rangefinding Assay I

Time After Dosing (hours)	Dose Level (mg/kg)	Observations
≈0.2	all	Normal
≈16.8	1000	Normal
	1510	Male # 9761 and Female #s 9776 & 9788 found dead. Remaining males appeared hunched and hypoactive. Remaining female appeared normal.
	2010, 2540, 3010	Normal
≈40.2	1000, 1510, 2010, 2540	Normal
	3010	Male #s 9765 & 9767 found dead. Remaining male and all females appear normal.
≈67.0	1000	Normal
	1510	Male # 9766 found dead. Remaining male and female appeared normal.
	2010, 2540, 3010	Normal
≈88.5	1000	Normal
	1510	Remaining male # 9774 found dead. Remaining female appeared normal.
	2010, 2540	Normal
	3010	Remaining male # 9764 appeared hypoactive and hunched with a rough hair coat. All females appeared normal.

The mortality data for this assay are summarized in the following table:

Summary of Mortalities for Dose Rangefinding I

Treatment	Male	Female
T-6564		
1000 mg/kg	0/3	0/3
1510 mg/kg	3/3	2/3
2010 mg/kg	0/3	0/3
2540 mg/kg	0/3	0/3
3010 mg/kg	2/3	0/3

10.4 Conclusion

Based on these results, the maximum tolerated dose could not be determined.

11.0 DOSE SELECTION STUDY II

11.1 Dose Selection

Dose levels of 1010, 1520, 2020 and 2530 mg/kg were administered by oral gavage for the second dose selection study.

11.2 Dosing Information

The animals used in the second dose selection assay were dosed on July 24, 1996. The weight range of the animals used in the second dose range finding assay was 30.1-35.8 and 23.6-28.4 grams, for the males and females, respectively. Dosing solutions were prepared just prior to dosing and were prepared by making a 253 mg/ml stock for the high dose (2530 mg/kg). This was prepared by adding deionized water (CHV, Lot # 20) up to a volume of 14.0 ml to 2.9 ml of T-6564, resulting in a clear colorless solution. Dilutions of this stock were prepared for the 2020, 1520 and 1010 mg/kg dose levels.

Dosing was achieved using a 10 ml/kg dosing volume. All animals were eight weeks and two days old at the time of dosing. An outline of the dosing scheme is found in the following table:

Dosing Scheme for Dose Selection Assay II

Treatment	Male	Female
T-6564		
1010 mg/kg	3	3
1520 mg/kg	3	3
2020 mg/kg	3	3
2530 mg/kg	3	3

A total of 24 animals was used in this assay. All doses given were on an acute (one-time only) basis.

11.3 Results and Interpretation

All animals were examined after dosing and daily throughout the duration of the study (three days) for toxic effects and/or mortalities. The animal observations for this assay are summarized in the following table:

Animal Observations for Toxicity for Dose Rangefinding Assay II

Time After Dosing (hours)	Dose Level (mg/kg)	Observations
≈0.1, 1.1 & 15.6	All	Normal
≈17.9	1520	Female # 1417 found dead.
≈21.6	1520	Male # 1405 found dead.
≈39.5	All	Normal
≈66.6	All	Normal
≈90.4	All	Normal

The mortality data for this assay are summarized in the following table:

Summary of Mortalities for Dose Rangefinding II

Treatment	Male	Female
T-6564		
1010 mg/kg	0/3	0/3
1520 mg/kg	1/3	1/3
2020 mg/kg	0/3	0/3
2530 mg/kg	0/3	0/3

11.4 Conclusion

Based on these results, the maximum tolerated dose was estimated as about 2000 mg/kg.

12.0 MICRONUCLEUS STUDY

12.1 Dose Selection

Based on results from the dose selection study, dose levels of 498, 995, and 1990 mg/kg were tested in this study.

12.2 Micronucleus Assay Dosing Information

The animals used in the micronucleus assay were dosed on July 30, 1996. Cyclophosphamide (CP), (CAS # 6055-19-2; Sigma, Lot # 26H0473), the positive control, was solubilized in sterile deionized water (Lot # 19, prepared at CHV) and was administered by oral gavage at 80.0 mg/kg. The vehicle control, deionized water (CHV, Lot # 20), was administered concurrently with the test article at a volume of 10 ml/kg. The weight range of the animals used in the micronucleus assay was 31.0-37.7 and 22.4-28.3 grams for the males and females, respectively. The dosing solutions for the assay were prepared by making a 199 mg/ml stock for the high dose (1990 mg/kg). This was prepared by adding deionized water (CHV, Lot # 20) up to a volume of 30.0 ml to 4.9 ml of T-6564, resulting in a clear colorless solution. Dilutions of this stock were prepared for the 995 and 498 mg/kg dose levels. A second group of animals (designated Secondary Dose Group) was also assigned to the study and was dosed with the high dose of the test article. These animals were only used in the assay as replacements for any which died in the primary dose group.

Ten animals (five males and five females) were randomly assigned to each dose/-harvest time group. Vehicle and positive control groups, euthanized approximately 24 hours after dosing, were included in the assay. The animals dosed with the test article were euthanized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow. An outline of the dosing scheme is found in the following table:

Dosing Scheme for Micronucleus Assay

Treatment	Number of Animals Assigned: Primary Dose Groups 24 Hr M	24 Hr F	48 Hr M	48 Hr F	72 Hr M	72 Hr F	Secondary Dose Group [a] M	Secondary Dose Group [a] F
T-6564								
498 mg/kg	5	5	5	5	5	5	-	-
995 mg/kg	5	5	5	5	5	5	-	-
1990 mg/kg	5	5	5	5	5	5	10	10
Vehicle Control, deionized water, 10 ml/kg	5	5	-	-	-	-	-	-
Positive Control, Cyclophosphamide, 80.0 mg/kg	5	5	-	-	-	-	-	-

[a] The animals assigned to the secondary dose groups were dosed and were only used to replace animals which died in the primary dose group at the high dose level. All extra animals not used as replacements were euthanized at the completion of the trial.

A total of 130 animals was used in this assay. The age of the animals at the time of dosing was eight weeks and one day.

Volumes dosed were 10 ml/kg and were based upon individual animal weights.

13.0 BONE MARROW HARVEST, SLIDE PREPARATION AND ANALYSIS

At the appropriate harvest time, the animals were euthanized by CO_2/O_2 inhalation, followed by CO_2 inhalation and penetration of the thorax. The adhering soft tissue and epiphyses of both femora were removed. The marrow was flushed from the bone and transferred to centrifuge tubes containing 3 - 5 ml bovine serum (one tube for each animal). Following centrifugation to pellet the tissue, the supernatant was removed by aspiration and portions of the pellet were spread on slides and air dried. The slides were fixed in methanol, and stained in May-Grunwald solution followed by Giemsa (Schmid, 1975). The air-dried slides were coverslipped.

C00189

The slides were coded for analysis, and scored for micronuclei and the polychromatic erythrocyte (PCE) to normochromatic erythrocyte (NCE) cell ratio. Standard forms were used to record these data. One thousand PCEs per animal were scored. The frequency of micronucleated cells was expressed as percent micronucleated cells based on the total PCEs present in the scored optic field. The normal frequency of micronuclei in this Crl:CD-1®(ICR) BR strain is about 0.0 - 0.4%.

The frequency of PCEs versus NCEs was determined by scoring the number of PCEs and NCEs observed in the optic fields while scoring the first 1000 erythrocytes.

14.0 EVALUATION CRITERIA

14.1 General

The criteria for the identification of micronuclei were those of Schmid (1976). Micronuclei were darkly stained and generally round, although almond and ringshaped micronuclei occasionally occurred. Micronuclei had sharp borders and were generally between 1/20 and 1/5 the size of the PCE. The unit of scoring was the micronucleated cell, not the micronucleus; thus the occasional cell with more than one micronucleus was counted as one micronucleated PCE, not two (or more) micronuclei. The staining procedure permitted the differentiation by color of PCEs and NCEs (bluish-grey and red, respectively).

14.2 Data Presentation and Interpretation

Data are summarized by sex and dose groups for the different time points. Individual animal data are also presented. The analysis of these data was performed using an analysis of variance (Winer, 1971) on either untransformed (when variances are homogeneous) and rank transformed (when variances are heterogeneous) proportions of cells with micronuclei per animal. If the analysis of variance was significant ($p<0.05$), a Dunnett's t-test (Dunnett, 1955; 1964) was used to determine which dose groups, if any, were significantly different from the negative control. Analyses were performed separately for each harvest time and sex combination. The criteria for determining a positive response involved a statistically significant dose-related increase in micronucleated PCEs, or the detection of a reproducible and statistically significant positive response for at least one dose level. A test article that induced neither a statistically significant dose response nor a statistically significant and reproducible increase at one dose level was considered negative. In either case, the final decision was based on scientific judgment.

15.0 RESULTS AND INTERPRETATION

All animals were observed immediately after dosing and periodically throughout the duration of the assay for toxic symptoms and/or mortalities. All animals in the vehicle and positive control groups appeared normal after dosing and remained healthy until the appropriate harvest times. All test article dosed groups appeared normal immediately after dosing. Approximately 22 hours after dosing, one male (#1605) from the secondary dose group was found dead. All other animals appeared normal at this time and remained healthy until the appropriate harvest times.

The test article, T-6564, induced no significant increases in micronucleated polychromatic erythrocytes over the levels observed in the vehicle controls in either sex or at any of the harvest times. The positive control, Cyclophosphamide, induced significant increases in micronucleated PCEs in both sexes as compared to the vehicle controls, with means and standard errors of 3.86% ± 0.55% and 3.58% ± 0.79% for the males and females, respectively. The data summarized by dose group are presented in Table 1 and individual animal data are found in Tables 2 through 7. Historical control data are presented in Table 8.

16.0 CONCLUSION

The test material, T-6564, did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes under the conditions of this assay and is considered negative in the mouse micronucleus assay.

17.0 REFERENCES

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18.0 DEVIATIONS FROM THE SIGNED PROTOCOL

1. In both trials of the dose rangefinding studies, animals were observed for four days and not three days after dosing. This had no impact on study integrity.

2. Due to a technical oversight, more than 1000 erythrocytes were analyzed for animal #'s 1576 and 1628. This had no impact on the integrity of the study.

3. On July 31, 1996, for the definitive study, the humidity was recorded as 75.1%. This had no impact on the integrity of the study.

19.0 EXPERIMENT DATA TABLES

TABLE 1

MICRONUCLEUS DATA SUMMARY TABLE

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY: 17750

TREATMENT	DOSE	HARVEST TIME (HR)	% MICRONUCLEATED PCEs MEAN OF 1000 PER ANIMAL ± S.E. MALES	FEMALES	TOTAL	RATIO PCE:NCE MEAN ± S.E. MALES	FEMALES
CONTROLS							
VEHICLE	Water	24 hr	0.08 ± 0.06	0.08 ± 0.04	0.08 ± 0.03	0.53 ± 0.08	0.73 ± 0.07
POSITIVE	CP 80.0 mg/kg	24 hr	3.86 ± 0.55*	3.58 ± 0.79*	3.72 ± 0.46*	0.61 ± 0.05	0.96 ± 0.17
TEST ARTICLE	498 mg/kg	24 hr	0.20 ± 0.06	0.06 ± 0.06	0.13 ± 0.05	0.71 ± 0.08	0.92 ± 0.05
		48 hr	0.02 ± 0.02	0.08 ± 0.04	0.05 ± 0.02	0.59 ± 0.05	0.53 ± 0.04
		72 hr	0.08 ± 0.06	0.12 ± 0.07	0.10 ± 0.04	0.52 ± 0.08	1.12 ± 0.43
	995 mg/kg	24 hr	0.12 ± 0.06	0.18 ± 0.16	0.15 ± 0.08	0.69 ± 0.12	1.03 ± 0.13
		48 hr	0.12 ± 0.04	0.06 ± 0.04	0.09 ± 0.03	0.63 ± 0.03	0.54 ± 0.06
		72 hr	0.10 ± 0.08	0.10 ± 0.06	0.10 ± 0.05	0.45 ± 0.08	0.85 ± 0.21
	1990 mg/kg	24 hr	0.30 ± 0.13	0.08 ± 0.06	0.19 ± 0.08	0.69 ± 0.07	0.75 ± 0.07
		48 hr	0.00 ± 0.00	0.04 ± 0.02	0.02 ± 0.01	0.60 ± 0.06	0.56 ± 0.07
		72 hr	0.08 ± 0.06	0.12 ± 0.04	0.10 ± 0.03	0.49 ± 0.11	0.78 ± 0.21

* Significantly greater than the corresponding vehicle control, $p<0.05$.
CP = Cyclophosphamide
PCE = Polychromatic erythrocyte
NCE = Normochromatic erythrocyte

TABLE 2

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
24 HOUR HARVEST	MALE			
VEHICLE CONTROL	Water	1557	1	0.52
		1574	0	0.79*
		1576	0	0.62
		1585	3	0.39
		1614	0	0.35
POSITIVE CONTROL	CP 80.0 mg/kg	1564	46	0.62
		1566	32	0.49
		1569	25	0.77
		1607	56	0.64
		1612	34	0.53
TEST ARTICLE	498 mg/kg	1562	3	0.73
		1570	1	0.73
		1581	3	0.97
		1586	3	0.61
		1587	0	0.48
	995 mg/kg	1568	1	0.69
		1571	0	0.64
		1591	3	1.04
		1598	2	0.80
		1602	0	0.29
	1990 mg/kg	1558	2	0.72
		1567	0	0.61
		1580	8	0.96
		1594	3	0.55
		1611	2	0.63

CP = Cyclophosphamide
PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte
* 1059 erythrocytes scored

TABLE 3

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
24 HOUR HARVEST	FEMALE			
VEHICLE CONTROL	Water	1669	1	0.65
		1671	2	0.81
		1678	0	0.82
		1679	1	0.88
		1683	0	0.50
POSITIVE CONTROL	CP 80.0 mg/kg	1641	51	0.72
		1653	33	1.06
		1663	56	0.57
		1664	25	0.89
		1667	14	1.56
TEST ARTICLE	498 mg/kg	1627	0	0.97
		1630	0	1.00
		1635	0	0.74
		1644	3	0.90
		1652	0	1.01
	995 mg/kg	1633	0	0.78
		1637	0	0.77
		1660	0	0.96
		1666	8	1.26
		1672	1	1.39
	1990 mg/kg	1643	0	0.89
		1650	0	0.67
		1668	1	0.88
		1681	3	0.53
		1682	0	0.78

CP = Cyclophosphamide
PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

TABLE 4

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
48 HOUR HARVEST	**MALE**			
TEST ARTICLE	498 mg/kg	1563	0	0.60
		1582	0	0.75
		1593	1	0.43
		1603	0	0.54
		1618	0	0.62
	995 mg/kg	1572	1	0.67
		1589	1	0.66
		1596	2	0.52
		1604	2	0.66
		1615	0	0.62
	1990 mg/kg	1577	0	0.75
		1579	0	0.68
		1583	0	0.60
		1595	0	0.41
		1606	0	0.53

PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

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TABLE 5

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
48 HOUR HARVEST	FEMALE			
TEST ARTICLE	498 mg/kg	1628	2	0.58*
		1636	1	0.66
		1638	0	0.39
		1654	1	0.48
		1662	0	0.54
	995 mg/kg	1621	1	0.36
		1649	0	0.44
		1651	0	0.57
		1657	0	0.71
		1665	2	0.59
	1990 mg/kg	1626	0	0.40
		1632	1	0.64
		1634	0	0.48
		1639	1	0.77
		1677	0	0.51

PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte
* 1005 erythrocytes scored

TABLE 6

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
72 HOUR HARVEST	**MALE**			
TEST ARTICLE	498 mg/kg	1561	0	0.65
		1565	0	0.74
		1599	0	0.44
		1600	3	0.34
		1609	1	0.42
	995 mg/kg	1555	1	0.48
		1556	0	0.17
		1559	0	0.58
		1590	4	0.45
		1597	0	0.57
	1990 mg/kg	1554	3	0.21
		1560	1	0.78
		1573	0	0.63
		1613	0	0.24
		1617	0	0.58

PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

TABLE 7

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation

TEST ARTICLE: T-6564

ASSAY NO.: 17750

TREATMENT		ANIMAL NUMBER	# MN PCEs/ 1000 PCEs	RATIO PCE:NCE
72 HOUR HARVEST	**FEMALE**			
TEST ARTICLE	498 mg/kg	1619	0	0.60
		1620	1	0.73
		1624	0	0.45
		1656	4	2.82
		1680	1	0.99
	995 mg/kg	1645	2	1.60
		1648	3	0.79
		1658	0	0.66
		1674	0	0.33
		1675	0	0.88
	1990 mg/kg	1622	1	0.67
		1625	2	0.73
		1629	0	0.34
		1640	2	1.58
		1642	1	0.56

PCE = Polychromatic erythrocyte
# MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

TABLE 8

MOUSE MICRONUCLEUS HISTORICAL CONTROL DATA 7/95 THROUGH 12/95

		% MICRONUCLEATED PCEs PER 1000 PCE MEAN OF 1000 PER ANIMAL ± S.E.			RATIO PCE:NCE MEAN ± S.E.	
		MALES	FEMALES	TOTAL	MALES	FEMALES
POOLED VEHICLE CONTROLS						
	MIN	0.00	0.00	0.01	0.31	0.24
	MAX	0.22	0.24	0.17	0.85	1.03
	AVG	0.087 ± 0.007	0.081 ± 0.008	0.084 ± 0.005	0.550 ± 0.021	0.587 ± 0.025
	N	47	47	47	47	47
POSITIVE CONTROLS Cyclophosphamide, 80.0 mg/kg						
	MIN	2.00	1.50	2.41	0.41	0.40
	MAX	5.68	6.36	5.38	0.72	0.79
	AVG	3.682 ± 0.240	3.170 ± 0.245	3.426 ± 0.184	0.577 ± 0.020	0.588 ± 0.026
	N	19	19	19	19	19

PCE = Polychromatic erythrocyte
NCE = Normochromatic erythrocyte
N = Number of harvests

CORNING Hazleton

MUTAGENICITY TEST ON

T-6564

MEASURING CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY (CHO) CELLS: WITH A CONFIRMATORY ASSAY WITH MULTIPLE HARVESTS

FINAL REPORT

AUTHOR

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PERFORMING LABORATORY

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LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17750-0-437CO

SUBMITTED TO

3M Corporation
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St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

September 16, 1996

000202

QUALITY ASSURANCE STATEMENT

Project Title: Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: With a Confirmatory Assay With Multiple Harvests

Project No.: 20990 Assay No.: 17750

Protocol No.: 437CO Edition No.: 4, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Dosing/06/20/1996	06/21/1996	C. Orantes
Draft Report Review/08/21/1996	08/22/1996	C. Orantes
Final Report Review/09/16/1996	09/16/1996	C. Orantes

Quality Assurance Unit 9/16/96 Date Released

000203

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Food and Drug Administration (FDA) Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

Hemalatha Murli

Hemalatha Murli, Ph.D.
Mammalian Cytogenetics
Department of Genetic and Cellular Toxicology

7/16/96

Study Completion Date

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ABSTRACT

The objective of this in vitro assay was to evaluate the ability of T-6564 to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells with and without metabolic activation.

The specific gravity of the neat test article was evaluated as 1.22 g/ml in the testing laboratory and this was used to calculate the dosing stock preparation. Dilutions of the test article were prepared in sterile deionized water. For the dose rangefinding assays with and without metabolic activation, concentrations of 0.169, 0.508, 1.69, 5.08, 16.9, 50.8, 169, 508, 1690, and 5080 µg/ml were tested. All dosing was achieved using a dosing volume of 1.0% (10 µl/ml). Complete cytotoxicity was observed in the cultures dosed with 5080 µg/ml with and without metabolic activation. A reduction of 92% was observed in the mitotic index of the culture dosed with 1690 µg/ml without metabolic activation as compared with the solvent control culture. Reductions of 44%, 15%, and 38% were observed in the mitotic indices of the cultures dosed with 169, 508, and 1690 µg/ml with metabolic activation, respectively, as compared with the solvent control culture.

Based on the data from the dose rangefinding assay, replicate cultures of CHO cells were incubated with 62.5, 125, 250, 500, 1000, 1500, and 2000 µg/ml without metabolic activation and with 250, 500, 1000, 2000, 3000, and 4000 µg/ml with metabolic activation in 20.0 hour assays. Cultures treated with 125, 250, 500, and 1000 µg/ml from the assay without metabolic activation assay and with 250, 500, 1000, and 2000 µg/ml with metabolic activation were analyzed for chromosomal aberrations. No significant increase in cells with chromosomal aberrations was observed at the concentrations analyzed.

In the confirmatory trial, replicate cultures of CHO cells were incubated with 100, 200, 400, 600, 800, 1000, and 1200 µg/ml and with 50.0, 100, 200, 400, 600, 800, 1000, and 1200 µg/ml without metabolic activation with 20.1 and 44.2 hour harvests, respectively. In the assay with metabolic activation, cultures were incubated with 500, 1000, 1500, 2000, 2250, 2500, 2750, and 3000 µg/ml with 20.1 and 44.2 hour harvests. Cultures treated with 200, 400, 600, and 800 µg/ml from the 20.1 hour nonactivation assay, with 100, 200, 400, and 600 µg/ml from the 44.2 hour nonactivation assay, with 1500, 2000, 2250, and 2500 µg/ml from the 20.1 hour activation assay, and with 2000, 2250, 2500, and 2750 µg/ml from the 44.2 hour activation assay were analyzed for chromosomal aberrations. No significant increase in cells with chromosomal aberrations was observed at the concentrations analyzed except for the highest dose analyzed (2500 µg/ml from the 20.1 hour activation assay and 2750 µg/ml from the 44.2 hour activation assay) from the activation.

T-6564 was considered negative for inducing chromosomal aberrations in CHO cells with and without metabolic activation, except at a single dose level with metabolic activation that induced significant toxicity.

Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells:
With a Confirmatory Assay With Multiple Harvests
With T-6564

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (TEST ARTICLE):

2.1 Client's Identification: T-6564 L-13167 FC-1015-X

2.2 Date Received: May 30, 1996

2.3 Physical Description: Clear, colorless liquid

2.4 Genetics Assay No.: 17750

3.0 TYPE OF ASSAY: Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: With a Confirmatory Assay With Multiple Harvests

4.0 PROTOCOL NO.: 437CO, Edition 4, Modified for 3M Corporation

5.0 STUDY DATES:

5.1 Initiation Date: June 4, 1996

5.2 Experimental Start Date: June 13, 1996

5.3 Experimental Termination Date: July 26, 1996

6.0 SUPERVISORY PERSONNEL:

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Carol S. Spicer, B.S.

7.0 OBJECTIVE:

The objective of this in vitro assay was to evaluate the ability of T-6564 to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells, with and without metabolic activation.

8.0 RATIONALE:

The assay is designed to establish whether the test article or its metabolites can interact with cells to induce chromosome breaks. Chemically induced lesions may result in breaks in chromatin that are either repaired by the cell in such a way as to be undetectable or result in visible damage. Aberrations are a consequence of failure or mistakes in repair processes such that breaks do not rejoin or rejoin in abnormal configurations (Evans, 1962).

9.0 EXPERIMENTAL DESIGN:

Results from the rangefinding assay were used to determine the dose range to be used in the chromosomal aberrations assay. In the rangefinding assay, the cultures were harvested 20.0 hours after initiation of treatment. Mitotic index and visual observation of the cultures were evaluated for evidence of toxicity. A summary of the treatment schedule for the rangefinding assay is given below.

Summary of Dose Rangefinding Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
- S9	0	17.8	18.0	20.0
+ S9	0	3.0	18.0	20.0

In the chromosomal aberrations assays, replicate cultures were used at each dose level, and negative and solvent controls. Single cultures were used for each of two doses of the positive control. The aberrations assays were conducted with a 20.0 hour harvest time in the initial trial and with 20.1 and 44.2 hour harvest times in the confirmatory trials. Chromosomal aberrations were analyzed from the cultures treated at four dose levels and from one of the positive control doses. A summary of the treatment schedule for the chromosomal aberrations assays is given on the following page.

Summary of Chromosomal Aberrations Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
Initial Trial				
- S9	0	17.8	18.0	20.0
+ S9	0	3.0	18.0	20.0
Confirmatory Trial				
- S9	0	17.8	18.1	20.1
+ S9	0	3.0	18.1	20.1
- S9	0	41.8	42.2	44.2
+ S9	0	3.0	42.2	44.2

10.0 MATERIALS AND METHODS:

10.1 Test Cells:

The Chinese hamster ovary cells (CHO-WBL) used in this assay were from a permanent cell line and were originally obtained from the laboratory of Dr. S. Wolff, University of California, San Francisco. The cells have since been recloned to maintain karyotypic stability. This cell line has an average cycle time of 12 to 14 hours with a modal chromosome number of 21.

10.2 Cell Culture Medium:

The CHO cells were grown in McCoy's 5a culture medium which was supplemented with 10 % fetal bovine serum (FBS), 1% L-glutamine, and 1% penicillin and streptomycin, at approximately 37°C, in an atmosphere of about 5% CO_2 in air.

10.3 Negative and Solvent Controls:

In the nonactivation assays, negative controls were cultures which contain only cells and culture medium. Solvent controls were cultures containing the solvent

for the test article, sterile deionized water, at the highest concentration used in test cultures, 10.0 µl/ml. In the activation assays, the negative and solvent controls were the same as described in the nonactivation assays but with the S9 activation mix included.

10.4 Positive Control Agents:

The positive control agents which were used in the assays were mitomycin C (MMC) for the nonactivation series and cyclophosphamide (CP) in the metabolic activation series. Mitomycin C (CAS# 50-07-7, Sigma, Lot # 25H0619) is a clastogen that does not require metabolic activation. Cyclophosphamide (CAS # 6055-19-2, Sigma, Lot # 67F0155) does not act directly but must be converted to active intermediates by microsomal enzymes. In the chromosomal aberrations assays, two concentrations of MMC (0.08 and 0.1 µg/ml) and CP (5.0 and 10.0 µg/ml) were used to induce chromosomal aberrations in the CHO cells. One of the dose levels was analyzed in each of the aberration assays. Both MMC and CP were dissolved in water.

10.5 Rangefinding Assays:

In these assays, the cells were cultured for approximately 24 hours prior to treatment by seeding approximately 0.3×10^6 cells per 25 cm^2 flask into 5 ml of complete McCoy's 5a culture medium.

10.5.1 Assay Without Metabolic Activation:

The cultures were incubated with the test article for 17.8 hours at ≈37°C. Then, the test article was washed from the cells with phosphate buffered saline and fresh complete medium containing Colcemid® (final concentration 0.1 µg/ml) was added. The cultures were then trypsinized and harvested 2.0 hours later. (See Sections on Harvest and Slide Preparation and Staining).

10.5.2 Assay With Metabolic Activation:

In this assay, the CHO cells were exposed to the test article for three hours at ≈37°C in the presence of a rat liver S9 reaction mixture (S9 15 µl/ml, NADP 1.5 mg/ml, and isocitric acid 2.7 mg/ml). The S9 fraction (Molecular Toxicology, Inc., Lot #0583 used for dose rangefinding assay and initial trial of chromosomal aberrations assay; Lot # 0667, used for the

confirmatory trial of chromosomal aberrations assay) was derived from the liver of male Sprague-Dawley rats which had been previously treated with Aroclor 1254 to induce the mixed function oxidase enzymes which are capable of metabolizing chemicals to more active forms. The three hour incubation time was used because prolonged exposure to the S9 mixture might be toxic to the cells and the enzyme activity of S9 is lost rapidly at about 37°C. The medium did not have FBS during the exposure period to avoid possible inactivation of short lived and highly reactive intermediates produced by the S9 enzymes by binding to serum proteins.

After the exposure period the cells were washed twice with buffered saline. Complete McCoy's 5a medium was added to the cultures which were then incubated for 17.8 hours with Colcemid® (final concentration 0.1 µg/ml) added for the last 2.0 hours to collect metaphase cells. The cultures were then trypsinized, harvested, fixed, and slides were prepared and stained as was described for the nonactivation rangefinding assay.

10.5.3 Assay Evaluation:

Mitotic index was analyzed from the highest four (nonactivation assay) and three (activation assay) surviving dose levels by analyzing the number of metaphases present in 1000 consecutive cells.

10.6 Aberrations Assay Without Metabolic Activation:

Cultures were initiated by seeding approximately 1.2 x 10^6 cells (≈20 hour assay) and 0.8 X 10^6 cells (44.2 hour assay) per 75 cm^2 flask into 10 ml of complete McCoy's 5a medium. One day after culture initiation, the cells were incubated at ≈37°C with the test article at predetermined doses for 17.8 or 41.8 hours. The cultures were then washed with buffered saline and complete McCoy's 5a medium containing 0.1 µg/ml Colcemid® was placed back onto the cells. Two hours later, the cells were harvested and air dried slides were made. The slides were then stained in 5 % Giemsa solution for the analysis of chromosomal aberrations.

10.7 Aberrations Assay With Metabolic Activation:

Cultures were initiated by seeding approximately 1.2 x 10^6 cells (≈20 hour assay) and 0.8 X 10^6 cells (44.2 hour assay) per 75 cm^2 flask into 10 ml of complete McCoy's 5a medium. One day after culture initiation, the cultures that were

treated under the conditions of metabolic activation were incubated at ≈37°C for three hours in the presence of the test article and the S9 reaction mixture in McCoy's 5a medium without FBS. After the three hour exposure period the cells were washed twice with buffered saline and the cells were refed with complete McCoy's 5a medium. The cells were incubated for the rest of the culture period up to the time of harvest with 0.1 µg/ml Colcemid® present during the last 2.0 hours of incubation. The metaphase cells were then harvested and prepared for cytogenetic analysis.

10.8 Harvest Procedure:

Prior to the harvest of the cultures, visual observations of toxicity were made. These observations included an assessment of the percent confluence of the cell monolayer within the culture flasks. The cultures were also evaluated for the presence of mitotic (large rounded cells) or dead cells floating in the medium. The cultures from the dose rangefinding assay were trypsinized first to collect mitotic and interphase cells and were treated with 0.075 M KCl hypotonic solution. This treatment helps to swell the cells and thus disperse the chromosomes. The cultures were then fixed with an absolute methanol: glacial acetic acid (3:1, v:v) fixative and were washed several times before air-dried slides were prepared.

10.9 Slide Preparation and Staining:

Slides were prepared by dropping the harvested cultures on clean slides. The slides were stained with 5% Giemsa solution for the analysis of mitotic index and chromosomal aberrations. All slides were then air-dried and cover slipped using Depex® mounting medium.

10.10 Aberrations Analysis and Assay Evaluation:

Cells were selected for good morphology and only cells with the number of centromeres equal to the modal number 21 ± 1 (range 20-22) were analyzed.

One hundred cells, if possible, from each replicate culture at four dose levels of the test article and from the negative and solvent control cultures were analyzed for the different types of chromosomal aberrations (Evans, 1962; See Section 16.0). At least 25 cells were analyzed for chromosomal aberrations from one of the positive control cultures and from those cultures that had greater than 50% of cells with one or more aberrations. For control of bias, all slides except for the positive controls were coded prior to analysis. Cells with aberrations were

recorded on the data sheets by the microscope stage location. Mitotic index was assessed by analyzing the number of mitotic cells in 1000 cells and the ratio was expressed as a percentage of mitotic cells.

The following factors were taken into account in the evaluation of the chromosomal aberrations data:

1. The percentage of cells with any aberrations.
2. The percentage of cells with more than one aberration.
3. Any evidence for increasing amounts of damage with increasing dose, i.e., a positive dose response.

Chromatid and isochromatid gaps, if observed, were noted in the raw data and were tabulated. They were not, however, considered in the evaluation of the ability of the test article to induce chromosomal aberrations since they may not represent true chromosomal breaks and may possibly be induced by toxicity. Percent polyploidy was analyzed from the 44.2 hour assay and results were tabulated. Historical control data are presented in Table 8.

A cell classified as "GT" is considered to contain 10 aberrations for statistical purposes but a ">" is also included in the tables for this classification to indicate that it is a minimum number.

Statistical analysis employed the Fisher's Exact Test (Sokal and Rohlf, 1981) to compare the percentage of cells with aberrations in each treatment group with the results from the solvent controls. A linear trend test of increasing number of cells with aberrations with increasing dose (Armitage, 1971) was also performed. Test article significance was established where $p<0.01$. All factors as stated previously were taken into account and the final evaluation of the test article was based upon scientific judgement.

11.0 RESULTS:

11.1 Solubility and Dose Determination

The test article was soluble in water. A clear, colorless solution was obtained at a concentration of 500 mg/ml in water. This solution was dosed in the absence of cells using a 1.0% (10 µl/ml) dosing volume in McCoy's 5a culture medium. At a dosed concentration of 5000 µg/ml, a clear solution was obtained and a pH of 8.0 (the same pH as that of McCoy's 5a culture medium) was determined. The

specific gravity of the test article was calculated in the testing laboratory as 1.22 g/ml. This specific gravity was used to prepare dosing stocks for the assay. Sterile deionized water (Batch # 19, prepared at CHV) was used as the vehicle in this assay. All dosing was achieved with a 1.0% (10.0 µl/ml) dosing of the dosing stocks and the solvent control culture was dosed with 10.0 µl/ml of sterile deionized water. Concentrations of 0.169, 0.508, 1.69, 5.08, 16.9, 50.8, 169, 508, 1690, and 5080 µg/ml were tested in the dose rangefinding assays. The stability of the test article under the preparation and dosing conditions used in this assay is the responsibility of the sponsor.

11.2 Rangefinding Assay Without Metabolic Activation

A dead cell monolayer, no visible mitotic cells, floating dead cells and debris, and <5% cell monolayer confluence were observed in the culture dosed with 5080 µg/ml. An unhealthy cell monolayer, a severe reduction in the number of visible mitotic cells, floating dead cells and debris, and ≈45% reduction in the cell monolayer confluence were observed in the culture dosed with 1690 µg/ml. A slightly unhealthy cell monolayer, floating dead cells and debris, and ≈30% reduction in the cell monolayer confluence were observed in the culture dosed with 508 µg/ml. Floating debris and ≈15% reduction in the cell monolayer confluence were observed in the culture dosed with 167 µg/ml. Floating debris was observed in the culture dosed with 50.8 µg/ml. Mitotic indices were analyzed from the cultures dosed with 50.8, 169, 508, and 1690 µg/ml (Table 1). A reduction of 92% was observed in the mitotic index of the culture dosed with 1690 µg/ml as compared with the solvent control culture. Based on these results, the initial aberrations assay without metabolic activation was conducted with a 20.0 hour harvest testing concentrations of 62.5, 125, 250, 500, 1000, 1500, and 2000 µg/ml.

11.3 Rangefinding Assay With Metabolic Activation

No cell monolayer and no visible mitotic cells were observed in the culture dosed with 5080 µg/ml. No other signs of visual toxicity were observed in any of the other cultures. Mitotic indices were analyzed from the cultures dosed with 169, 508, and 1690 µg/ml (Table 1). Reductions of 44%, 15%, and 38% were observed in the mitotic indices of the cultures dosed with 169, 508, and 1690 µg/ml, respectively, as compared with the solvent control culture. Based on these results, the initial aberrations assay with metabolic activation was conducted with a 20.0 hour harvest testing concentrations of 250, 500, 1000, 2000, 3000, and 4000 µg/ml.

11.4 Chromosomal Aberrations Assay Without Metabolic Activation

Initial Trial

Dead cell monolayers, floating dead cells and debris, no visible mitotic cells, and ≈95% reduction in the cell monolayer confluence were observed in the cultures dosed with 2000 µg/ml. Unhealthy cell monolayers, severe reductions in the number of visible mitotic cells, floating dead cells and debris, and ≈45% reduction in the cell monolayer confluence were observed in the cultures dosed with 1500 µg/ml. Unhealthy cell monolayers, severe reductions in the number of visible mitotic cells, floating dead cells and debris, and ≈30% reduction in the cell monolayer confluence were observed in the cultures dosed with 1000 µg/ml. Slightly unhealthy cell monolayers, floating debris, and ≈15% reduction in the cell monolayer confluence were observed in the cultures dosed with 500 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 125, 250, 500, and 1000 µg/ml (Table 2). Reductions of 25%, 30%, 87%, and 96% were observed in the mitotic indices of the cultures dosed with 125, 250, 1000, and 1500 µg/ml, respectively, as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations were observed at the concentrations analyzed.

Based on the results from this trial, the confirmatory trial of the nonactivation aberrations assay was conducted testing concentrations of 100, 200, 400, 600, 800, 1000, and 1200 µg/ml and 50.0, 100, 200, 400, 600, 800, 1000, and 1200 µg/ml with 20.1 and 44.2 hour harvests, respectively.

Confirmatory Trial

In the 20.1 hour assay, very unhealthy cell monolayers, severe reductions in the number of visible mitotic cells, floating dead cells and debris, and ≈15% reduction in the cell monolayer confluence were observed in the cultures dosed with 1200 µg/ml. Unhealthy cell monolayers, floating dead cells and debris, and severe reductions in the number of visible mitotic cells were observed in the cultures dosed with 1000 µg/ml. Unhealthy cell monolayers, floating debris, and reductions in the number of visible mitotic cells were observed in the cultures dosed with 800 µg/ml. Slightly unhealthy cell monolayers, floating debris, and slight reductions in the number of visible mitotic cells were observed in the cultures dosed with 600 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 200, 400, 600, and 800 µg/ml (Table 3). Reductions of 73%, 84%, and 95% were observed the mitotic indices of the cultures dosed with 800,

1000, and 1200 µg/ml, respectively, as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations were observed at the concentrations analyzed.

In the 44.2 hour assay, dead cell monolayers, no visible mitotic cells, floating dead cells and debris, and ≈45% reduction in the cell monolayer confluence were observed in the cultures dosed with 1000 and 1200 µg/ml. Very unhealthy cell monolayers, floating dead cells and debris, severe reductions in the number of visible mitotic cells, and ≈30% reduction in the cell monolayer confluence were observed in the cultures dosed with 800 µg/ml. Unhealthy cell monolayers, floating dead cells and debris, reductions in the number of visible mitotic cells, and ≈15% reduction in the cell monolayer confluence were observed in the cultures dosed with 600 µg/ml. Slightly unhealthy cell monolayers, floating debris, and slight reductions in the number of visible mitotic cells were observed in the cultures dosed with 400 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 100, 200, 400, and 600 µg/ml (Table 4). Reductions of 12%, 61%, 63%, and 92% were observed the mitotic indices of the cultures dosed with 50.0, 400, 600, and 800 µg/ml, respectively, as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations or in polyploidy were observed at the concentrations analyzed.

The sensitivity of the cell culture for induction of chromosomal aberrations is shown by the increased frequency of aberrations in the cells exposed to mitomycin C, the positive control agent. The test article is considered negative for inducing chromosomal aberrations and polyploidy under nonactivation conditions.

11.5 Chromosomal Aberrations Assay With Metabolic Activation

Initial Trial

No cell monolayers and no visible mitotic cells were observed in the cultures dosed with 3000 and 4000 µg/ml. Slightly unhealthy cell monolayers and ≈30% reduction in the cell monolayer confluence were observed in the cultures dosed with 2000 µg/ml. A reduction of ≈15% in the cell monolayer confluence was observed in the cultures dosed with 1000 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 250, 500, 1000, and 2000 µg/ml (Table 5). Reductions of 2% were observed in the mitotic indices of the cultures dosed with 250 µg/ml as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations were observed at the concentrations analyzed.

Based on the results from the initial trial, the confirmatory trial of the aberrations assay with metabolic activation was conducted testing concentrations of 500, 1000, 1500, 2000, 2250, 2500, 2750, and 3000 µg/ml with 20.1 and 44.2 hour harvests.

Confirmatory Trial

In the 20.1 hour assay, dead cell monolayers, floating dead cells and debris, no visible mitotic cells, and <5% cell monolayer confluence were observed in the cultures dosed with 2750 and 3000 µg/ml. Slightly unhealthy cell monolayers, reductions in the number of visible mitotic cells, floating dead cells and debris, and ≈45% reduction in the cell monolayer confluence were observed in the cultures dosed with 2500 µg/ml. Floating debris, slight reductions in the number of visible mitotic cells, and ≈30% reduction in the cell monolayer confluence were observed in the cultures dosed with 2250 µg/ml. Reductions of ≈15% in the cell monolayer confluence were observed in the cultures dosed with 2000 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 1500, 2000, 2250, and 2500 µg/ml (Table 6). Reductions of 13%, 38%, 15%, 11%, and 30% were observed in the mitotic indices of the cultures dosed with 1000, 1500, 2000, 2250, and 2500 µg/ml, respectively, as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations were observed at the concentrations analyzed, except in the cultures dosed with 2500 µg/ml. In addition, an increase in endoreduplicated cells were observed in the cultures dosed with 2250 and 2500 µg/ml.

In the 44.2 hour assay, dead cell monolayers, floating dead cells and debris, no visible mitotic cells, and ≈95% reduction in the cell monolayer confluence were observed in the cultures dosed with 3000 µg/ml. Unhealthy cell monolayers, severe reductions in the number of visible mitotic cells, floating dead cells and debris, and ≈55% reduction in the cell monolayer confluence were observed in the cultures dosed with 2750 µg/ml. Slightly unhealthy cell monolayers, floating dead cells and debris, and ≈45% reduction in the cell monolayer confluence were observed in the cultures dosed with 2500 µg/ml. Reductions of ≈15% in the cell monolayer confluence were observed in the cultures dosed with 2250 µg/ml. Chromosomal aberrations were analyzed from the cultures dosed with 2000, 2250, 2500 and 2750 µg/ml (Table 7). Reductions of 14%, 17%, 56%, and 53% were observed in the mitotic indices of the cultures dosed with 1000, 2250, 2500, and 2750 µg/ml, respectively, as compared with the solvent control cultures. No significant increases in cells with chromosomal aberrations were observed at the concentrations analyzed, except in the cultures dosed with 2750 µg/ml. In addition, a significant increase in polyploidy was observed in the cultures dosed

with 2250, 2500, and 2750 µg/ml. The dose levels with increased endoreduplication was in the cultures dosed with 2250 and 2500 µg/ml in the 20.1 hour assay.

The successful activation by the metabolic system is illustrated by the increased incidence of cells with chromosomal aberrations in the cultures induced with cyclophosphamide, the positive control agent. The test article is considered negative for inducing chromosomal aberrations except at a single high dose that induced significant toxicity. In addition the test article is considered positive for inducing endoreduplication and polyploidy.

12.0 CONCLUSION:

T-6564 was considered negative for inducing chromosomal aberrations in CHO cells with and without metabolic activation except at a single dose level with metabolic activation that induced significant toxicity.

13.0 REFERENCES:

Armitage, P. Statistical Methods in Medical Research, John Wiley & Sons, Inc., New York, NY, 1971.

Evans, H.J.: Chromosomal aberrations produced by ionizing radiation. International Review of Cytology, 13:221-321, 1962.

Sokal, R.R., and Rohlf, F.J.: Biometry, Ed. 2, W.H. Freeman and Company, New York, 1981.

14.0 DEVIATION FROM THE SIGNED PROTOCOL:

Endoreduplication and polyploidy were analyzed separately since there were some dose levels with increased endoreduplication and some with polyploidy. This added greater scientific information to the study.

15.0 EXPERIMENTAL DATA TABLES

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TABLE 1

RANGEFINDING ASSAY FOR ASSESSING TOXICITY

Assay No.: 17750 Trial No.: I Date: 06/13/96
Lab No.: CY6156

Compound: T-6564

Metabolic Activation: -S9

Treatment			% Mitotic Index	Confluence * % Solvent Control
NEGATIVE CONTROL	McCoy's 5a		2.5	100
SOLVENT CONTROL	Water	10.0 µl/ml	2.4	100
TEST ARTICLE		50.8 µg/ml	4.7	100
		169 µg/ml	4.9	85
		508 µg/ml	5.7	71
		1690 µg/ml	0.2	57

Metabolic Activation: +S9

Treatment			% Mitotic Index	Confluence * % Solvent Control
NEGATIVE CONTROL	McCoy's 5a		10.2	100
SOLVENT CONTROL	Water	10.0 µl/ml	10.9	100
TEST ARTICLE		169 µg/ml	6.1	100
		508 µg/ml	9.3	100
		1690 µg/ml	6.8	100

*This endpoint is based upon visual observations which are made prior to the harvest of the metaphase cells. Actual cell counts are not taken and any hypertrophy of the attached cells cannot be evaluated. At the time of the confluence observation the flasks are also evaluated for the appearance of floating mitotic cells and dead cells.
McCoy's 5a = culture medium

TABLE 2
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.0 Hours After Treatment

Assay No.: 17750 Trial #: 1 Date: 06/20/96 Lab #: CY6196 Metabolic Activation: -S9

Compound: T-6564

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																					
NEGATIVE:	McCoy's 5a		A 100	2	1													0.00	0.0	0.0	5.3
			B 100	5	1			2										0.02	1.0	1.0	4.2
			A+B 200	7	2			2										0.01	0.5	0.5	4.8
SOLVENT:	Water	10.0 µl/ml	A 100															0.00	0.0	0.0	5.7
			B 100	4									1					0.01	1.0	0.0	4.8
			A+B 200	4									1					0.01	0.5	0.0	5.3
POSITIVE:	MMC	0.080 µg/ml	50	1	1		8	1	2		2				1			0.28	22.0*	4.0*	6.9
TEST ARTICLE		125 µg/ml	A 100					1					1					0.02	2.0	0.0	3.9
			B 100										1					0.01	1.0	0.0	4.1
			A+B 200					1					2					0.02	1.5	0.0	4.0
		250 µg/ml	A 100	2									1					0.01	1.0	0.0	2.7
			B 100	2														0.00	0.0	0.0	4.6
			A+B 200	4									1					0.01	0.5	0.0	3.7
		500 µg/ml	A 100		1													0.00	0.0	0.0	6.2
			B 100	3			1											0.01	1.0	0.0	5.6
			A+B 200	3	1		1											0.01	0.5	0.0	5.9
		1000 µg/ml	A 100	2									1					0.01	1.0	0.0	0.8
			B 100	2														0.00	0.0	0.0	0.5
			A+B 200	4									1					0.01	0.5	0.0	0.7
		1500 µg/ml**	A+B 0																		0.2

* Significantly greater than the solvent controls, $p<0.01$.
** Chromosome aberrations not analyzed due to excessive toxicity.
McCoy's 5a = culture medium MMC = Mitomycin C

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TABLE 3
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.1Hours After Treatment

Assay No.: 17750 Trial #: 2 Date: 07/10/96 Lab #: CY7116 Metabolic Activation: -S9

Compound: T-6564

				CELLS SCORED	NUMBER AND TYPE OF ABERRATION: NOT COMPUTED TG	NOT COMPUTED SG	NOT COMPUTED UC	SIMPLE TB	SIMPLE SB	COMPLEX ID	COMPLEX TR	COMPLEX QR	COMPLEX CR	COMPLEX D	COMPLEX R	COMPLEX CI	COMPLEX DF	OTHER GT	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% MITOTIC INDEX
CONTROLS NEGATIVE:	McCoy's 5a		A	100	1			1											0.01	1.0	0.0	7.6
			B	100	2	1		1											0.01	1.0	0.0	8.7
			A+B	200	3	1		2											0.01	1.0	0.0	8.2
SOLVENT:	Water	10.0 µl/ml	A	100	2	1		1	1		1			1					0.04	2.0	1.0	4.3
			B	100		1													0.00	0.0	0.0	4.4
			A+B	200	2	2		1	1		1			1					0.02	1.0	0.5	4.4
POSITIVE:	MMC	0.080 µg/ml		50	2			4	4		5	7	1			1			0.44	28.0*	12.0*	3.1
TEST ARTICLE		100 µg/ml**	A+B	0																		6.4
		200 µg/ml	A	100	5									2					0.02	2.0	0.0	7.2
			B	100	6									1					0.01	1.0	0.0	5.7
			A+B	200	11									3					0.02	1.5	0.0	6.5
		400 µg/ml	A	100	4									2					0.02	2.0	0.0	8.7
			B	100	4	1													0.00	0.0	0.0	6.9
			A+B	200	8	1								2					0.01	1.0	0.0	7.8
		600 µg/ml	A	100	3														0.00	0.0	0.0	5.0
			B	100															0.00	0.0	0.0	5.2
			A+B	200	3														0.00	0.0	0.0	5.1
		800 µg/ml	A	100	3										1				0.01	1.0	0.0	1.0
			B	100	4	1													0.00	0.0	0.0	1.3
			A+B	200	7	1									1				0.01	0.5	0.0	1.2
		1000 µg/ml***	A+B	0																		0.7
		1200 µg/ml***	A+B	0																		0.2

* Significantly greater than the solvent controls, $p<0.01$.
** Chromosome aberrations not analyzed due to higher doses available for analysis.
*** Chromosome aberrations not analyzed due to excessive toxicity.
McCoy's 5a = culture medium MMC = Mitomycin C

C00223

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TABLE 4
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 44.2 Hours After Treatment

Assay No.: 17750 Trial #: 2 Date: 07/10/96 Lab #: CY7116 Metabolic Activation: -S9

Compound: T-6564

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	%[a] POLYPLOID CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT					
CONTROLS NEGATIVE:	McCoy's 5a		A 100															0.00	0.0	0.0	0.0	6.9
			B 100	2														0.00	0.0	0.0	0.0	6.0
			A+B 200	2														0.00	0.0	0.0	0.0	6.5
SOLVENT:	Water	10.0 µl/ml	A 100	5		1							1					0.01	1.0	0.0	2.0	5.8
			B 100	3		1												0.00	0.0	0.0	0.0	4.4
			A+B 200	8		2							1					0.01	0.5	0.0	1.0	5.1
TEST ARTICLE		50.0 µg/ml*	A+B 0																			4.5
		100 µg/ml	A 100	1		1							1					0.01	1.0	0.0	3.0	3.7
			B 100	1														0.00	0.0	0.0	1.0	6.6
			A+B 200	2		1							1					0.01	0.5	0.0	2.0	5.2
		200 µg/ml	A 100	1														0.00	0.0	0.0	4.0	4.1
			B 100					1										0.01	1.0	0.0	3.0	6.1
			A+B 200	1				1										0.01	0.5	0.0	3.5	5.1
		400 µg/ml	A 100	1		1												0.00	0.0	0.0	0.0	2.6
			B 100															0.00	0.0	0.0	1.0	1.3
			A+B 200	1		1												0.00	0.0	0.0	0.5	2.0
		600 µg/ml	A 100	4						1								0.01	0.0	0.0	1.0	2.4
			B 100	2	1	3	1	1										0.02	2.0	0.0	0.0	1.4
			A+B 200	6	1	3	1	1		1								0.02	1.0	0.0	0.5	1.9
		800 µg/ml**	A+B 0																			0.4

* Chromosome aberrations not analyzed due to higher doses available for analysis.

** Chromosome aberrations not analyzed due to excessive toxicity.

McCoy's 5a = culture medium

[a] Includes polyploidy and endoreduplication

TABLE 5
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.0 Hours After Treatment

Assay No.: 17750 Trial #: 1 Date: 06/20/96 Lab #: CY6196 Metabolic Activation: +S9

Compound: T-6564

				NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% MITOTIC INDEX
			CELLS SCORED		TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																						
NEGATIVE:	McCoy's 5a		A	100	1	1													0.00	0.0	0.0	9.4
			B	100	5	1													0.00	0.0	0.0	10.1
			A+B	200	6	2													0.00	0.0	0.0	9.8
SOLVENT:	Water	10.0 µl/ml	A	100		2													0.00	0.0	0.0	8.2
			B	100	6									1					0.01	1.0	0.0	9.9
			A+B	200	6	2								1					0.01	0.5	0.0	9.1
POSITIVE:	CP	5.00 µg/ml		25	7			6	1	6	11	6	5			3			1.52	64.0*	40.0*	2.5
TEST ARTICLE		250 µg/ml	A	100	3														0.00	0.0	0.0	9.6
			B	100	3	1					1			1					0.02	2.0	0.0	8.2
			A+B	200	6	1					1			1					0.01	1.0	0.0	8.9
		500 µg/ml	A	100	6			1						1					0.02	2.0	0.0	8.6
			B	100		1					1								0.01	1.0	0.0	10.6
			A+B	200	6	1		1			1			1					0.02	1.5	0.0	9.6
		1000 µg/ml	A	100	3									1					0.01	1.0	0.0	9.8
			B	100															0.00	0.0	0.0	11.5
			A+B	200	3									1					0.01	0.5	0.0	10.7
		2000 µg/ml	A	100	2	1			1		3								0.04	3.0	1.0	8.5
			B	100	2	1													0.00	0.0	0.0	9.8
			A+B	200	4	2			1		3								0.02	1.5	0.5	9.2

* Significantly greater than the solvent controls, $p<0.01$.
McCoy's 5a = culture medium CP = Cyclophosphamide

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TABLE 6
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.1 Hours After Treatment

Assay No.: 17750 Trial #: 2 Date: 07/10/96 Lab #: CY7116 Metabolic Activation: +S9

Compound: T-6564

				NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT					
CONTROLS NEGATIVE:	McCoy's 5a		A 100	3									1					0.01	1.0	0.0		8.5
			B 100	3			1											0.01	1.0	0.0		8.8
			A+B 200	6			1						1					0.01	1.0	0.0		8.7
SOLVENT:	Water	10.0 µl/ml	A 100	2									1					0.01	1.0	0.0		8.1
			B 100	2	1								1					0.01	1.0	0.0		7.7
			A+B 200	4	1								2					0.01	1.0	0.0		7.9
POSITIVE:	CP	5.00 µg/ml	25	4			4	2	1	1	4				1			0.52	28.0*	12.0*		3.0
TEST ARTICLE		1000 µg/ml**	A+B 0																			6.9
		1500 µg/ml	A 100	1														0.00	0.0	0.0		4.6
			B 100	2	2								1					0.01	1.0	0.0		5.2
			A+B 200	3	2								1					0.01	0.5	0.0		4.9
		2000 µg/ml	A 100	5									1	1				0.02	2.0	0.0		6.9
			B 100	1	1								1					0.01	1.0	0.0		6.5
			A+B 200	6	1								2	1				0.02	1.5	0.0		6.7
		2250 µg/ml	A 100	4					1	2	1		1		2			0.07	4.0	2.0	20.0	7.2
			B 100	2														0.00	0.0	0.0	16.0	6.7
			A+B 200	6					1	2	1		1		2			0.04	2.0	1.0	18.0*	7.0
		2500 µg/ml	A 100	7			4	4	4		1		2		3			0.18	10.0	5.0	32.0	7.3
			B 100	5	4		13	3	2	4	9		1		3			0.35	15.0	10.0	35.0	3.7
			A+B 200	12	4		17	7	6	4	10		3		6			0.27	12.5*	7.5*	33.5*	5.5

* Significantly greater than the solvent controls, $p<0.01$.
McCoy's 5a = culture medium CP = Cyclophosphamide

** Chromosome aberrations not analyzed due to higher doses available for analysis.
* Endoreduplication scored due to noticible increase in incidence.

TABLE 7
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 44.2 Hours After Treatment

Assay No.: 17750 Trial #: 2 Date: 07/10/96 Lab #: CY7116 Metabolic Activation: +S9

Compound: T-6564

					NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	%[a] POLYPLOID CELLS	% MITOTIC INDEX
			CELLS SCORED		TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT					
CONTROLS NEGATIVE:	McCoy's 5a		A	100	3	1													0.00	0.0	0.0	0.0	7.0
			B	100	1														0.00	0.0	0.0	1.0	6.6
			A+B	200	4	1													0.00	0.0	0.0	0.5	6.8
SOLVENT:	Water	10.0 µl/ml	A	100		1		1											0.01	1.0	0.0	2.0	6.9
			B	100	1														0.00	0.0	0.0	1.0	5.8
			A+B	200	1	1		1											0.01	0.5	0.0	1.5	6.4
TEST ARTICLE		1000 µg/ml**	A+B	0																			5.5
		1500 µg/ml**	A+B	0																			7.0
		2000 µg/ml	A	100	1														0.00	0.0	0.0	4.0	7.6
			B	100	1	3		1											0.01	1.0	0.0	3.0	8.7
			A+B	200	2	3		1											0.01	0.5	0.0	3.5	8.2
		2250 µg/ml	A	100	3									1					0.01	1.0	0.0	7.0	6.2
			B	100	1	1			1										0.01	1.0	0.0	5.0	4.3
			A+B	200	4	1			1					1					0.01	1.0	0.0	6.0*	5.3
		2500 µg/ml	A	100	3	1								2			1		0.03	3.0	0.0	17.0	1.6
			B	100	1				1					2					0.03	3.0	0.0	14.0	4.0
			A+B	200	4	1			1					4			1		0.03	3.0	0.0	15.5*	2.8
		2750 µg/ml	A	81	6	1	1	2	6			1		4		4	2		0.23	13.6	4.9	46.0	2.8
			B	84	4	1	3		2		2			6	2				0.14	11.9	2.4	39.0	3.1
			A+B	165	10	2	4	2	8		2	1		10	2	4	2		0.19	12.7*	3.6*	42.5*	3.0

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

McCoy's 5a = culture medium

[a] Includes polyploidy and endoreduplication

TABLE 8

CONTROL DATA OF CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
8/95 THROUGH 12/95

	Activation		# Of Aberrations Per Cell	% Of Cells With Aberrations	% Of Cells With >1 Aberrations	% Endore-duplicated Cells	% Poly-ploidy Cells
Negative Control							
	Without	MIN	0.00	0.0	0.0	0.0	0.0
		MAX	0.04	4.0	0.5	5.0	9.5
		AVG	0.012	1.04	0.01	0.19	1.93
		N	36	36	36	39	45
Solvent Control							
	Without	MIN	0.00	0.0	0.0	0.0	0.0
		MAX	0.05	5.0	0.5	2.0	10.0
		AVG	0.012	0.93	0.01	0.14	2.20
		N	36	36	36	39	45
Positive Control Mitomycin C	Without	MIN	0.24	20.0	0.0		
		MAX	2.96	84.0	60.0		
		AVG	0.770	39.70	16.52		
		N	27	27	27		
Negative Control							
	With	MIN	0.00	0.0	0.0	0.0	0.0
		MAX	0.03	2.5	1.0	3.0	12.5
		AVG	0.017	1.40	0.10	0.45	2.33
		N	31	31	31	28	30
Solvent Control							
	With	MIN	0.00	0.0	0.0	0.0	0.0
		MAX	0.12	7.0	4.0	4.0	13.0
		AVG	0.023	1.78	0.26	0.64	2.28
		N	29	29	29	28	30
Positive Control Cyclophosphamide	With	MIN	0.40	32.0	8.0		
		MAX	8.88	100.0	100.0		
		AVG	1.728	57.17	32.83		
		N	24	24	24		

16.0 DEFINITIONS OF CHROMOSOME ABERRATIONS FOR GIEMSA STAINED CELLS

NOT COMPUTED

TG	Chromatid gap:	("tid gap"). An achromatic (unstained) region in one chromatid, the size of which is equal to or smaller than the width of a chromatid. These are noted but not usually included in final totals of aberrations as they may not all be true breaks.
SG	Chromosome gap:	("isochromatid gap, IG"). Same as chromatid gap but at the same locus in both sister chromatids.
UC	Uncoiled chromosome:	Failure of chromatin packing. Probably not a true aberration.
PP	Polyploid cell:	A cell containing multiple copies of the haploid number (n) of chromosomes. Not counted in the cells scored for aberrations.
E	Endoreduplication:	4n cell in which separation of chromosome pairs has failed. Not counted in the cells scored for aberrations.

SIMPLE

TB	Chromatic break:	An achromatic region in one chromatid, larger than the width of a chromatid. The associated fragment may be partially or completely displaced.
SB	Chromosome break:	Chromosome has a clear break, forming an abnormal (deleted) chromosome with an acentric fragment that is dislocated. This classification now includes the acentric fragment (AF). The AF was different from the SB only in that it was not apparently related to any specific chromosome.
DM	"Double Minute " fragment:	These are small double dots, some of which are terminal deletions and some interstitial deletions and probably small rings. Their origins are not distinguishable.

COMPLEX

ID	Interstitial deletion:	Length of chromatid "cut out" from midregion of a chromatid resulting in a small fragment of ring lying beside a shortened chromatid of a gap in the chromatid.
TR	Triradial:	An exchange between two chromosomes, or one chromosome and an acentric fragment, which results in a three-armed configuration.
QR	Quadri radial:	As triradial, but resulting in a four-armed configuration.
D	Dicentric:	An exchange between two chromosomes which results in a chromosome with two centromeres. This is often associated with an acentric fragment in which case it is classified as DF.
DF		Dicentric with fragment.
TC	Tricentric:	An exchange between three chromosomes which results in a chromosome with three centromeres. Often associated with two to three AF. Such exchanges can involve many chromosomes and are named as follows:
QC	Quadricentric:	four centromeres, up to four AF
PC	Pentacentric:	five centromeres, up to five AF
HC	Hexacentric:	six centromeres, up to six AF
R	Ring	A chromosome which forms a circle containing a centromere. This is often associated with an acentric fragment in which case it is classed as RF.
RC	Ring Chromatid:	Single chromatid ring (acentric).
RF		Ring with associated acentric fragment.
CI	Chromosome Intrachange:	Exchange within a chromosome; e.g., a ring that does not include the entire chromosome.

T	Translocation:	Obvious transfer of material between two chromosomes resulting in two abnormal chromosomes. When identifiable, scored as "T" not "2Ab."
AB		Abnormal monocentric chromosome. This is a chromosome whose morphology is abnormal for the karyotype, and often the result of a translocation, pericentric inversion, etc. Classification used if abnormality cannot be ascribed to; e.g., a reciprocal translocation.
Other		
GT/>		A cell which contains more than 10 aberrations. A heavily damaged cell should be analyzed to identify the types of aberrations and may not actually have >10, e.g., multiple fragments such as those found associated with a tricentric.

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MUTAGENICITY TEST WITH

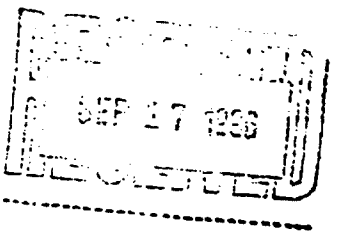
T-6564

IN THE *SALMONELLA - ESCHERICHIA COLI*/MAMMALIAN-MICROSOME REVERSE MUTATION ASSAY WITH A CONFIRMATORY ASSAY

FINAL REPORT

AUTHOR

Timothy E. Lawlor, M.A.



PERFORMING LABORATORY

Corning Hazleton Inc. (CHV)
9200 Leesburg Pike
Vienna, Virginia 22182

LABORATORY PROJECT ID

CHV Study No.: 17750-0-409R

SUBMITTED TO

3M Corporation
Building 220-2E-02 3M Center
St. Paul, MN 55144-1000

STUDY COMPLETION DATE

September 13, 1996

000232

QUALITY ASSURANCE STATEMENT

STUDY TITLE: *Salmonella - Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay

ASSAY NO.: 17750-0-409R

PROTOCOL NO.: 409R, Edition 4, Modified for 3M

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Scoring Plates - 06/28/96	06/28/96	P. Conley
Draft Report Review - 08/29/96	08/30/96	C. Orantes
Final Report Review - 09/13/96	09/13/96	C. Orantes

Quality Assurance Unit — Date Released 9/13/96

STUDY COMPLIANCE AND CERTIFICATION

The study was conducted in compliance with the Good Laboratory Practice regulations as set forth by the Food and Drug Administration (FDA) in Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) with any applicable amendments. There were no deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

Study Director:

Timothy E. Lawlor, M.A.
Bacterial Mutagenesis
Genetic and Cellular Toxicology

9·13·96
Study Completion Date

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SECTION I. SUMMARY

INTRODUCTION AND CONCLUSIONS

SUMMARY

A. Introduction

At the request of 3M Corporation , Corning Hazleton Inc. investigated **T-6564** for mutagenic activity in the *Salmonella - Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay. This assay evaluated the test article and/or its metabolites for their ability to induce reverse mutations at the histidine locus in the genome of specific *Salmonella typhimurium* tester strains and at the tryptophan locus in an *Escherichia coli* tester strain both in the presence and absence of an exogenous metabolic activation system of mammalian microsomal enzymes derived from Aroclor™-induced rat liver (S9).

The doses tested in the mutagenicity assay were selected based on the results of a dose rangefinding study using tester strains TA100 and WP2*uvr*A and ten doses of test article ranging from 5,000 to 6.67 µg per plate, one plate per dose, both in the presence and absence of S9 mix.

The tester strains used in the mutagenicity assay were *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* tester strain WP2*uvr*A. The assay was conducted with five doses of test article in both the presence and absence of S9 mix along with concurrent vehicle and positive controls using three plates per dose. The doses tested were 5,000, 3,330, 1,000; 333, and 100 µg per plate in both the presence and absence of S9 mix. The results of the initial mutagenicity assay were confirmed in an independent experiment.

B. Conclusions

The results of the *Salmonella - Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay indicate that, under the conditions of this study, 3M Corporation 's test article, **T-6564**, did not cause a positive increase in the number of revertants per plate of any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor™-induced rat liver (S9).

SECTION II. STUDY INFORMATION

STUDY INFORMATION

A. Sponsor: **3M Corporation**

B. Test Article: **T-6564**
L-13167 FC1015-X

1. Physical Description: **clear colorless liquid**

2. Date Received: **05/30/96**

C. Type of Assay: *Salmonella-Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay

1. Protocol Number: CHV Protocol 409R, Edition 4

2. CHV Study Number: **17750-0-409R**

D. Study Dates

1. Study Initiation Date: **06/04/96**

2. Experimental Start Date: **06/12/96**

3. Experimental Termination Date: **08/27/96**

E. Study Supervisory Personnel

Study Director: Timothy E. Lawlor, M.A.

Laboratory Supervisor: Michael S. Mecchi, B.S.

SECTION III. MATERIALS AND METHODS

MATERIALS AND METHODS

The experimental materials, methods and procedures are based on those described by Ames *et al* (1975) and Green and Muriel (1976).

MATERIALS

A. Tester Strains

1. *Salmonella typhimurium*

The tester strains used were the *Salmonella typhimurium* histidine auxotrophs TA98, TA100, TA1535, and TA1537 as described by Ames *et al* (1975). The specific genotypes of these strains are shown in Table I.

TABLE I. TESTER STRAIN GENOTYPES

Histidine Mutation			Additional Mutations		
*his*G46	*his*C3076	*his*D3052	LPS	Repair	R Factor
TA1535	TA1537		*rfa*	*uvr*B	-
TA100		TA98	*rfa*	*uvr*B	+R

In addition to a mutation in the histidine operon, the tester strains contain two additional mutations which enhance their sensitivity to some mutagenic compounds. The *rfa* wall mutation results in the loss of one of the enzymes responsible for the synthesis of part of the lipopolysaccharide barrier that forms the surface of the bacterial cell wall. The resulting cell wall deficiency increases permeability to certain classes of chemicals such as those containing large ring systems (i.e. benzo(a)pyrene) that would otherwise be excluded by a normal intact cell wall.

The second mutation, a deletion of the *uvr*B gene, results in a deficient DNA excision repair system which greatly enhances the sensitivity of these strains to some mutagens. Since the *uvr*B deletion extends through the *bio* gene, all of the tester strains containing this deletion require the vitamin biotin for growth.

Strains TA98 and TA100 also contain the R-factor plasmid, pKM101, which further increases the sensitivity of these strains to some mutagens. The mechanism by which this plasmid increases sensitivity to mutagens has been suggested to be by modifying an existing bacterial DNA repair polymerase complex involved with the mismatch-repair process.

Tester strains TA98 and TA1537 are reverted from histidine dependence (auxotrophy) to histidine independence (prototrophy) by frameshift mutagens. TA1535 is reverted by base substitution mutagens and TA100 is reverted by mutagens which cause both frameshifts and base substitution mutations.

2. *Escherichia coli*

The tester strain used was the tryptophan auxotroph WP2*uvr*A as described by Green and Muriel (1976).

In addition to a mutation in the tryptophan operon, the tester strain contains a *uvr*A DNA repair deficiency which enhances its sensitivity to some mutagenic compounds. This deficiency allows the strain to show enhanced mutability since the *uvr*A repair system would normally act to remove the damaged part of the DNA molecule and accurately repair it afterwards.

Tester strain WP2*uvr*A is reverted from tryptophan dependence (auxotrophy) to tryptophan independence (prototrophy) by base substitution mutagens.

3. Source of Tester Strains

a. *Salmonella typhimurium*

The tester strains in use at CHV were received directly from Dr. Bruce Ames, Department of Biochemistry, University of California, Berkeley.

b. *Escherichia coli*

The tester strain, WP2*uvr*A, in use at CHV was received from the National Collection of Industrial Bacteria, Torrey Research Station, Scotland (United Kingdom).

4. Storage of the Tester Strains

a. Frozen Permanent Stocks

Frozen permanent stocks were prepared by growing fresh overnight cultures, adding DMSO (0.09 ml/ml of culture) and freezing small aliquots (0.5-1.5 ml) at ≤-70°C.

b. Master Plates

Master plates were prepared by streaking each tester strain from a frozen permanent stock onto minimal agar appropriately supplemented with 1) for *Salmonella typhimurium*, an excess of histidine, and biotin, and for tester strains TA98 and TA100, ampicillin (25 µg/ml), to ensure the stable maintenance of the pKM101 plasmid; and 2) for *Escherichia coli*, an excess of tryptophan. Tester strain master plates were stored at 5 ± 3 °C.

5. Preparation of Overnight Cultures

a. Inoculation

Overnight cultures for use in all testing procedures were inoculated by transferring a colony from the appropriate master plate to a flask containing culture medium. Inoculated flasks were placed in a shaker/incubator which was programmed to begin operation (shaking, 125 ± 25 rpm; incubation, 37 ± 2 °C) so that the overnight cultures were in log phase or late log phase when turbidity monitoring began.

b. Harvest

To ensure that cultures were harvested in late log phase, the length of incubation was determined by spectrophotometric monitoring of culture turbidity. Cultures were harvested once a predetermined turbidity was reached as determined by a percent transmittance (%T) reading on a spectrophotometer. This target turbidity ensures that cultures have reached a density of at least 0.5×10^9 cells per ml and that the cultures have not overgrown. Overgrown (stationary) cultures may exhibit decreased sensitivity to some mutagens. Cultures were removed from incubation when the target %T was reached and were placed at 5 ± 3 °C.

6. Confirmation of Tester Strain Genotypes

Tester strain cultures were checked for the following genetic markers on the day of their use in the mutagenicity assay:

a. *Salmonella typhimurium*

1) *rfa* Wall Mutation

The presence of the *rfa* wall mutation was confirmed by demonstration of the sensitivity of the culture to crystal violet. An aliquot of an overnight

culture of each strain was overlaid onto plates containing selective media and an antibiotic sensitivity disk containing 10 µg of crystal violet was added. Sensitivity was demonstrated by inhibition of bacterial growth in a zone immediately surrounding the disk.

2) pKM101 Plasmid R-factor

The presence of the pKM101 plasmid was confirmed for tester strains TA98 and TA100 by demonstration of resistance to ampicillin. An aliquot of an overnight culture of each strain was overlaid onto plates containing selective media and an antibiotic sensitivity disk containing 10 µg of ampicillin was added. Resistance was demonstrated by bacterial growth in the zone immediately surrounding the disk.

3) Characteristic Number of Spontaneous Revertants

The mean number of spontaneous revertants per plate in the vehicle controls that are characteristic of the respective strains were demonstrated by plating 100 µl aliquots of the culture along with the appropriate vehicle on selective media.

b. *Escherichia coli*

1) Characteristic Number of Spontaneous Revertants

The mean number of spontaneous revertants per plate in the vehicle controls that are characteristic of the respective strains were demonstrated by plating 100 µl aliquots of the WP2*uvr*A culture along with the appropriate vehicle on selective media.

7. Tester Strain Media

a. Culturing Broth

The broth used to grow overnight cultures of the tester strains was Vogel-Bonner salt solution (Vogel and Bonner, 1956) supplemented with 2.5% (w/v) Oxoid Nutrient Broth No. 2 (dry powder).

b. Agar Plates

Bottom agar (25 ml per 15 x 100 mm petri dish) was Vogel-Bonner minimal medium E (Vogel and Bonner, 1956), supplemented with 1.5% (w/v) agar and 0.2% (w/v) glucose.

c. Overlay Agar for Selection of Revertants

Overlay (top) agar was prepared with 0.7% agar (w/v) and 0.5% NaCl (w/v) and was supplemented with 10 ml of 1) 0.5 mM histidine/biotin solution per 100 ml agar for selection of histidine revertants, or 2) 0.5 mM tryptophan solution per 100 ml of agar for selection of tryptophan revertants. When S9 mix was required, 2.0 ml of the supplemented top agar was used in the overlay. However, when S9 mix was not required, water was added to the supplemented top agar (0.5 ml of water per 2 ml of supplemented top agar) and the resulting 2.5 ml of diluted supplemented top agar was used for the overlay. This dilution ensured that the final top agar and amino acid supplement concentrations remained the same both in the presence and absence of S9 mix.

B. Liver Microsomal Enzyme Reaction Mixture (S9 Mix)

1. S9 Homogenate

Liver microsomal enzymes (S9 homogenate) were purchased from Molecular Toxicology, Inc., Annapolis, MD 21401, Batch 0642 (39.5 mg of protein per ml) and Batch 0646 (43.4 mg of protein per ml). The homogenate was prepared from male Sprague-Dawley rats that had been injected (i.p.) with Aroclor™ 1254 (200 mg per ml in corn oil) at 500 mg/kg as described by Ames *et al*, 1975.

2. S9 Mix

The S9 mix was prepared immediately prior to its use in any experimental procedure. The S9 mix contained the components indicated in Table II.

TABLE II. S9 MIX COMPONENTS

H_2O	0.70 ml
1M NaH_2PO_4/Na_2HPO_4, pH 7.4	0.10 ml
0.25M Glucose-6-phosphate	0.02 ml
0.10M NADP	0.04 ml
0.825M KCl/0.2M $MgCl_2$	0.04 ml
S9 Homogenate	0.10 ml
	1.00 ml

C. Controls

1. Vehicle Controls

Vehicle controls were plated for all tester strains both in the presence and absence of S9 mix. The vehicle control was plated, using a 50 µl aliquot of vehicle (equal to the maximum aliquot of test article dilution plated), along with a 100 µl aliquot of the appropriate tester strain and a 500 µl aliquot of S9 mix (when necessary), on selective agar.

2. Positive Controls

The combinations of positive controls, activation condition and tester strains plated concurrently with the assay are indicated in Table III.

TABLE III. POSITIVE CONTROLS

Tester Strain	S9 Mix	Positive Control	Conc per plate
TA98	+	2-aminoanthracene	2.5 µg
TA98	-	2-nitrofluorene	1.0 µg
TA100	+	2-aminoanthracene	2.5 µg
TA100	-	sodium azide	2.0 µg
TA1535	+	2-aminoanthracene	2.5 µg
TA1535	-	sodium azide	2.0 µg
TA1537	+	2-aminoanthracene	2.5 µg
TA1537	-	ICR-191	2.0 µg
WP2*uvr*A	+	2-aminoanthracene	25.0 µg
WP2*uvr*A	-	4-nitroquinoline-N-oxide	1.0 µg

a. Source and Grade of Positive Control Articles

2-aminoanthracene (CAS #613-13-8), Sigma Chemical Co., purity ≥ 97.5%; 2-nitrofluorene (CAS #607-57-8), Aldrich Chemical Co., purity 98%; sodium azide (CAS #26628-22-8), Sigma Chemical Co., purity >98%; ICR-191 (CAS #1707-45-0), Polysciences Inc., purity >95% and Sigma Chemical Co., purity 98%; 4-nitroquinoline-N-oxide (CAS #56-57-5), Sigma Chemical Co., purity >99%.

3. Sterility Controls

a. Test Article

The most concentrated test article dilution was checked for sterility by plating a 50 µl aliquot (the same volume used in the assay) on selective agar.

b. S9 Mix

The S9 mix was checked for sterility by plating 0.5 ml on selective agar.

METHODS

A. Dose Rangefinding Study

The growth inhibitory effect (cytotoxicity) of the test article to the test system was determined in order to allow the selection of appropriate doses to be tested in the mutagenicity assay.

1. Design

The dose rangefinding study was performed using tester strains TA100 and WP2*uvr*A both in the presence and absence of S9 mix. Ten doses of test article were tested at one plate per dose. The test article was checked for cytotoxicity up to a maximum concentration of 5 mg per plate.

a. Rationale

The cytotoxicity of the test article observed on tester strain TA100 is generally representative of that observed on the other tester strains and because of TA100's comparatively high number of spontaneous revertants per plate, gradations of cytotoxicity can be readily discerned from routine experimental variation. The *Escherichia coli* tester strain WP2*uvr*A does not possess the *rfa* wall mutation that the *Salmonella typhimurium* strains have and thus, a different range of cytotoxicity may be observed. Also, the cytotoxicity induced by a test article in the presence of S9 mix may vary greatly from that observed in the absence of S9 mix. Therefore, this would require that different test article dose ranges be tested in the mutagenicity assay based on the presence or absence of the S9 mix.

2. Evaluation of the Dose Rangefinding Study

Cytotoxicity is detectable as a decrease in the number of revertant colonies per plate and/or by a thinning or disappearance of the bacterial background lawn.

3. Selection of the Maximum Dose for the Mutagenicity Assay

a. No Cytotoxicity Observed

Since no cytotoxicity was observed in the dose rangefinding study, the highest dose level of test article used in the mutagenicity assay was the same as that tested in the rangefinding study.

B. Mutagenicity Assay

1. Design

The assay was performed using tester strains TA98, TA100, TA1535, TA1537, and WP2*uvr*A both in the presence and absence of S9 mix. Five doses of test article were tested along with the appropriate vehicle and positive controls. The doses of test article were selected based on the results of the dose rangefinding study. The results of the initial mutagenicity assay were confirmed in an independent experiment.

2. Frequency and Route of Administration

The tester strains were exposed to the test article via the plate incorporation methodology originally described by Ames *et al* (1975) and Maron and Ames (1983). This methodology has been shown to detect a wide range of classes of chemical mutagens. In the plate incorporation methodology, the test article, the tester strain and the S9 mix (where appropriate) were combined in molten agar which was overlaid onto a minimal agar plate. Following incubation at 37 ± 2°C for 48 ± 8 hr, revertant colonies were counted. All doses of the test article, the vehicle controls and the positive controls were plated in triplicate.

C. Plating Procedures

These procedures were used in both the dose rangefinding study and the mutagenicity assay.

Each plate was labeled with a code which identified the test article, test phase, tester strain, activation condition and dose level. The S9 mix and dilutions of the test article were prepared immediately prior to their use.

When S9 mix was not required, 100 µl of tester strain and 50 µl of vehicle or test article dose was added to 2.5 ml of molten selective top agar (maintained at 45 ± 2°C). When S9 mix was required, 500 µl of S9 mix, 100 µl of tester strain and 50 µl of vehicle or test article dose was added to 2.0 ml of molten selective top agar. After the required components had been added, the mixture was vortexed and overlaid onto the surface of 25 ml of minimal bottom agar contained in a 15 x 100 mm petri dish. After the overlay had solidified, the plates were inverted and incubated for 48 ± 8 hr at 37 ± 2°C. Positive control articles were plated using a 50 µl plating aliquot.

D. Scoring the Plates

Plates which were not evaluated immediately following the incubation period were held at 5 ± 3°C until such time that colony counting and bacterial background lawn evaluation could take place.

1. Bacterial Background Lawn Evaluation

The condition of the bacterial background lawn was evaluated for evidence of cytotoxicity and test article precipitate. Evidence of cytotoxicity was scored relative to the vehicle control plate and was recorded along with the revertant counts for all plates at that dose level on the data tables using the code system presented at the end of the Materials and Methods Section.

2. Counting Revertant Colonies

The number of revertant colonies per plate for the vehicle controls and all plates containing test article were counted manually. The number of revertant colonies per plate for the positive controls were counted by automated colony counter with the exception of the positive controls for tester strain WP2*uvr*A in the absence of S9 mix, in Experiment 17750-B1, which were counted manually.

E. Analysis of Data

For all replicate platings, the mean revertants per plate and the standard deviation were calculated. The results of these calculations are presented in tabular form in the Data Tables Section of this report.

EVALUATION OF TEST RESULTS

Before assay data were evaluated, the criteria for a valid assay had to be met.

A. Criteria For A Valid Assay

The following criteria were used to determine a valid assay:

1. Tester Strain Integrity : *Salmonella typhimurium*

a. *rfa* Wall Mutation

To demonstrate the presence of the *rfa* wall mutation, tester strain cultures exhibited sensitivity to crystal violet.

b. pKM101 Plasmid

To demonstrate the presence of the R-factor plasmid, pKM101, cultures of tester strains TA98 and TA100 exhibited resistance to ampicillin.

c. Characteristic Number of Spontaneous Revertants

To demonstrate the requirement for histidine, the tester strain cultures exhibited a characteristic number of spontaneous revertants per plate when plated along with the vehicle under selective conditions. The acceptable ranges for the mean vehicle controls were as follows:

TA98	8 - 60
TA100	60 - 240
TA1535	4 - 45
TA1537	2 - 25

2. Tester Strain Integrity : *Escherichia coli*

a. Characteristic Number of Spontaneous Revertants

To demonstrate the requirement for tryptophan, the tester strain culture exhibited a characteristic number of spontaneous revertants per plate when plated along

with the vehicle under selective conditions. The acceptable range for the WP2*uvr*A mean vehicle controls was 5 to 40 revertants per plate.

3. Tester Strain Culture Density

To demonstrate that appropriate numbers of bacteria are plated, the density of tester strain cultures were greater than or equal to 0.5×10^9 bacteria per ml and/or had reached a target level of turbidity demonstrated to produce cultures with a density greater than or equal to 0.5×10^9 bacteria per ml.

4. Positive Control Values

a. Positive Control Values in the Absence of S9 Mix

To demonstrate that the tester strains were capable of identifying a mutagen, the mean value of a positive control for a respective tester strain exhibited at least a 3-fold increase over the mean value of the vehicle control for that strain.

b. Positive Control Values in the Presence of S9 Mix (S9 Mix Integrity)

To demonstrate that the S9 mix was capable of metabolizing a promutagen to its mutagenic form(s), the mean value of the positive control for a respective tester strain in the presence of the S9 mix exhibited at least a 3-fold increase over the mean value of the vehicle control for that strain.

An acceptable positive control in the presence of S9 mix for a specific strain was evaluated as having demonstrated both the integrity of the S9 mix and the ability of the tester strain to detect a mutagen.

5. Cytotoxicity

A minimum of three non-toxic doses were required to evaluate assay data.

B. Criteria For A Positive Response

Once the criteria for a valid assay had been met, responses observed in the assay were evaluated as follows:

1. Tester Strains TA98, TA100, and WP2*uvr*A

For a test article to be considered positive, it had to produce at least a 2-fold increase in the mean revertants per plate of at least one of these tester strains over the mean revertants per plate of the appropriate vehicle control. This increase in the mean number of revertants per plate had to be accompanied by a dose response to increasing concentrations of the test article.

2. Tester Strains TA1535 and TA1537

For a test article to be considered positive, it had to produce at least a 3-fold increase in the mean revertants per plate of at least one of these tester strains over the mean revertants per plate of the appropriate vehicle control. This increase in the mean number of revertants per plate had to be accompanied by a dose response to increasing concentrations of the test article.

RECORDS TO BE MAINTAINED

All raw data, documentation, records, the protocol, and the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time or sent to a storage facility designated by the Sponsor.

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BACTERIAL BACKGROUND LAWN EVALUATION CODE

The condition of the background bacterial lawn is evaluated both macroscopically and microscopically (using a dissecting microscope) for indications of cytotoxicity and test article precipitate as follows:

CODE	DEFINITION	CHARACTERISTICS OF BACKGROUND LAWN
1	Normal	A healthy microcolony lawn.
2	Slightly Reduced	A noticeable thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
3	Moderately Reduced	A marked thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
4	Extremely Reduced	An extreme thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
5	Absent	A complete lack of any microcolony lawn.
6	Obscured by Precipitate	The background bacterial lawn cannot be accurately evaluated due to microscopic and/or macroscopic test article precipitate.

Evidence of macroscopic test article precipitate on the plates is recorded by addition of the following precipitate code to the code number used to evaluate the condition of the background bacterial lawn.

sp	Slight Precipitate	Noticeable macroscopic precipitate on the plate, however, the precipitate does not influence automated counting of the plate.
mp	Moderate Precipitate	The amount of macroscopic precipitate on the plate would interfere with automated counting, thus requiring the plate to be hand counted.
hp	Heavy Precipitate	The large amount of macroscopic precipitate on the plate makes the required hand counting difficult.

Example: 4mp would indicate a plate observed to have an extremely reduced background lawn which had to be counted manually due to the marked amount of macroscopic test article precipitate.

SECTION IV. RESULTS AND CONCLUSIONS

RESULTS

A. Test Article Handling

The test article, **T-6564**, was stored at room temperature. Deionized water (CHV Lots 347, 349, and 352) was used as the vehicle. At 100 mg per ml, which was the most concentrated stock dilution prepared, the test article formed a clear, colorless solution. The test article remained a solution in all succeeding dilutions prepared for the mutagenicity assay.

B. Dose Rangefinding Study

Doses to be tested in the mutagenicity assay were selected based on the results of the dose rangefinding study conducted on the test article using tester strains TA100 and WP2*uvr*A in both the presence and absence of S9 mix (one plate per dose). Ten doses of test article, from 5,000 to 6.67 µg per plate, were tested and the results are presented in Tables 1 and 2. These data were generated in Experiment 17750-A1. No cytotoxicity was observed in either the presence or absence of S9 mix as evidenced by a normal background lawn and no decrease in the number of revertants per plate.

C. Mutagenicity Assay

The mutagenicity assay results for **T-6564** are presented in Tables 3 through 7. These data were generated in Experiments 17750-B1, 17750-C1, and 17750-D1. The data are presented as mean revertants per plate ± standard deviation for each treatment and control group (Tables 4, 6, and 7) and as individual plate counts (Tables 3, 5, and 7).

The results of the dose rangefinding study were used to select five doses to be tested in the mutagenicity assay. The doses tested were 5,000, 3,330, 1,000, 333, and 100 µg per plate in both the presence and absence of S9 mix.

In the initial mutagenicity assay, Experiment 17750-B1 (Tables 3 and 4), and in the confirmatory assay, Experiment 17750-C1 (Tables 5 and 6), all data were acceptable and no positive increases in the number of revertants per plate were observed with any of the tester strains either in the presence or absence of S9 mix. In Experiment 17750-C1, a non-dose responsive 5.0-fold increase which did not meet the criteria for a positive response was observed with tester strain TA1537 in the absence of S9 mix. For this reason tester strain TA1537 was retested in the absence of S9 mix in Experiment 17750-D1.

In Experiment 17750-D1 (Table 7), all data were acceptable and and no positive increases in the number of revertants per plate were observed with tester strain TA1537 in the absence of S9 mix.

All criteria for a valid study were met.

CONCLUSIONS

The results of the *Salmonella - Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay indicate that, under the conditions of this study, 3M Corporation's test article, **T-6564**, did not cause a positive increase in the number of revertants per plate of any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor™-induced rat liver (S9).

SECTION V. DATA TABLES

TABLE 1

DOSE RANGEFINDING STUDY

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-A1 DATE PLATED: 12-Jun-96

VEHICLE: Deionized water DATE COUNTED: 18-Jun-96

	TA100 REVERTANTS PER PLATE			
	WITH S9		WITHOUT S9	
µg/PLATE	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*
0.00 (Vehicle) (50 µl)	85	1	78	1
Test Article				
6.67	106	1	91	1
10.0	128	1	96	1
33.3	120	1	78	1
66.7	122	1	105	1
100	113	1	84	1
333	126	1	113	1
667	121	1	96	1
1000	110	1	86	1
3330	112	1	81	1
5000	118	1	99	1

* Background Lawn Evaluation Codes:
1 = normal; 2 = slightly reduced; 3 = moderately reduced
4 = extremely reduced; 5 = absent; 6 = obscured by precipitate
sp = slight precipitate; mp = moderate precipitate (requires hand count); hp = heavy precipitate (requires hand count)

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TABLE 2

DOSE RANGEFINDING STUDY

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-A1 DATE PLATED: 12-Jun-96

VEHICLE: Deionized water DATE COUNTED: 18-Jun-96

µg/PLATE	WP2uvrA REVERTANTS PER PLATE WITH S9		WITHOUT S9	
	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*
0.00 (Vehicle) (50 µl)	10	1	12	1
Test Article				
6.67	13	1	14	1
10.0	12	1	11	1
33.3	16	1	16	1
66.7	9	1	22	1
100	15	1	10	1
333	16	1	8	1
667	10	1	20	1
1000	9	1	14	1
3330	11	1	6	1
5000	10	1	5	1

* Background Lawn Evaluation Codes:
1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

TABLE 3
MUTAGENICITY ASSAY RESULTS
INDIVIDUAL PLATE COUNTS

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-B1

DATE PLATED: 20-Jun-96 VEHICLE: Deionized water

DATE COUNTED: 28-Jun-96 PLATING ALIQUOT: 50 µl

		REVERTANTS PER PLATE															BACKGROUND LAWN*
DOSE/PLATE		TA98			TA100			TA1535			TA1537			WP2uvrA			
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	
MICROSOMES: Rat Liver																	
VEHICLE CONTROL		25	22	13	118	106	103	15	17	9	9	10	5	15	12	12	1
TEST ARTICLE	100 µg	21	29	18	85	109	102	13	13	10	10	11	5	11	10	19	1
	333 µg	16	27	25	101	104	96	8	11	15	5	6	2	20	24	9	1
	1000 µg	27	16	29	106	100	101	10	12	15	8	5	12	14	14	14	1
	3330 µg	25	17	19	114	110	125	18	10	13	12	8	10	11	16	8	1
	5000 µg	23	25	25	117	99	109	12	12	10	7	7	5	13	13	5	1
POSITIVE CONTROL **		860	852	970	936	892	810	141	134	124	240	202	190	314	279	270	1
MICROSOMES: None																	
VEHICLE CONTROL		12	12	12	91	74	85	14	10	6	5	4	7	15	14	10	1
TEST ARTICLE	100 µg	14	10	13	81	104	83	11	9	5	6	7	1	8	7	13	1
	333 µg	13	11	4	101	95	86	10	13	5	6	6	6	12	12	11	1
	1000 µg	16	11	12	97	98	92	11	10	7	6	6	5	8	12	9	1
	3330 µg	15	10	2	108	93	75	12	10	6	4	5	1	12	8	11	1
	5000 µg	11	11	13	106	108	104	16	14	12	9	5	4	13	13	9	1
POSITIVE CONTROL ***		105	99	86	470	419	460	460	427	400	1233	918	1110	135	102	85	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

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TABLE 4
MUTAGENICITY ASSAY RESULTS
SUMMARY

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-B1

DATE PLATED: 20-Jun-96 VEHICLE: Deionized water

DATE COUNTED: 28-Jun-96 PLATING ALIQUOT: 50 µl

		MEAN REVERTANTS PER PLATE WITH STANDARD DEVIATION										BACKGROUND LAWN*
	DOSE/PLATE	TA98		TA100		TA1535		TA1537		WP2uvrA		
		MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	
MICROSOMES: Rat Liver												
VEHICLE CONTROL		20	6	109	8	14	4	8	3	13	2	1
TEST ARTICLE	100 µg	23	6	99	12	12	2	9	3	13	5	1
	333 µg	23	6	100	4	11	4	4	2	18	8	1
	1000 µg	24	7	102	3	12	3	8	4	14	0	1
	3330 µg	20	4	116	8	14	4	10	2	12	4	1
	5000 µg	24	1	108	9	11	1	6	1	10	5	1
POSITIVE CONTROL **		894	66	879	64	133	9	211	26	288	23	1
MICROSOMES: None												
VEHICLE CONTROL		12	0	83	9	10	4	5	2	13	3	1
TEST ARTICLE	100 µg	12	2	89	13	8	3	5	3	9	3	1
	333 µg	9	5	94	8	9	4	6	0	12	1	1
	1000 µg	13	3	96	3	9	2	6	1	10	2	1
	3330 µg	9	7	92	17	9	3	3	2	10	2	1
	5000 µg	12	1	106	2	14	2	6	3	12	2	1
POSITIVE CONTROL ***		97	10	450	27	429	30	1087	159	107	25	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

000262

TABLE 5
MUTAGENICITY ASSAY RESULTS
INDIVIDUAL PLATE COUNTS

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-C1

DATE PLATED: 25-Jul-96 VEHICLE: Deionized water

DATE COUNTED: 30-Jul-96, 31-Jul-96 PLATING ALIQUOT: 50 µl

		REVERTANTS PER PLATE															BACKGROUND LAWN*
DOSE/PLATE		TA98			TA100			TA1535			TA1537			WP2uvrA			
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	
MICROSOMES: Rat Liver																	
VEHICLE CONTROL		25	25	18	94	76	103	17	14	17	4	7	6	12	14	18	1
TEST ARTICLE	100 µg	21	21	28	89	99	95	8	11	9	11	4	11	14	16	10	1
	333 µg	27	33	25	102	105	76	16	16	9	8	6	19	10	15	9	1
	1000 µg	33	26	29	87	115	108	12	10	8	7	7	10	24	13	14	1
	3330 µg	24	30	27	106	96	114	9	18	12	8	4	4	24	16	13	1
	5000 µg	25	33	25	107	87	89	8	6	17	8	7	8	21	14	20	1
POSITIVE CONTROL **		769	624	815	949	1108	1066	146	196	136	89	129	91	151	90	108	1
MICROSOMES: None																	
VEHICLE CONTROL		13	18	15	79	89	70	16	9	19	1	4	2	13	16	23	1
TEST ARTICLE	100 µg	16	17	17	71	105	76	16	17	17	6	5	4	15	10	10	1
	333 µg	21	8	16	74	89	73	14	9	8	6	6	8	15	15	19	1
	1000 µg	20	9	8	74	71	88	9	9	8	1	6	7	6	13	19	1
	3330 µg	21	15	11	78	75	78	15	14	10	16	10	3	13	9	6	1
	5000 µg	10	17	17	99	80	77	16	13	16	8	7	1	9	17	10	1
POSITIVE CONTROL ***		207	208	172	548	597	595	644	619	663	462	477	463	187	207	160	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal 2 = slightly reduced 3 = moderately reduced
4 = extremely reduced 5 = absent 6 = obscured by precipitate
sp = slight precipitate mp = moderate precipitate (requires hand count) hp = heavy precipitate (requires hand count)

000263

TABLE 6
MUTAGENICITY ASSAY RESULTS
SUMMARY

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-C1

DATE PLATED: 25-Jul-96 VEHICLE: Deionized water

DATE COUNTED: 30-Jul-96, 31-Jul-96 PLATING ALIQUOT: 50 µl

		MEAN REVERTANTS PER PLATE WITH STANDARD DEVIATION										BACKGROUND LAWN*
	DOSE/PLATE	TA98		TA100		TA1535		TA1537		WP2uvrA		
		MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	
MICROSOMES: Rat Liver												
VEHICLE CONTROL		23	4	91	14	16	2	6	2	15	3	1
TEST ARTICLE	100 µg	23	4	94	5	9	2	9	4	13	3	1
	333 µg	28	4	94	16	14	4	11	7	11	3	1
	1000 µg	29	4	103	15	10	2	8	2	17	6	1
	3330 µg	27	3	105	9	13	5	5	2	18	6	1
	5000 µg	28	5	94	11	10	6	8	1	18	4	1
POSITIVE CONTROL **		736	100	1041	82	160	32	103	23	116	31	1
MICROSOMES: None												
VEHICLE CONTROL		15	3	79	10	15	5	2	2	17	5	1
TEST ARTICLE	100 µg	17	1	84	18	17	1	5	1	12	3	1
	333 µg	15	7	79	9	10	3	7	1	16	2	1
	1000 µg	12	7	78	9	9	1	5	3	13	7	1
	3330 µg	16	5	77	2	13	3	10	7	9	4	1
	5000 µg	15	4	85	12	15	2	5	4	12	4	1
POSITIVE CONTROL ***		196	21	580	28	642	22	467	8	185	24	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal 2 = slightly reduced 3 = moderately reduced
4 = extremely reduced 5 = absent 6 = obscured by precipitate
sp = slight precipitate mp = moderate precipitate (requires hand count) hp = heavy precipitate (requires hand count)

000264

TABLE 7
MUTAGENICITY ASSAY RESULTS
INDIVIDUAL PLATE COUNTS AND SUMMARY

TEST ARTICLE ID: T-6564

EXPERIMENT ID: 17750-D1

DATE PLATED: 25-Aug-96 VEHICLE: Deionized water

DATE COUNTED: 27-Aug-96 PLATING ALIQUOT: 50 µl

DOSE/PLATE		REVERTANTS PER PLATE TA1537			MEAN REVERTANTS PER PLATE WITH STANDARD DEVIATION TA1537		BACKGROUND LAWN*
		1	2	3	MEAN	S.D.	
MICROSOMES: None							
VEHICLE CONTROL		10	2	9	7	4	1
TEST ARTICLE	100 µg	9	6	5	7	2	1
	333 µg	9	5	4	6	3	1
	1000 µg	5	6	8	6	2	1
	3330 µg	6	8	5	6	2	1
	5000 µg	3	1	9	4	4	1
POSITIVE CONTROL ***		128	63	60	84	38	1

*** TA1537 ICR-191 2.0 µg/plate

* Background Lawn Evaluation Codes:

1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

000265

CORNING Hazleton

MUTAGENICITY TEST ON

T-6342

MEASURING CHROMOSOME ABERRATIONS IN HUMAN WHOLE BLOOD LYMPHOCYTES WITH A CONFIRMATORY ASSAY WITH MULTIPLE HARVESTS

FINAL REPORT

AUTHOR

Hemalatha Murli, Ph.D.

PERFORMING LABORATORY

Corning Hazleton Inc. (CHV)
9200 Leesburg Pike
Vienna, Virginia 22182

LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17073-0-449CO

SUBMITTED TO

3M Corporation
Building 220-2E-02
3M Center
St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

November 1, 1996

000266

QUALITY ASSURANCE STATEMENT

Project Title: Chromosome Aberrations in Human Whole Blood Lymphocytes With a Confirmatory Assay With Multiple Harvests

Project No.: 20990 Assay No.: 17073

Protocol No.: 449CO Edition No.: 2, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Addition of Colcemid/08/15/1996	08/15/1996	C. Orantes
Draft Report Review/09/18-20/1996	09/20/1996	C. Orantes
Final Report Review/11/01/1996	11/01/1996	C. Smith

Quality Assurance Unit — Date Released: 11/1/96

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Organization for Economic Cooperation and Development Principles of Good Laboratory Practice C(81)30 (Final) Annex 2, issued 1979-1980 (effective 1981) with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

Hemalatha Murli

Hemalatha Murli, Ph.D.
Mammalian Cytogenetics
Department of Genetic and Cellular Toxicology

11/1/96
Study Completion Date

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ABSTRACT

The objective of this in vitro assay was to evaluate the ability of T-6342 to induce chromosomal aberrations in cultured whole blood human lymphocytes with and without metabolic activation.

The test article was dissolved in deionized water at a concentration of 500 mg/ml. The test article solutions and the vehicle control, deionized water, were dosed with a dosing volume of 1% (10 µl/ml) for this assay.

For the dose rangefinding assay with and without metabolic activation, concentrations of 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml were tested. Reductions of 35%, 6%, 38%, 15%, 18%, 57%, and 100% were observed in the mitotic indices of the cultures dosed with 0.500, 1.67, 5.00, 16.7, 500, 1670, and 5000 µg/ml without metabolic activation, respectively, as compared with the solvent control culture. Reductions of 8%, 5%, 4%, 1%, and 100% were observed in the mitotic indices of the cultures dosed with 1.67, 50.0, 500, 1670, and 5000 µg/ml with metabolic activation, respectively, as compared with the solvent control culture.

Based on these data, the initial trial of the chromosomal aberrations assay was conducted testing concentrations of 127, 253, 505, 1010, 1510, 2010, and 2510 µg/ml without metabolic activation and of 253, 505, 1010, 1510, 2010, 2510, 3010, and 4010 µg/ml with metabolic activation in 22.0 hour assays. Cultures dosed with 253, 505, 1010, and 1510 µg/ml without metabolic activation and with 505, 1010, 1510 and 2010 µg/ml with metabolic activation were evaluated for chromosomal aberrations. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the confirmatory assay, replicate cultures were incubated with 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml in a 22.1 hour assay and with 62.5, 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml in a 46.0 hour assay under nonactivation conditions. Replicate cultures were incubated with 250, 500, 1000, 1500, 2000, 2500, and 3000 µg/ml in 22.1 and 46.0 hour assays with metabolic activation. Cultures dosed with 125, 250, 500, and 900 µg/ml from the 22.1 and 46.0 hour nonactivation assays, with 250, 500, 1000, and 1500 µg/ml from the 22.1 hour activation assay, and with 500, 1000, 1500, and 2000 µg/ml from the 46.0 hour activation assay were evaluated for chromosomal aberrations. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed, except for a weak increase in endoreduplication at 2000 µg/ml, an extremely toxic dose level, from the 45.9 hour activation assay.

The test article, T-6342, was considered negative for inducing chromosomal aberrations in cultured whole blood human lymphocytes with and without metabolic activation. These results were verified in independently conducted confirmatory trials.

Chromosomal Aberrations in Human Whole Blood Lymphocytes
With a Confirmatory Assay With Multiple Harvests
With T-6342

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (TEST ARTICLE):

2.1 Client's Identification: T-6342

2.2 Date Received: July 21, 1995

2.3 Physical Description: Clear, colorless liquid

2.4 Genetics Assay No.: 17073

3.0 TYPE OF ASSAY: Chromosomal Aberrations in Human Whole Blood Lymphocytes With a Confirmatory Assay With Multiple Harvests

4.0 PROTOCOL NO.: 449CO, Edition 2, Modified for 3M Corporation

5.0 STUDY DATES:

5.1 Initiation Date: July 9, 1996

5.2 Experimental Start Date: July 31, 1996

5.3 Experimental Termination Date: August 26, 1996

6.0 SUPERVISORY PERSONNEL:

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Carol S. Spicer, B.S.

7.0 OBJECTIVE:

The objective of this in vitro assay was to evaluate the ability of the test article, T-6342, to induce chromosomal aberrations in cultured human whole blood lymphocytes, with and without metabolic activation.

8.0 RATIONALE:

The assay is designed to establish whether the test article or its metabolites can interact with cells to induce chromosome breaks. Chemically induced lesions may result in breaks in chromatin that are either repaired by the cell in such a way as to be undetectable or result in visible damage. Aberrations are a consequence of failure or mistakes in repair processes such that breaks do not rejoin or rejoin in abnormal configurations (Evans, 1962).

In order to detect chromosomal aberrations, cells must be in metaphase so that chromosomes are visible. The lymphocytes in blood do not usually divide and are stimulated to divide in culture by phytohemagglutinin (PHA). The cells are later arrested at the appropriate stage (metaphase) by Colcemid®.

9.0 EXPERIMENTAL DESIGN:

Results from the dose rangefinding assay were used to determine the dose range to be used in the chromosomal aberrations assay. In the dose rangefinding assay, the cultures were harvested 20.1 hours after initiation of treatment. Mitotic indices of the cultures were evaluated for evidence of toxicity. A summary of the treatment schedule for the preliminary test is given below.

Summary of Dose Rangefinding Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
- S9	0	19.5	20.1	22.1
+ S9	0	3	20.1	22.1

In the chromosomal aberrations assays, replicate cultures were used at each dose level, and negative, solvent controls, and for each dose of the positive control. The aberrations assays were conducted with a 22.0 hour harvest time in the initial trial and with 22.1 and 46.0 hour harvest times in the confirmatory trials. Chromosomal aberrations were analyzed from the cultures treated at four dose levels and from one of the positive control doses. A summary of the treatment schedule for the chromosomal aberrations assays is given below.

Summary of Chromosomal Aberrations Assay Treatment Schedule in Hours

Test	Culture Initiation	Chemical	Wash	Colcemid®	Fixation
Initial Trial					
- S9	-48	0	19.2	20.0	22.0
+ S9	-48	0	3.0	20.0	22.0
Confirmatory Trial					
- S9	-48	0	19.3	20.1	22.1
+ S9	-48	0	3.0	20.1	22.1
- S9	-48	0	43.3	44.0	46.0
+ S9	-48	0	3.0	44.0	46.0

10.0 MATERIALS AND METHODS:

10.1 Cells Used:

Human venous blood from a single, normal, healthy male donor was drawn into sterile, heparinized Vacutainers. Cultures were initiated with 0.3 ml of blood per 5 ml culture for the dose rangefinding assay and 0.6 ml of blood per 10.0 ml culture for the chromosomal aberrations assays in 15 ml centrifuge tubes.

10.2 Cell Culture Medium:

The cells were incubated at about 37°C on a slope, with loose caps, in an atmosphere of about 5 % CO_2 in air. The culture medium used was RPMI 1640 (JRH Biosciences) supplemented with 15% fetal bovine serum (FBS; Biochemed, Lot#E5331, dose rangefinding assay; Lot No.:T06024, chromosomal aberrations assay), 1% phytohemagglutinin (PHA-M; Gibco), penicillin (100 units/ml; Quality Biologicals) and streptomycin (100 µg/ml; Quality Biologicals), and 2mM L-glutamine (Quality Biologicals).

10.3 Negative and Solvent Controls:

In the nonactivation assays, negative controls were cultures which contain only cells and culture medium. Solvent controls were cultures containing deionized water at the highest concentration used in test cultures (1% or 10.0 µl/ml). In the

activation assays, the negative and solvent controls were the same as described in the nonactivation assays but with the S9 activation mix included.

10.4 Positive Control Agents:

The positive control agents which were used in the assays were mitomycin C (MMC) for the nonactivation series and cyclophosphamide (CP) in the metabolic activation series. Mitomycin C (CAS# 50-07-7, Sigma, Lot # 40H2508) is a clastogen that does not require metabolic activation. Cyclophosphamide (CAS # 6055-19-2, Sigma, Lot # 43H0269) does not act directly but must be converted to active intermediates by microsomal enzymes. In the chromosomal aberrations assays, three concentrations of MMC (0.1, 0.2, and 0.3 µg/ml) and CP (20, 30, and 50 µg/ml) were used to induce chromosomal aberrations. One of the dose levels was analyzed in each of the aberration assays. Both MMC and CP were dissolved in water.

10.5 Dose Rangefinding Assay:

In these tests, cultures were initiated with 0.3 ml of blood per 5 ml culture and were incubated for two days prior to treatment.

10.5.1 Test Without Metabolic Activation:

The lymphocytes were incubated with the test article for 19.5 hours at ≈37°C. Then, the test article was washed from the cells with phosphate buffered saline and fresh complete medium containing Colcemid® (final concentration 0.1 µg/ml) was added. The cultures were then harvested 2.0 hours later. (See Sections on Harvest and Slide Preparation and Staining).

10.5.2 Test With Metabolic Activation:

In this test, the lymphocytes were incubated to the test article for three hours at ≈37°C in the presence of a rat liver S9 reaction mixture (S9 15 µl/ml, NADP 1.5 mg/ml, and isocitric acid 2.7 mg/ml). The S9 fraction (Molecular Toxicology, Inc., Lot #0667) was derived from the liver of male Sprague-Dawley rats which had been previously treated with Aroclor 1254 to induce the mixed function oxidase enzymes which are capable of metabolizing chemicals to more active forms. The three hour incubation time was used because prolonged exposure to the S9 mixture might be toxic to the cells and the enzyme activity of S9 is lost rapidly at

about 37°C. The medium did not have FBS during the exposure period to avoid possible inactivation of short lived and highly reactive intermediates produced by the S9 enzymes by binding to serum proteins.

After the exposure period the cells were washed twice with buffered saline. Complete RPMI culture medium was added to the cultures which were then incubated for 18.5 hours with Colcemid® (final concentration 0.1 µg/ml) added for the last 2.0 hours to collect metaphase cells. The cultures were then harvested, fixed, and slides were prepared and stained as was described for the nonactivation dose rangefinding assay .

10.5.3 Assay Evaluation:

Mitotic index was analyzed from the surviving dose levels by analyzing the number of metaphases present in 1000 consecutive cells.

10.6 Aberrations Assay Without Metabolic Activation:

Cultures were initiated two days prior to treatment with 0.6 ml of whole blood per 10.0 ml culture in 15 ml centrifuge tubes. Two days after culture initiation, the cells were treated with the test article at predetermined concentrations for about 19.3 and 43.3 hours. The cultures were then washed with buffered saline and complete RPMI 1640 medium containing 0.1 µg/ml Colcemid® was placed back onto the cells. Two hours later, the cells were harvested and air dried slides were made. The slides were then stained in 5 % Giemsa solution for the analysis of chromosomal aberrations.

10.7 Aberrations Assay With Metabolic Activation:

Cultures were initiated two days prior to treatment with 0.6 ml of whole blood per 10.0 ml culture in 15 ml centrifuge tubes. Two days after culture initiation, the cultures were incubated at ≈37°C for three hours in the presence of the test article and the S9 reaction mixture. After the three hour exposure period, the cells were washed twice with buffered saline and the cells were refed with complete RPMI 1640 medium. The cells were incubated for the rest of the culture period up to the time of harvest with 0.1 µg/ml Colcemid® present during the last 2.0 hours of incubation. The metaphase cells were then harvested and prepared for cytogenetic analysis.

10.8 Harvest Procedure:

The cell suspension was centrifuged, the supernatant was discarded and cells were treated with hypotonic KCl (0.075 M) for approximately 10 minutes. This treatment helps to swell the cells and thus disperse the chromosomes. After centrifugation and removal of the KCl, the cells were washed three times with freshly prepared fixative (absolute methanol:glacial acetic acid, 3:1, v:v). Air-dried slides were prepared from the harvested cells.

10.9 Slide Preparation and Staining:

Slides were prepared by dropping the harvested cultures on clean slides. The slides were stained with 5% Giemsa solution for the analysis of mitotic index and chromosomal aberrations. All slides were then air-dried and cover slipped.

10.10 Aberrations Analysis and Assay Evaluation:

Cells were selected for good morphology and only cells with the number of centromeres equal to the modal number 46 were analyzed.

One hundred cells, if available, from each replicate culture at four dose levels of the test article, the negative, solvent, and positive control cultures were analyzed for the different types of chromosomal aberrations (Evans, 1962; See Section 15.0). At least 25 cells were analyzed for chromosomal aberrations from those cultures with >25% cells with chromosomal aberrations. For control of bias, all slides were coded prior to analysis. Cells with aberrations were recorded on the data sheets by the microscope stage location. Mitotic index was assessed by analyzing the number of mitotic cells in 1000 cells and the ratio was expressed as a percentage of mitotic cells.

The following factors were taken into account in the evaluation of the chromosomal aberrations data:

1. The percentage of cells with any aberrations.
2. The percentage of cells with more than one aberration.
3. Any evidence for increasing amounts of damage with increasing dose, i.e., a positive dose response.

Chromatid and isochromatid gaps, if observed, were noted in the raw data and were tabulated. They were not, however, considered in the evaluation of the ability of the test article to induce chromosomal aberrations since they may not represent true chromosomal breaks and may possibly be induced by toxicity. Percent polyploidy and endoreduplication were analyzed and results were tabulated. Historical control data are presented in Table 8.

A cell classified as "GT" is considered to contain 10 aberrations for statistical purposes but a ">" is also included in the tables for this classification to indicate that it is a minimum number.

Statistical analysis employed a Cochran-Armitage test for linear trend and Fisher's Exact Test (Thakur *et al.*, 1985) to compare the percentage of cells with aberrations (and, if applicable, the percentage of cells with more than one aberration), polyploidy, and endoreduplication in treated cells with results from vehicle controls. Test article significance was established where $p<0.01$. All factors as stated previously were taken into account and the final evaluation of the test article was based upon scientific judgement.

11.0 RESULTS:

11.1 Solubility and Dose Determination

Deionized water (Prepared at CHV, Lot # 20) was the solvent of choice for this assay. T-6342 was dissolved in deionized water at a concentration of 500 mg/ml for the dose rangefinding assay . The test article solutions and the vehicle control, deionized water, were dosed with a dosing volume of 1% (10 µl/ml) for this assay. Concentrations of 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml were tested in the dose rangefinding assay with and without metabolic activation. The stability of the test article under the preparation and dosing conditions used in this assay is the responsibility of the sponsor.

11.2 Dose Rangefinding Assay Without Metabolic Activation

Hemolysis was observed prior to wash in the cultures dosed with 5000 µg/ml. Mitotic indices were analyzed from the cultures dosed with 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml (Table 1). Reductions of 35%, 6%, 38%, 15%, 18%, 57%, and 100% were observed in the mitotic indices of the cultures dosed with 0.500, 1.67, 5.00, 16.7, 500, 1670, and 5000 µg/ml. Based on these results, the initial trial of the aberrations assay without metabolic activation

was conducted with a 22.0 hour harvest testing concentrations of 127, 253, 505, 1010, 1510, 2010, and 2510 µg/ml.

11.3 Dose Rangefinding Assay With Metabolic Activation

Hemolysis was observed prior to wash in the cultures dosed with 5000 µg/ml. Mitotic indices were analyzed from the cultures dosed with 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml (Table 1). Reductions of 8%, 5%, 4%, 1%, and 100% were observed in the mitotic indices of the cultures dosed with 1.67, 50.0, 500, 1670, and 5000 µg/ml, as compared with the solvent control culture. Based on these results, the initial trial of the aberrations assay with metabolic activation was conducted with a 22.0 hour harvest testing concentrations of 253, 505, 1010, 1510, 2010, 2510, 3010, and 4010 µg/ml.

11.4 Chromosomal Aberrations Assay Without Metabolic Activation

INITIAL TRIAL

Hemolysis was observed prior to wash in the cultures dosed with 2510 µg/ml. Reductions of 38%, 18%, 18%, 50%, 55%, and 95% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 127, 253, 505, 1010, 1510, and 2010 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 253, 505, 1010, and 1510 µg/ml (Table 2). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

Based on these results, the confirmatory trial under nonactivation conditions were conducted testing dose levels of 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml with a 22.1 harvest and 62.5, 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml with a 46.0 harvest.

CONFIRMATORY TRIAL

In the 22.1-hour confirmatory trial, hemolysis was observed prior to wash of the cultures dosed with 1600 and 2000 µg/ml, and a slight evidence of hemolysis was evident at harvest of the cultures dosed with 1600 µg/ml. Reductions of 2%, 14%, 64%, 74%, 93%, and 93% in the mitotic indices as compared with the solvent control cultures were observed in the cultures dosed with 125, 500, 900, 1200, 1600, and 2000 µg/ml, respectively. Chromosomal aberrations were ana-

lyzed from the cultures treated with 125, 250, 500, and 900 µg/ml (Table 3). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the 46.0-hour confirmatory trial, hemolysis was observed prior to wash of the cultures dosed with 1600 and 2000 µg/ml. Reductions of 59%, 93%, 98%, and 98% in the mitotic indices as compared with the solvent control cultures were observed in the cultures dosed with 900, 1200, 1600, and 2000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 125, 250, 500, and 900 µg/ml (Table 4). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

The sensitivity of the cell culture for induction of chromosomal aberrations is shown by the increased frequency of aberrations in the cells exposed to MMC, the positive control agent. The test article is considered negative for inducing chromosomal aberrations, polyploidy, and endoreduplication under nonactivation conditions.

11.5 Chromosomal Aberrations Assay With Metabolic Activation

INITIAL TRIAL

Hemolysis was observed prior to wash in the cultures dosed with 2010, 2510, 3010, and 4010 µg/ml. No cells were visible prior to the addition of Colcemid® to the cultures dosed with 4010 µg/ml, and hemolysis was observed prior to the addition of Colcemid® in the cultures dosed with 3010 µg/ml. Reductions of 15%, 20%, 15%, 43%, 77%, and 95% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 253, 505, 1010, 1510, 2010, and 2510 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 505, 1010, 1510, and 2010 µg/ml (Table 5). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

Based on these results, the confirmatory trial under activation conditions were conducted testing dose levels of 250, 500, 1000, 1500, 2000, 2500, and 3000 µg/ml with 22.1 and 46.0 hour harvests.

CONFIRMATORY TRIAL

In the 22.1-hour confirmatory trial, hemolysis was observed prior to wash and prior to harvest of the cultures dosed with 2000, 2500, and 3000 µg/ml. Reductions of 15%, 5%, 69%, 82%, 97%, and 100% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 500, 1000, 1500, 2000, 2500, and 3000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 250, 500, 1000, and 1500 µg/ml (Table 6). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the 46.0-hour confirmatory trial, hemolysis was observed prior to wash and prior to harvest of the cultures dosed with 2000, 2500, and 3000 µg/ml. Reductions of 15%, 80%, 100%, and 100% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 1500, 2000, 2500, and 3000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 500, 1000, 1500 and 2000 µg/ml (Table 7). Due to toxicity, only 52 metaphases were available for analysis in one of the cultures dosed with 2000 µg/ml. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed, except for a weak increase in endoreduplication at 2000 µg/ml, an extremely toxic dose level.

The successful activation of the metabolic system is illustrated by the increased incidence of cells with chromosomal aberrations in the cultures induced with cyclophosphamide, the positive control agent. The test article is considered negative for inducing chromosomal aberrations, polyploidy, and endoreduplication under conditions of metabolic activation, except for a weak increase in endoreduplication at an extremely toxic dose level in the 46.0 hour assay.

12.0 CONCLUSION:

The test article, T-6342, was considered negative for inducing chromosomal aberrations in cultured whole blood human lymphocytes cells with and without metabolic activation. These results were verified in independently conducted confirmatory trials.

13.0 REFERENCES:

Evans, H.J. (1962) Chromosomal aberrations produced by ionizing radiation, International Review of Cytology, 13, 221-321.

Thakur, A.J., Berry, K.J., and Mielke, P.W. Jr (1985) A FORTRAN program for testing trend and homogeneity in proportions, Computer Programs in Biomedicine, 19, 229-233.

14.0 EXPERIMENTAL DATA TABLES

TABLE 1

DOSE RANGEFINDING ASSAY

Assay No.: 17073 Trial No.: I Date: 07/31/96
Compound: T-6342 Lab No.: CY7316

Metabolic Activation: -S9

Treatment			% Mitotic Index
NEGATIVE CONTROL	RPMI 1640		5.9
SOLVENT CONTROL	Water	10.0 µl/ml	6.8
TEST ARTICLE		0.167 µg/ml	7.4
		0.500 µg/ml	4.4
		1.67 µg/ml	6.4
		5.00 µg/ml	4.2
		16.7 µg/ml	5.8
		50.0 µg/ml	7.2
		167 µg/ml	7.1
		500 µg/ml	5.6
		1670 µg/ml	2.9
		5000 µg/ml*	0.0

Metabolic Activation: +S9

Treatment			% Mitotic Index
NEGATIVE CONTROL	RPMI 1640		7.4
SOLVENT CONTROL	Water	10.0 µl/ml	8.3
TEST ARTICLE		0.167 µg/ml	9.4
		0.500 µg/ml	8.6
		1.67 µg/ml	7.6
		5.00 µg/ml	8.3
		16.7 µg/ml	8.4
		50.0 µg/ml	7.9
		167 µg/ml	8.6
		500 µg/ml	8.0
		1670 µg/ml	8.2
		5000 µg/ml*	0.0

*Toxic dose level RPMI 1640 = Culture medium

C00284

TABLE 2
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.0 Hours After Treatment

Assay No.: 17073 Trial #: 1 Date: 08/07/96 Lab #: CY8066 Metabolic Activation: -S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	2	1		1											0.01	1.0	0.0	0.0	0.0	2.0
			B 100	1														0.00	0.0	0.0	0.0	0.0	3.7
			A+B 200	3	1		1											0.01	0.5	0.0	0.0	0.0	2.9
SOLVENT:	Water	10.0 µl/ml	A 100	3														0.00	0.0	0.0	0.0	0.0	4.2
			B 100	3														0.00	0.0	0.0	0.0	0.0	3.8
			A+B 200	6														0.00	0.0	0.0	0.0	0.0	4.0
POSITIVE:	MMC	0.300 µg/ml	A 25	4	2			1	4	3	1							0.36	32.0	4.0	0.0	0.0	3.3
			B 25	7	1		5		2		4							0.44	44.0	0.0	0.0	0.0	2.2
			A+B 50	11	3		5	1	6	3	5							0.40	38.0*	2.0	0.0	0.0	2.8
TEST ARTICLE		127 µg/ml**	A+B 0																				2.5
		253 µg/ml	A 100	7														0.00	0.0	0.0	0.0	0.0	3.5
			B 100	2			1											0.01	1.0	0.0	0.0	0.0	3.0
			A+B 200	9			1											0.01	0.5	0.0	0.0	0.0	3.3
		505 µg/ml	A 100	5			1											0.01	1.0	0.0	0.0	0.0	3.4
			B 100	6														0.00	0.0	0.0	0.0	0.0	3.2
			A+B 200	11			1											0.01	0.5	0.0	0.0	0.0	3.3
		1010 µg/ml	A 100				1	2										0.03	2.0	1.0	0.0	0.0	2.2
			B 100	3	1		1											0.01	1.0	0.0	0.0	0.0	1.7
			A+B 200	3	1		2	2										0.02	1.5	0.5	0.0	0.0	2.0
		1510 µg/ml	A 100	4	3		2											0.02	2.0	0.0	0.0	0.0	2.1
			B 100	2			1			1								0.02	2.0	0.0	0.0	0.0	1.5
			A+B 200	6	3		3			1								0.02	2.0	0.0	0.0	0.0	1.8
		2010 µg/ml***	A+B 0																				0.2

RPMI 1640 = Culture medium MMC = Mitomycin C

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

TABLE 3
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.1 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: -S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	2														0.00	0.0	0.0	0.0	0.0	4.2
			B 100	1														0.00	0.0	0.0	0.0	0.0	4.4
			A+B 200	3														0.00	0.0	0.0	0.0	0.0	4.3
SOLVENT:	Water	10.0 µl/ml	A 100	2			1											0.01	1.0	0.0	0.0	0.0	4.0
			B 100				1											0.01	1.0	0.0	0.0	0.0	4.3
			A+B 200	2			2											0.01	1.0	0.0	0.0	0.0	4.2
POSITIVE:	MMC	0.300 µg/ml	A 25	5			6	2	4		2	1						0.60	40.0	20.0	0.0	0.0	1.2
			B 25	1	1		3	2	3		1							0.36	32.0	4.0	0.0	0.0	2.2
			A+B 50	6	1		9	4	7		3	1						0.48	36.0*	12.0*	0.0	0.0	1.7
TEST ARTICLE		125 µg/ml	A 100	6														0.00	0.0	0.0	0.0	0.0	3.7
			B 100	3	1													0.00	0.0	0.0	0.0	0.0	4.5
			A+B 200	9	1													0.00	0.0	0.0	0.0	0.0	4.1
		250 µg/ml	A 100															0.00	0.0	0.0	0.0	0.0	4.0
			B 100				1											0.01	1.0	0.0	0.0	0.0	4.4
			A+B 200				1											0.01	0.5	0.0	0.0	0.0	4.2
		500 µg/ml	A 100	6	1													0.00	0.0	0.0	0.0	0.0	4.0
			B 100	3														0.00	0.0	0.0	0.0	0.0	3.1
			A+B 200	9	1													0.00	0.0	0.0	0.0	0.0	3.6
		900 µg/ml	A 100	3	1													0.00	0.0	0.0	0.0	0.0	1.4
			B 100	4				1										0.01	1.0	0.0	0.0	0.0	1.6
			A+B 200	7	1			1										0.01	0.5	0.0	0.0	0.0	1.5
		1200 µg/ml**	A+B 0																				1.1
		1600 µg/ml**	A+B 0																				0.3
		2000 µg/ml**	A+B 0																				0.3

RPMI 1640 = Culture medium MMC = Mitomycin C * Significantly greater than the solvent controls, $p<0.01$.
** Chromosome aberrations not analyzed due to excessive toxicity.

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TABLE 4
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 46.0 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: -S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	1			3											0.03	2.0	1.0	0.0	0.0	5.3
			B 100	2			1	1										0.02	2.0	0.0	0.0	0.0	4.5
			A+B 200	3			4	1										0.03	2.0	0.5	0.0	0.0	4.9
SOLVENT:	Water	10.0 µl/ml	A 100				2											0.02	2.0	0.0	0.0	0.0	6.0
			B 100	2			1	1										0.02	2.0	0.0	0.0	0.0	4.8
			A+B 200	2			3	1										0.02	2.0	0.0	0.0	0.0	5.4
TEST ARTICLE		62.5 µg/ml*	A+B 0																				5.6
		125 µg/ml	A 100	5			1											0.01	1.0	0.0	0.0	0.0	6.3
			B 100	6														0.00	0.0	0.0	0.0	0.0	6.0
			A+B 200	11			1											0.01	0.5	0.0	0.0	0.0	6.2
		250 µg/ml	A 100	5														0.00	0.0	0.0	0.0	0.0	5.4
			B 100	4														0.00	0.0	0.0	0.0	0.0	7.2
			A+B 200	9														0.00	0.0	0.0	0.0	0.0	6.3
		500 µg/ml	A 100	4			1	1										0.02	2.0	0.0	0.0	0.0	5.9
			B 100	5	1													0.00	0.0	0.0	0.0	0.0	5.6
			A+B 200	9	1		1	1										0.01	1.0	0.0	0.0	0.0	5.8
		900 µg/ml	A 100	4	1		1											0.01	1.0	0.0	0.0	0.0	1.9
			B 100	4														0.00	0.0	0.0	0.0	0.0	2.4
			A+B 200	8	1		1											0.01	0.5	0.0	0.0	0.0	2.2
		1200 µg/ml**	A+B 0																				0.4
		1600 µg/ml**	A+B 0																				0.1
		2000 µg/ml**	A+B 0																				0.1

RPMI 1640 = Culture medium

* Chromosome aberrations not analyzed due to higher doses available for analysis.

** Chromosome aberrations not analyzed due to excessive toxicity.

TABLE 5
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.0 Hours After Treatment

Assay No.: 17073 Trial #: 1 Date: 08/07/96 Lab #: CY8066 Metabolic Activation: +S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS NEGATIVE:	RPMI 1640		A 100	1	1													0.00	0.0	0.0	0.0	0.0	4.8
			B 100															0.00	0.0	0.0	0.0	0.0	5.0
			A+B 200	1	1													0.00	0.0	0.0	0.0	0.0	4.9
SOLVENT:	Water	10.0 µl/ml	A 100	3			2											0.02	2.0	0.0	0.0	0.0	6.8
			B 100	3	1													0.00	0.0	0.0	0.0	0.0	5.2
			A+B 200	6	1		2											0.01	1.0	0.0	0.0	0.0	6.0
POSITIVE:	CP	50.0 µg/ml*	A 25	4			7	1		2	3							0.52	44.0	8.0	0.0	0.0	1.7
			B 25	4	5		14	1		2	3	2						0.88	52.0	28.0	0.0	0.0	1.2
			A+B 50	8	5		21	2		4	6	2						0.70	48.0*	18.0*	0.0	0.0	1.5
TEST ARTICLE		253 µg/ml**	A+B 0																				5.1
		505 µg/ml	A 100	2														0.00	0.0	0.0	0.0	0.0	4.7
			B 100	2														0.00	0.0	0.0	0.0	0.0	4.9
			A+B 200	4														0.00	0.0	0.0	0.0	0.0	4.8
		1010 µg/ml	A 100															0.00	0.0	0.0	0.0	0.0	4.2
			B 100	6														0.00	0.0	0.0	0.0	0.0	5.9
			A+B 200	6														0.00	0.0	0.0	0.0	0.0	5.1
		1510 µg/ml	A 100	4	1		3											0.03	2.0	1.0	1.0	0.0	3.1
			B 100	7	1		1											0.01	1.0	0.0	1.0	0.0	3.7
			A+B 200	11	2		4											0.02	1.5	0.5	1.0	0.0	3.4
		2010 µg/ml	A 100	2			1											0.01	1.0	0.0	0.0	0.0	1.1
			B 100	7	2		1											0.01	1.0	0.0	0.0	0.0	1.7
			A+B 200	9	2		2											0.01	1.0	0.0	0.0	0.0	1.4
		2510 µg/ml***	A+B 0																				0.3

RPMI 1640 = Culture medium CP = Cyclophosphamide

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

[a] Due to toxicity, only 83 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 6
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.1 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: +S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLI-CATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	T	GT						
CONTROLS																								
NEGATIVE:	RPMI 1640		A 100	8														0.00	0.0	0.0	0.0	0.0	4.5
			B 100	6				1										0.01	1.0	0.0	0.0	0.0	4.7
			A+B 200	14				1										0.01	0.5	0.0	0.0	0.0	4.6
SOLVENT:	Water	10.0 µl/ml	A 100	3			2									1		0.03	3.0	0.0	0.0	0.0	4.1
			B 100	5	2													0.00	0.0	0.0	0.0	0.0	3.6
			A+B 200	8	2		2									1		0.02	1.5	0.0	0.0	0.0	3.9
POSITIVE:	CP	50.0 µg/ml***	A 25	4	2		7		2		1							0.40	32.0	8.0	0.0	0.0	0.7
			B 25	5	1		6	2			1							0.36	36.0	0.0	0.0	0.0	0.3
			A+B 50	9	3		13	2	2		2							0.38	34.0*	4.0	0.0	0.0	0.5
TEST ARTICLE		250 µg/ml	A 100	5	1	1												0.00	0.0	0.0	0.0	0.0	4.4
			B 100	2	1													0.00	0.0	0.0	0.0	0.0	4.2
			A+B 200	7	2	1												0.00	0.0	0.0	0.0	0.0	4.3
		500 µg/ml	A 100	3			1											0.01	1.0	0.0	0.0	0.0	2.1
			B 100	5	1		2											0.02	2.0	0.0	1.0	0.0	4.4
			A+B 200	8	1		3											0.02	1.5	0.0	0.5	0.0	3.3
		1000 µg/ml	A 100	7			1											0.01	1.0	0.0	0.0	0.0	3.6
			B 100	7			1											0.01	1.0	0.0	0.0	0.0	3.8
			A+B 200	14			2											0.01	1.0	0.0	0.0	0.0	3.7
		1500 µg/ml	A 100	9	2		2	1										0.03	2.0	1.0	0.0	0.0	1.2
			B 100	10			4											0.04	4.0	0.0	1.0	0.0	1.1
			A+B 200	19	2		6	1										0.04	3.0	0.5	0.5	0.0	1.2
		2000 µg/ml**	A+B 0																				0.7
		2500 µg/ml**	A+B 0																				0.1
		3000 µg/ml**	A+B 0																				0.0

RPMI 1640 = Culture medium CP = Cyclophosphamide

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to excessive toxicity.

*** Due to toxicity, only 56 metaphases from the A culture and 36 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 7
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 46.0 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: +S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS NEGATIVE:	RPMI 1640		A 100	3														0.00	0.0	0.0	1.0	0.0	8.0
			B 100	2			1											0.01	1.0	0.0	0.0	0.0	8.1
			A+B 200	5			1											0.01	0.5	0.0	0.5	0.0	8.1
SOLVENT:	Water	10.0 µl/ml	A 100	1	1		1											0.01	1.0	0.0	0.0	0.0	6.3
			B 100	3			1											0.01	1.0	0.0	0.0	0.0	6.9
			A+B 200	4	1		2											0.01	1.0	0.0	0.0	0.0	6.6
TEST ARTICLE		250 µg/ml**	A+B 0																				7.7
		500 µg/ml	A 100	3														0.00	0.0	0.0	1.0	0.0	7.8
			B 100	1	1													0.00	0.0	0.0	0.0	0.0	8.1
			A+B 200	4	1													0.00	0.0	0.0	0.5	0.0	8.0
		1000 µg/ml	A 100	3														0.00	0.0	0.0	0.0	0.0	6.4
			B 100	2			1											0.01	1.0	0.0	1.0	0.0	7.7
			A+B 200	5			1											0.01	0.5	0.0	0.5	0.0	7.1
		1500 µg/ml	A 100	4														0.00	0.0	0.0	1.0	1.0	5.6
			B 100	9	1		1											0.01	1.0	0.0	1.0	0.0	5.5
			A+B 200	13	1		1											0.01	0.5	0.0	1.0	0.5	5.6
		2000 µg/ml[a]	A 52	2	2		1	1										0.04	3.8	0.0	0.0	7.4	0.8
			B 148	2			2			1	1							0.03	2.0	0.7	0.0	5.2	1.8
			A+B 200	4	2		3	1		1	1							0.03	2.5	0.5	0.0	6.3*	1.3
		2500 µg/ml***	A+B 0																				0.0
		3000 µg/ml***	A+B 0																				0.0

RPMI 1640 = Culture medium

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

[a] Due to toxicity, only 54 metaphases from the A culture and 58 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 8

CONTROL DATA OF CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
4-95 THROUGH 12-95

	Activation		# Of Aberrations Per Cell	% Of Cells With Aberrations	% Of Cells With >1 Aberration	% Poly-ploidy	% Endore-duplicated Cells	% Mitotic Index
Negative Control								
	Without	MIN	0.00	0.0	0.0	0.0	0.0	0.4
		MAX	0.06	2.5	0.5	1.0	1.0	7.1
		AVG	0.012	0.72	0.06	0.18	0.03	3.57
		N	18	18	18	17	35	18
Solvent Control								
	Without	MIN	0.00	0.0	0.0	0.0	0.0	0.5
		MAX	0.06	2.5	0.5	1.0	2.0	10.9
		AVG	0.011	0.78	0.05	0.14	0.10	4.52
		N	29	29	29	18	35	29
Positive Control Mitomycin C	Without	MIN	0.02	1.5	0.0	0.0	0.0	0.1
		MAX	0.60	39.5	15.0	0.0	0.0	6.6
		AVG	0.267	22.22	3.63	0.00	0.00	2.46
		N	19	19	19	11	31	19
Negative Control								
	With	MIN	0.00	0.0	0.0	0.0	0.0	0.6
		MAX	0.03	2.0	0.5	1.0	0.5	9.6
		AVG	0.010	0.75	0.06	0.28	0.02	4.68
		N	18	18	18	17	27	18
Solvent Control								
	With	MIN	0.00	0.0	0.0	0.0	0.0	0.5
		MAX	0.02	2.0	0.5	2.0	0:0	10.7
		AVG	0.009	0.66	0.05	0.25	0.00	6.13
		N	28	28	28	17	27	28
Positive Control Cyclophosphamide	With	MIN	0.28	21.7	0.0	0.0	0.0	0.1
		MAX	2.52	40.0	40.0	1.0	0.0	5.9
		AVG	0.647	31.45	12.90	0.22	0.00	1.35
		N	17	17	17	9	25	17

15.0 DEFINITIONS OF CHROMOSOME ABERRATIONS FOR GIEMSA STAINED CELLS

SIMPLE

TB	Chromatid Break:	An achromatic region in one chromatid, larger than the width of a chromatid. The associated fragment may be partially or completely displaced.
SB	Chromosome Break:	Chromosome has a clear break, forming an abnormal (deleted) chromosome with an acentric fragment that is dislocated. This classification now includes the acentric fragment (AF). An AF is different from a SB only in that it can not be related to any specific chromosome.
DM	"Double Minute" Fragment:	These are small double dots, which may represent terminal or interstitial deletions, or even small rings. These possible origins are not distinguishable.

COMPLEX

ID	Interstitial Deletion:	Length of chromatid "cut out" from midregion of a chromatid, resulting in a small fragment or ring lying beside a shortened chromatid or a gap in the chromatid.
TR	Triradial:	An exchange between two chromosomes, or one chromosome and an acentric fragment, which results in a three-armed configuration.
QR	Quadriradial:	An exchange like a triradial, but resulting in a four-armed configuration.
CR	Complex Rearrangement:	An exchange among more than two chromosomes or fragments, caused by the induction of several breaks.
D	Dicentric:	An exchange between two chromosomes which results in a chromosome with two centromeres. This is often associated with an acentric fragment in which case it is classified as DF.
DF		Dicentric with fragment.

COMPLEX (Continued)

TC	Tricentric:	An exchange involving three chromosomes and resulting in a chromosome with three centromeres. Often associated with two to three AF. Such exchanges can involve many chromosomes and are named as follows:
QC	Quadricentric:	four centromeres, up to four AF
PC	Pentacentric:	five centromeres, up to five AF
HC	Hexacentric:	six centromeres, up to six AF
R	Ring:	A chromosome which forms a circle containing a centromere. This is often associated with an acentric fragment, in which case it is classed as RF.
RC	Ring Chromatid:	Single chromatid ring (acentric).
RF		Ring with associated acentric fragment.
CI	Chromosome Intrachange:	Exchange within a chromosome; e.g., a ring that does not include the entire chromosome.
T	Translocation:	Obvious transfer of material between two chromosomes resulting in two abnormal chromosomes. When identifiable, scored as "T" not "2AB".
AB	Abnormal:	Abnormal monocentric chromosome. This is a chromosome whose morphology is abnormal for the karyotype, and often the result of a translocation, pericentric inversion, etc. Classification used if abnormality cannot be ascribed to, e.g., a reciprocal translocation.

OTHER

GT	Greater than Ten:	Greater than 10 aberrations: A cell which contains more than 10 aberrations. Heavily damaged cells will be analyzed to identify the types of aberrations because multiple fragments, such as those found associated with a tricentric, do not count as independent aberrations.
PP	Polyploid Cell:	A cell containing multiple copies of the haploid number (n) of chromosomes.
E	Endoreduplication:	A failure of chromosomes to separate, resulting in a 4n cell.

NOT COMPUTED

TG	Chromatid Gap:	("tid gap"). An achromatic (unstained) region in one chromatid, the size of which is equal to or smaller than the width of a chromatid. These are noted but not usually included in final totals of aberrations as they may not all be true breaks.
SG	Chromosome Gap:	("isochromatid gap, IG"). Same as chromatid gap but at the same locus in both sister chromatids.
UC	Uncoiled Chromosome:	Failure of chromatin packing. Probably not a true aberration.

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MUTAGENICITY TEST ON

T-6342

MEASURING CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY (CHO) CELLS: WITH A CONFIRMATORY ASSAY WITH MULTIPLE HARVESTS

FINAL REPORT

AUTHOR

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LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17073-0-437CO

SUBMITTED TO

3M Corporation
Building 220-2E-02 3M Center
St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

September 16, 1996

000295

QUALITY ASSURANCE STATEMENT

Project Title: Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: With a Confirmatory Assay With Multiple Harvests

Project No.: 20990 Assay No.: 17073

Protocol No.: 437CO Edition No.: 4, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Dosing-09/06/1995	09/06/1995	M. Murphy
Draft Report Review-11/06,07/1995	11/07/1995	C. Orantes, K. Newland
Revised Draft Report Review-01/04/1996	01/04/1996	C. Orantes
Final Report Review-09/16/1996	09/16/1996	C. Orantes

Arthur L. Orantes 9/16/96

Quality Assurance Unit Date Released

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Food and Drug Administration (FDA) Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) with any applicable amendments . There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

Hemalatha Murli

Hemalatha Murli, Ph.D.
Mammalian Cytogenetics
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9/16/96

Study Completion Date

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ABSTRACT

The objective of this in vitro assay was to evaluate the ability of T-6342 to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells with and without metabolic activation.

For the dose rangefinding assay with and without metabolic activation, the test article was dissolved in sterile deionized water at a concentration of 498 mg/ml. Concentrations of 0.166, 0.498, 1.66, 4.98, 16.6, 49.8, 166, 498, 1660, and 4980 µg/ml were tested in the dose rangefinding assays. All dosing was achieved using a dosing volume of 1% (10 µl/ml). In the nonactivation assay, complete cytotoxicity was observed in the culture dosed with 4980 µg/ml, and reductions of 100% in the mitotic index as compared with the solvent control cultures were observed in the culture dosed with 1660 µg/ml. In the activation assay, reductions of 19%, 33%, 27%, and 63% as compared with the solvent control cultures were observed in the cultures dosed with 166, 498, 1660, and 4980 µg/ml, respectively.

Based on the data from the dose rangefinding assay, replicate cultures of CHO cells were incubated with 125, 250, 500, 750, 1000, 1500, and 2000 µg/ml without metabolic activation and with 250, 500, 1250, 2500, 3750, and 5000 µg/ml with metabolic activation in 20.0 hour aberrations assays. Cultures treated with 750, 1000, 1500, and 2000 µg/ml without metabolic activation and with 1250, 2500, 3750, and 5000 µg/ml with metabolic activation were analyzed for chromosomal aberrations. No significant increase in cells with chromosomal aberrations was observed in the nonactivation assay. A significant increase in cells with chromosomal aberrations was observed in the cultures dosed with 3750 and 5000 µg/ml with metabolic activation.

In the confirmatory trial, replicate cultures of CHO cells were incubated with 125, 249, 498, 746, 995, 1490, and 1990 µg/ml without metabolic activation and with 249, 498, 1250, 2490, 3730, and 4970 µg/ml with metabolic activation in 20.0 and 44.1 hour assays. Cultures treated with 746, 995, 1490, and 1990 µg/ml from the 20.0 hour assay and with 249, 498, 746 and 995 µg/ml from the 44.1 hour assay without metabolic activation, and with 1250, 2490, 3730, and 4970 µg/ml from the 20.0 and 44.1 hour assays with metabolic activation were analyzed for chromosomal aberrations. No significant increase in cells with chromosomal aberrations was observed in the nonactivation assay. A significant increase in cells with chromosomal aberrations was observed in the cultures dosed with 4970 µg/ml in the 20.0 hour assay with metabolic activation. A significant increase in percent polyploidy was observed in the cultures dosed with 4970 µg/ml in the 44.1 hour assay with metabolic activation. This positive response was investigated under nonactivation conditions by treating cells for 3 hours under the same conditions as the assay with metabolic activation.

In this repeat trial, replicate cultures of CHO cells were incubated with 250, 500, 1250, 2490, 3740, and 4980 µg/ml without metabolic activation for 3 hours and harvested 20.0 and 44.0 hours after initiation of treatment. Cultures treated with 250, 500, 1250 and 2490 µg/ml from the 20.0 hour assay and with 500, 1250, 2490, and 3740 µg/ml from the 44.0 hour assay were analyzed for chromosomal aberrations. No significant increase in cells with chromosomal aberrations was observed in the 20.0 hour assay. A weakly significant increase in cells with chromosomal aberrations was observed in the cultures dosed with 3740 µg/ml in the 44.0 hour assay. A significant increase in percent polyploidy was observed in the cultures dosed with 3740 µg/ml in the 44.0 hour assay.

The test article, T-6342, was considered weakly positive for inducing chromosomal aberrations in CHO cells without metabolic activation with a three hour treatment. T-6342 was considered positive for inducing chromosomal aberrations in CHO cells with metabolic activation. T-6342 was considered positive for inducing polyploidy with and without metabolic activation.

Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells: With a Confirmatory Assay With Multiple Harvests With T-6342

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (TEST ARTICLE):

2.1 Client's Identification: T-6342

2.2 Date Received: July 21, 1995

2.3 Physical Description: Clear, colorless liquid

2.4 Genetics Assay No.: 17073

3.0 TYPE OF ASSAY: Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells

4.0 PROTOCOL NO.: 437CO, Edition 4, Modified for 3M Corporation

5.0 STUDY DATES:

5.1 Initiation Date: August 15, 1995

5.2 Experimental Start Date: August 24, 1995

5.3 Experimental Termination Date: December 04, 1995

6.0 SUPERVISORY PERSONNEL:

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Carol S. Spicer, B.S.

7.0 OBJECTIVE:

The objective of this in vitro assay was to evaluate the ability of the test article, T-6342, to induce chromosomal aberrations in Chinese hamster ovary (CHO) cells, with and without metabolic activation.

8.0 RATIONALE:

The assay is designed to establish whether the test article or its metabolites can interact with cells to induce chromosome breaks. Chemically induced lesions may result in breaks in chromatin that are either repaired by the cell in such a way as to be undetectable or result in visible damage. Aberrations are a consequence of failure in repair processes such that breaks do not rejoin or rejoin in abnormal configurations (Evans, 1962).

9.0 EXPERIMENTAL DESIGN:

Results from the rangefinding assay were used to determine the dose range to be used in the chromosomal aberrations assay. In the rangefinding assay, the cultures were harvested 20.0 hours after initiation of treatment. Mitotic index and visual observations of the cultures were evaluated for evidence of toxicity. A summary of the treatment schedule for the rangefinding assay is given below.

Summary of Rangefinding Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
- S9	0	17.8	17.9	20
+ S9	0	3	17.9	20

In the chromosomal aberrations assays, replicate cultures were used at each dose level, and negative and solvent controls. Single cultures were used for each of two doses of the positive control. The aberrations assays were conducted with a 20.0 hour harvest time in the initial trial and with 20.0 and 44.1 hour harvest times in the confirmatory trials. Chromosomal aberrations were analyzed from the cultures treated at four dose levels and from only one of the positive control doses. A summary of the treatment schedule for the chromosomal aberrations assays is on the following page.

Summary of Chromosomal Aberrations Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
Initial Trial				
- S9	0	17.8	18	20
+ S9	0	3	18	20
Confirmatory Trial				
- S9	0	17.6	18	20
+ S9	0	3	17.9	20
- S9	0	41.8	42.1	44.1
+ S9	0	3	42.1	44.1
Repeat Trial				
- S9	0	3	18	20
- S9	0	3	42	44

10.0 MATERIALS AND METHODS:

10.1 Test Cells:

The Chinese hamster ovary cells (CHO-WBL) used in this assay were from a permanent cell line and were originally obtained from the laboratory of Dr. S. Wolff, University of California, San Francisco. The cells have since been recloned to maintain karyotypic stability. This cell line has an average cycle time of 12 to 14 hours with a modal chromosome number of 21.

10.2 Cell Culture Medium:

The CHO cells were grown in McCoy's 5a culture medium which was supplemented with 10 % fetal bovine serum (FBS), 1% L-glutamine, and 1% penicillin and streptomycin, at approximately 37°C, in an atmosphere of about 5% CO_2 in air.

10.3 Negative and Solvent Controls:

In the nonactivation assays, negative controls were cultures which contained only cells and culture medium. Solvent controls were cultures containing the solvent for the test article at the highest concentration used in test cultures. In the activation assays, the negative and solvent controls were the same as described in the nonactivation assays but with the S9 activation mix included.

10.4 Positive Control Agents:

The positive control agents which were used in the assays were mitomycin C (MMC) for the nonactivation series and cyclophosphamide (CP) in the metabolic activation series. Mitomycin C (CAS# 50-07-7, Sigma, Lot # 25H0619) is a clastogen that does not require metabolic activation. Cyclophosphamide (CAS # 6055-19-2, Sigma, Lot # 67F0155) does not act directly but must be converted to active intermediates by microsomal enzymes. In the chromosomal aberrations assays, two concentrations of MMC (0.08 and 0.10 µg/ml, initial and confirmatory trials; 0.50 and 1.0 µg/ml, third trial) and CP (5.0 and 10.0 µg/ml) were used to induce chromosomal aberrations in the CHO cells. One of the dose levels was analyzed in each of the aberration assays. Both MMC and CP were dissolved in water.

10.5 Rangefinding Assays:

In these assays, the cells were cultured for approximately 24 hours prior to treatment by seeding approximately 0.3 x 10^6 cells per 25 cm^2 flask into 5 ml of complete McCoy's 5a culture medium.

10.5.1 Assay Without Metabolic Activation:

The cultures were incubated with the test article for 17.8 hours at ≈37°C. Then, the test article was washed from the cells with phosphate buffered saline and fresh complete medium containing Colcemid® (final concentration 0.1 µg/ml) was added. The cultures were then trypsinized and harvested 2.0 hours later. (See Sections on Harvest and Slide Preparation and Staining).

10.5.2 Assay With Metabolic Activation:

In this assay, the CHO cells were exposed to the test article for three hours

at ≈37°C in the presence of a rat liver S9 reaction mixture (S9 15 µl/ml, NADP 1.5 mg/ml, and isocitric acid 2.7 mg/ml). The S9 fraction (Molecular Toxicology, Inc., Lot #0583) was derived from the liver of male Sprague-Dawley rats which had been previously treated with Aroclor 1254 to induce the mixed function oxidase enzymes which are capable of metabolizing chemicals to more active forms. The three hour incubation time was used because prolonged exposure to the S9 mixture might be toxic to the cells and the enzyme activity of S9 is lost rapidly at about 37°C. The medium did not have FBS during the exposure period to avoid possible inactivation of short lived and highly reactive intermediates produced by the S9 enzymes by binding to serum proteins.

After the exposure period the cells were washed twice with buffered saline. Complete McCoy's 5a medium was added to the cultures which were then incubated for 16.8 hours with Colcemid® (final concentration 0.1 µg/ml) added for the last 2.0 hours to collect metaphase cells. The cultures were then trypsinized, harvested, fixed, and slides were prepared and stained as was described for the nonactivation rangefinding assay.

10.5.3 Assay Evaluation:

Mitotic index was analyzed from the highest five surviving dose levels by analyzing the number of metaphases present in 1000 consecutive cells.

10.6 Aberrations Assay Without Metabolic Activation:

Cultures were initiated by seeding approximately 1.2 x 10^6 cells (20.0 hour assay) and 0.8 X 10^6 cells (≈44.0 hour assay) per 75 cm^2 flask into 10 ml of complete McCoy's 5a medium. One day after culture initiation, for the initial and confirmatory trials, the cells were incubated at ≈37°C with the test article at predetermined doses for about 17.7 (20.0 hour assay) and 41.8 (44.1 hour assay) hours. The cultures were then washed with buffered saline and complete McCoy's 5a medium containing 0.1 µg/ml Colcemid® was placed back onto the cells. Approximately two hours later, the cells were harvested and air dried slides were made. The slides were then stained in 5 % Giemsa solution for the analysis of chromosomal aberrations. For the third trial, one day after culture initiation, the cultures were incubated at ≈37°C for three hours in the presence of the test article in McCoy's 5a medium without FBS. After the three hour exposure period the cells were washed twice with buffered saline and the cells were refed with complete McCoy's 5a medium. The cells were incubated for the rest of the

culture period up to the time of harvest with 0.1 µg/ml Colcemid® present during the last ≈2.0 hours of incubation. The metaphase cells were then harvested and prepared for cytogenetic analysis.

10.7 Aberrations Assay With Metabolic Activation:

Cultures were initiated by seeding approximately 1.2 x 10^6 cells (20.0 hour assay) and 0.8 X 10^6 cells (44.1 hour assay) per 75 cm^2 flask into 10 ml of complete McCoy's 5a medium. One day after culture initiation, the cultures that were treated under the conditions of metabolic activation were incubated at ≈37°C for three hours in the presence of the test article and the S9 reaction mixture in McCoy's 5a medium without FBS. After the three hour exposure period the cells were washed twice with buffered saline and the cells were refed with complete McCoy's 5a medium. The cells were incubated for the rest of the culture period up to the time of harvest with 0.1 µg/ml Colcemid® present during the last ≈2.0 hours of incubation. The metaphase cells were then harvested and prepared for cytogenetic analysis.

10.8 Harvest Procedure:

Prior to the harvest of the cultures, visual observations of toxicity were made. These observations included an assessment of the percent confluence of the cell monolayer within the culture flasks. The cultures were also evaluated for the presence of mitotic (large rounded cells) or dead cells floating in the medium. The cultures from the dose rangefinding assay were trypsinized first to collect mitotic and interphase cells and were treated with 0.075 M KCL hypotonic solution. This treatment helps to swell the cells and thus disperse the chromosomes. The cultures were then fixed with an absolute methanol: glacial acetic acid (3:1, v:v) fixative and were washed several times before air-dried slides were prepared.

10.9 Slide Preparation and Staining:

Slides were prepared by dropping the harvested cultures on clean slides. The slides were stained with 5% Giemsa solution for the analysis of mitotic index and chromosomal aberrations. All slides were then air-dried and cover slipped using Depex® mounting medium.

10.10 Aberrations Analysis and Assay Evaluation:

Cells were selected for good morphology and only cells with the number of centromeres equal to the modal number 21 ± 1 (range 20-22) were analyzed.

One hundred cells, if possible, from each replicate culture at four dose levels of the test article and from the negative and solvent control cultures were analyzed for the different types of chromosomal aberrations (Evans, 1962; See Section 15.0). At least 25 cells were analyzed for chromosomal aberrations from one of the positive control cultures. For control of bias, all slides except for the positive controls were coded prior to analysis. Cells with aberrations were recorded on the data sheets by the microscope stage location. Mitotic index was assessed by analyzing the number of mitotic cells in 1000 cells and the ratio was expressed as a percentage of mitotic cells.

The following factors were taken into account in the evaluation of the chromosomal aberrations data:

1. The percentage of cells with any aberrations.

2. The percentage of cells with more than one aberration.

3. Any evidence for increasing amounts of damage with increasing dose, i.e., a positive dose response.

Chromatid and isochromatid gaps, if observed, were noted in the raw data and were tabulated. They were not, however, considered in the evaluation of the ability of the test article to induce chromosomal aberrations since they may not represent true chromosomal breaks and may possibly be induced by toxicity. Percent polyploidy was analyzed from the ≈44.0 hour assay and results were tabulated. Historical control data are presented in Table 10.

A cell classified as "GT" is considered to contain 10 aberrations for statistical purposes but a ">" is also included in the tables for this classification to indicate that it is a minimum number.

Statistical analysis employed the Fisher's Exact Test with an adjustment for multiple comparisons (Sokal and Rohlf, 1981) to compare the percentage of cells with aberrations in each treatment group with the results from the solvent controls. A linear trend test of increasing number of cells with aberrations with

increasing dose (Armitage, 1971) was also performed. Test article significance was established where $p<0.01$. All factors as stated previously were taken into account and the final evaluation of the test article was based upon scientific judgement.

11.0 RESULTS:

11.1 Solubility and Dose Determination

T-6342 was described as being freely soluble in water, so its solubility for this study was evaluated in sterile deionized water (Lot #17, prepared 06/16/95 at CHV). A clear, colorless solution was obtained at a concentration of 498 mg/ml. This solution was diluted to 1% (10 µl/ml) in McCoy's 5a culture medium in the absence of any cells. At a concentration of 4980 µg/ml in culture medium, the test article remained completely soluble and a pH of 7.5 was determined. Sterile deionized water was therefore chosen as an appropriate vehicle for this assay. A stock concentration of 498 mg/ml and dilutions thereof were prepared for dosing the rangefinding assays. All dosing was achieved with a 1% (10 µl/ml) dosing of each stock solution, and the solvent control culture was dosed with 10 µl/ml of sterile deionized water. Concentrations of 0.166, 0.498, 1.66, 4.98, 16.6, 49.8, 166. 498, 1660, and 4980 µg/ml were tested in the rangefinding assays with and without the S9 metabolic activation system.

The stability of the test article under the preparation and dosing conditions used in this assay is the responsibility of the Sponsor.

11.2 Rangefinding Assay Without Metabolic Activation

In the culture treated with 4980 µg/ml, no visible mitotic cells were observed; the cell monolayer was <5% confluent, and the culture consisted only of debris and dead cells, floating or attached. A severe reduction in the number of visible mitotic cells was observed in the culture dosed with 1660 µg/ml. The cell monolayer looked unhealthy and the degree of confluency was reduced about 15%; floating dead cells and debris were noted. Floating debris also was observed in the culture dosed with 498 µg/ml, but the culture otherwise was similar to the negative control.

Mitotic indices were analyzed from the cultures dosed with 16.6, 49.8, 166, 498, and 1660 µg/ml (Table 1) and compared to the solvent control. At 1660 µg/ml, the mitotic index was essentially zero. However, little or no reduction in mitotic

index was observed at the next lowerdose of 498 µg/ml. Based on these results, the first trial of the chromosomal aberrations assay without metabolic activation was conducted with a 20 hour harvest at test article concentrations of 125, 250, 500, 750, 1000, 1500, and 2000 µg/ml in order to ensure a wide toxicity range.

11.3 Rangefinding Assay With Metabolic Activation

With S9 metabolic activation, an unhealthy cell monolayer was observed in the culture dosed with 4980 µg/ml. The cell monolayer confluence was reduced by approximately 85%, and a severe reduction in the number of visible mitotic cells occurred (about 63%, Table 1). At the next lower dose of 1660 µg/ml, the monolayer confluence was the same as the solvent control, and the mitotic index was only somewhat reduced (about 27%). Based on these results, the initial aberrations assay with metabolic activation was conducted with a 20 hour harvest at test article concentrations of 250, 500, 1250, 2500, 3750 and 5000 µg/ml.

11.4 Chromosomal Aberrations Assay Without Metabolic Activation

Initial Trial

Chromosomal aberrations were analyzed from the cultures dosed with 750, 1000, 1500, and 2000 µg/ml (Table 2). No significant increases in cells with chromosomal aberrations were observed for the cultures analyzed.

This assay covered a wide range of toxicity. Unhealthy cell monolayers, floating dead cells and debris, severe loss of visible mitotic cells, and about 25% reduction in cell monolayer confluence were observed in the cultures dosed with 1500 and 2000 µg/ml. Slightly unhealthy cell monolayers, floating dead cells and debris, a reduction in the number of visible mitotic cells, and about 15% reduction in cell monolayer confluence were observed in the cultures dosed with 1000 µg/ml. At the lowest analyzed dose of 750 µg/ml, the cell monolayers appeared to be almost normal, with only a slight reduction in the number of visible mitotic cells and about a 15% reduction in the degree of confluence. Severe reductions in mitotic index relative to the solvent control cultures occurred at all dose levels, eg., 95%, 86%, 67%, and 57% at 2000, 1500, 1000, and 750 µg/ml, respectively.

Based on the toxicities obtained in this trial, the confirmatory trial of the nonactivation aberrations assay was conducted at test article concentrations of 125, 249, 498, 746, 995, 1490, and 1990 µg/ml, using two harvest times of 20 and 44.1 hours.

Confirmatory Trial

For the 20 hour harvest, chromosomal aberrations were analyzed from the cultures dosed with 746, 995, 1490, and 1990 µg/ml (Table 3). No significant increases in cells with chromosomal aberrations were observed for any of the cultures analyzed. As obtained in the first trial, the toxicity range was wide, ranging from a severe 95% reduction in mitotic index at 1990 µg/ml to 25% reduction at 746 µg/ml. The cell monolayer confluence was reduced by about 25% at 1990 µg/ml, and only 83 metaphases could be scored from one of the replicate cultures. To compensate, 117 metaphases were scored from the replicate culture, in order to score a total of 200 metaphases for this dose.

For the 44.1 hour harvest, chromosomal aberrations were analyzed from the cultures dosed with 249, 498, 746, and 995 µg/ml (Table 4). Again, no significant increases in cells with chromosomal aberrations were observed for any of the cultures analyzed. The percent polyploidy is scored at this harvest time, and no significant increases were noted. The concentrations of test article were lower relative to the 20 hour harvest because the longer exposure time caused greater toxicity. The two highest applied doses of 1990 µg/ml and 1490 µg/ml were lethal. Treatment with 995 µg/ml was severely toxic, resulting in about 40% reductions in monolayer confluence and 79% reduction in mitotic index. At 746 µg/ml, however, the toxicity was much less (about 15% reduction in confluency and 18% reduction in mitotic index compared to the solvent control cultures).

The results obtained from the two assay trials in the absence of an S9 metabolic activation system appeared to show the lack of any clastogenic activity by the test article. However, in another assay having an exposure time of only 3 hours, the induction of chromosomal aberrations was demonstrated (see Section 11.6).

11.5 Chromosomal Aberrations Assay With Metabolic Activation

Initial Trial

Chromosomal aberrations were analyzed from the cultures dosed with 1250, 2500, 3750, and 5000 µg/ml in the presence of the rat liver S9 metabolic activation system (Table 5). Significant increases in cells with chromosomal aberrations were observed in the cultures dosed with 3750 and 5000 µg/ml. The treatment with 3750 µg/ml was only slightly toxic, but the 5000 µg/ml treatment was highly toxic, causing about 95% reduction in monolayer confluency for one culture and

about 75% reduction for the replicate culture. Floating dead cells and debris were abundant, and only 94 metaphases were analyzable from the culture with greater toxicity. However, the mitotic index was reduced by only 13% compared to the solvent control cultures.

Based on these results, the confirmatory trial was conducted with essentially the same test article concentrations, using two harvest times of 20 and 44.1 hours.

Confirmatory Trial

For the 20 hour harvest, a significant increase in cells with chromosomal aberrations was observed only for the cultures dosed with 4970 µg/ml (Table 6). This toxic treatment reduced the confluency by about 70% and caused a 43% reduction in the mitotic index. The treatment with 3730 µg/ml was much less toxic, causing about 30% reduction in confluency and 18% reduction in mitotic index. Even though the treatment with 3730 µg/ml appeared to be somewhat more toxic than the similar dose in the initial trial, there was no hint of any clastogenic activity. Therefore, only the highly toxic treatment at the dose limit of the assay (5000 µg/ml) induced a repeatable, but large, increase in percent cells with chromosomal aberrations. In both trials, both simple and complex aberrations were observed.

For the 44.1 hour harvest, chromosomal aberrations were analyzed from the cultures dosed with 498, 1250, 2490, and 3730 µg/ml (Table 7). No significant increases in cells with chromosomal aberrations were observed for any of the cultures analyzed. Although the 4970 µg/ml treatment was too toxic to yield sufficient metaphases for analysis, it was nevertheless noted that the percent polyploid cells increased significantly. At 3730 µg/ml, there was little or no toxicity evident.

The successful activation by the metabolic system was illustrated by the large increase in percent cells with chromosomal aberrations (at 20 hours harvest) in the cultures exposed to cyclophosphamide, the positive control article, which requires metabolic activation to become clastogenic.

The initial interpretation of these results was that the test article was converted to clastogenic substance(s) in the presence of the S9 metabolic activation system. However, according to information provided by the Sponsor, the test article is not metabolized. The appearance of clastogenic activity in the activation portion of the assay was not in doubt, but this activity should also have been observed under

nonactivation conditions if the S9 system had no effect on the test article. This situation raised the possibility that an unrecognized toxicity in the nonactivation assay was actually eliminating the cells with induced aberrations before the cultures were analyzed. The treatment periods under nonactivation conditions were only about 2 hours less than the harvest times, whereas the test article was removed after 3 hours exposure for the activation assays. If the continued presence of the test article was causing the demise of cells with induced aberrations, then the aberrations should be observable if the treatment time was made equivalent to the activation assay, ie, reduced to 3 hours. Accordingly, the nonactivation assay was repeated, using a 3 hour exposure period.

11.6 Chromosomal Aberrations Assay Without Metabolic Activation; 3-Hour Treatment

The positive response observed in the assay with metabolic activation was investigated by treating cells under the same conditions without metabolic activation. Cells were treated for 3 hours at test article concentrations of 250, 500, 1250, 2490, 3740, and 4980 µg/ml, using harvest times of 20 and 44 hours after the initiation of treatment.

For the 20 hour harvest, chromosomal aberrations were analyzed from the cultures dosed with 250, 500, 1250, and 2490 µg/ml (Table 8). No significant increases in cells with chromosomal aberrations were observed. Unfortunately, these treatments were not very toxic (about 30% reduction in confluency at 2490 µg/ml), and the next higher dose of 3740 µg/ml was so toxic that only a small number of metaphases could be examined. As footnoted in the table, 7 of 38 metaphases obtained from the replicate cultures had chromosomal aberrations. Thus, approximately 18% of the cells were indicated as having aberrations. Due to the severe depression of mitotic index, the percent cells with aberrations likely would have been higher at a longer harvest time. Obviously, much closer dose steps would have been necessary to achieve toxicities comparable to the activation assays and to compare the observable clastogenic responses.

It is interesting to note that the test article was clearly more toxic for the 3 hour treatment period than when the S9 activation system was present. Genotoxic events (mutation or chromosomal changes) are necessarily associated with toxicity, and the metabolism of test articles to clastogenic substances is therefore expected to be accompanied by increased toxicity, not less toxicity. Thus, the observation of more toxicity in the absence of S9 was very suggestive that the

controlling factor in observing clastogenic activity for this test article was the attainment of a certain high toxicity for a short time period, and not the metabolic conversion of the test article.

For the 44 hour harvest, chromosomal aberrations were analyzed from the cultures dosed with 500, 1250, 2490, and 3740 µg/ml (Table 9). A small, but significant 7.5% of cells with chromosomal aberrations was observed in the cultures dosed with 3740 µg/ml. A significant increase in percent polyploidy also was observed in these cultures. The 3740 µg/ml treatment resulted in about 55% reduction in monolayer confluency relative to the solvent controls, and the 2490 µg/ml treatment gave about 30% reduction. The mitotic index was also significantly reduced (57%) for the high dose.

These results were consistent with the interpretation that a highly toxic treatment with this test article, applied for a short period of time, will give rise to cells containing chromosomal aberrations that can be observed in the 20 or 44 hour time period after initiation of treatment. The harvest time for the observation of maximum numbers of aberrant cells was not determined. The addition of S9 to the cultures simply reduced the test article toxicity, so that finer adjustments in the dose levels than achieved in this study are necessary to make comparisons between equi-toxic treatments under activation and nonactivation assay conditions. The initial observations of clastogenic activity only in the presence of the S9 activation system can be interpreted to be a consequence of a more limited toxic action over 3 hours exposure, compared to the long exposures for the standard nonactivation assays, rather than being due to a metabolic effect. The test article is therefore evaluated as clastogenic only for highly toxic treatments for short enough exposure periods (eg, 3 hours) such that the cells containing chromosome aberrations do not disintegrate before they can be observed at 20 to 44 hour harvest times.

12.0 CONCLUSION:

The test article, T-6342, was evaluated as being clastogenic to cultured CHO cells for highly toxic treatments of short duration (eg., 3 hours) both in the presence and absence of an S9 metabolic activation system. Polyploidy was also induced for the highly toxic treatments.

13.0 REFERENCES:

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Sokal, R.R., and Rohlf, F.J.: Biometry, Ed. 2, W.H. Freeman and Company, New York, 1981.

14.0 EXPERIMENTAL DATA TABLES

TABLE 1

RANGEFINDING ASSAY FOR ASSESSING TOXICITY

Compound: T-6342

Assay No.: 17073 Trial No.: I Date: 08/24/95

Metabolic Activation: -S9 Lab No.: CY8225

Treatment				% Mitotic Index	Confluence[a] % Solvent Control
NEGATIVE CONTROL	McCoy's 5a			9.8	100
SOLVENT CONTROL	Water	10.0	µl/ml	2.0	100
TEST ARTICLE		16.6	µg/ml	5.4	100
		49.8	µg/ml	9.7	100
		166	µg/ml	9.1	100
		498	µg/ml	9.2	100
		1660**	µg/ml	0.0	85

Metabolic Activation: +S9 Lab No.: CY8225 Trial No.:I

Treatment				% Mitotic Index	Confluence[a] % Solvent Control
NEGATIVE CONTROL	McCoy's 5a			14.8	100
SOLVENT CONTROL	Water	10.0	µl/ml	17.1	100
TEST ARTICLE		49.8	µg/ml	17.3	100
		166	µg/ml	13.9	100
		498	µg/ml	11.5	100
		1660	µg/ml	12.5	100
		4980	µg/ml	6.3	14

[a] This endpoint is based upon visual observations which are made prior to the harvest of the metaphase cells. Actual cell counts are not taken and any hypertrophy of the attached cells cannot be evaluated. At the time of the confluence observation the flasks are also evaluated for the appearance of floating mitotic cells and dead cells.

** Toxic dose level.

TABLE 2
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.0 Hours After Treatment

Assay No.:17073 Trial #:1 Lab #: CY9055 Metabolic Activation:-S9

Compound:T-6342 Date:09/06/95

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% MITOTIC INDEX
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																						
NEGATIVE:	McCoy's 5a		A	100	2	1								1					0.01	1.0	0.0	4.4
			B	100	3														0.00	0.0	0.0	5.6
			A+B	200	5	1								1					0.01	0.5	0.0	5.0
SOLVENT:	Water	10.0µl/ml	A	100	2									1					0.01	1.0	0.0	8.6
			B	100	2	1													0.00	0.0	0.0	7.2
			A+B	200	4	1								1					0.01	0.5	0.0	7.9
POSITIVE:	MMC	0.08µg/ml	A	25	9		2	7	5			3							0.60	28.0*	8.0**	4.5
TEST ARTICLE		750µg/ml	A	100	2	1								1					0.01	1.0	0.0	3.5
			B	100	4														0.00	0.0	0.0	3.3
			A+B	200	6	1								1					0.01	0.5	0.0	3.4
		1000µg/ml	A	100	8	1													0.00	0.0	0.0	2.5
			B	100	4														0.00	0.0	0.0	2.6
			A+B	200	12	1													0.00	0.0	0.0	2.6
		1500µg/ml	A	100	4														0.00	0.0	0.0	1.4
			B	100										2					0.02	2.0	0.0	0.7
			A+B	200	4									2					0.01	1.0	0.0	1.1
		2000µg/ml	A	100															0.00	0.0	0.0	0.3
			B	100	4														0.00	0.0	0.0	0.4
			A+B	200	4														0.00	0.0	0.0	0.4

* Significantly greater than the solvent controls, $p<0.01$
** Significantly greater than the solvent controls, $p<0.05$

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TABLE 3
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.0 Hours After Treatment

Assay No.:17073 Trial #:2 Lab #: CY9155 Metabolic Activation:-S9

Compound:T-6342 Date:09/13/95

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% MITOTIC INDEX
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																						
NEGATIVE:	McCoy's 5a		A	100	8	1											1		0.01	1.0	0.0	6.1
			B	100	8			1						1					0.02	2.0	0.0	6.4
			A+B	200	16	1		1						1			1		0.02	1.5	0.0	6.3
SOLVENT:	Water	10.0µl/ml	A	100	7	1		1											0.01	1.0	0.0	7.4
			B	100	1	2													0.00	0.0	0.0	8.3
			A+B	200	8	3		1											0.01	0.5	0.0	7.9
POSITIVE:	MMC	0.100µg/ml	A	25	3			6	1		7	4		2	1		1		0.88	52.0*	24.0*	4.2
TEST ARTICLE		746µg/ml	A	100	3				1					1					0.02	2.0	0.0	5.8
			B	100	4									1					0.01	1.0	0.0	6.0
			A+B	200	7				1					2					0.02	1.5	0.0	5.9
		995µg/ml	A	100	9			1						1			1		0.03	3.0	0.0	2.3
			B	100	1	1		1											0.01	1.0	0.0	2.1
			A+B	200	10	1		2						1			1		0.02	2.0	0.0	2.2
		1490µg/ml	A	100	3			1						1					0.02	2.0	0.0	0.6
			B	100	4	1	1							1					0.01	1.0	0.0	1.3
			A+B	200	7	1	1	1						2					0.02	1.5	0.0	1.0
		1990µg/ml	A	83	4	1	1		1										0.01	1.2	0.0	0.2
			B	117	12	1	1												0.00	0.0	0.0	0.4
			A+B	200	16	2	2		1										0.01	0.5	0.0	0.3

* Significantly greater than the solvent controls, p<0.01

C00319

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TABLE 4

CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS

Cells Fixed 44.1 Hours After Treatment

Assay No.:17073 Trial #:2 Lab #: CY9155 Metabolic Activation:-S9

Compound:T-6342 Date:09/13/95

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% POLY-PLOIDY	% MITOTIC INDEX
			CELLS SCORED		TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT					
CONTROLS																							
NEGATIVE:	McCoy's 5a		A	100	3	2								1					0.00	0.0	0.0	0.0	4.4
			B	100		1													0.01	1.0	0.0	2.0	4.9
			A+B	200	3	3								1					0.01	0.5	0.0	1.0	4.7
SOLVENT:	Water	10.0µl/ml	A	100	3														0.00	0.0	0.0	4.0	3.4
			B	100	2	1		1									1		0.02	2.0	0.0	1.0	3.3
			A+B	200	5	1		1									1		0.01	1.0	0.0	2.5	3.4
TEST ARTICLE		249µg/ml	A	100	4	2								3		1			0.04	3.0	1.0	0.0	5.1
			B	100	2	2								2	1				0.03	3.0	0.0	2.0	4.8
			A+B	200	6	4								5	1	1			0.04	3.0	0.5	1.0	5.0
		498µg/ml	A	100	4	2								1					0.01	1.0	0.0	0.0	4.2
			B	100	2	1													0.00	0.0	0.0	0.0	2.8
			A+B	200	6	3								1					0.01	0.5	0.0	0.0	3.5
		746µg/ml	A	100	3	1		2						1	2				0.05	4.0	1.0	2.0	2.5
			B	100	5									1	1				0.02	2.0	0.0	2.0	3.0
			A+B	200	8	1		2						2	3				0.04	3.0	0.5	2.0	2.8
		995µg/ml	A	100	2	1		1	1					1					0.03	3.0	0.0	5.0	0.9
			B	100	3									1					0.01	1.0	0.0	4.0	0.5
			A+B	200	5	1		1	1					2					0.02	2.0	0.0	4.5	0.7

C00320

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TABLE 5
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 20.0 Hours After Treatment

Assay No.: 17073 Trial #: 3 Lab #: CY11275 Metabolic Activation: -S9

Compound: T-6342 Date: 11/28/95

					NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% MITOTIC INDEX
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																							
NEGATIVE:	McCoy's 5a		A	100	2	1								1					0.01	1.0	0.0	7.9
			B	100	2			1											0.01	1.0	0.0	7.8
			A+B	200	4	1		1						1					0.01	1.0	0.0	7.9
SOLVENT:	Water	10.0µl/ml	A	100	2									3					0.03	3.0	0.0	5.2
			B	100		1		1						1	1				0.03	3.0	0.0	7.4
			A+B	200	2	1		1						4	1				0.03	3.0	0.0	6.3
POSITIVE:	MMC	0.500µg/ml	A	25	5	3		6	1	2	6	4				1			0.80	64.0*	16.0*	7.2
TEST ARTICLE		250µg/ml	A	100										3					0.03	3.0	0.0	8.9
			B	100	2										1				0.01	1.0	0.0	7.6
			A+B	200	2									3	1				0.02	2.0	0.0	8.3
		500µg/ml	A	100	2	1					1			3					0.04	4.0	0.0	10.2
			B	100				1						3					0.04	4.0	0.0	10.7
			A+B	200	2	1		1			1			6					0.04	4.0	0.0	10.5
		1250µg/ml	A	100	4									1					0.01	1.0	0.0	16.9
			B	100	1	1								1					0.01	1.0	0.0	12.3
			A+B	200	5	1								2					0.01	1.0	0.0	14.6
		2490µg/ml	A	100	2	1			1					1					0.02	2.0	0.0	6.3
			B	100	10			2						2			1		0.05	5.0	0.0	3.1
			A+B	200	12	1		2	1					3			1		0.04	3.5	0.0	4.7
		3740µg/ml**	A	0																		0.3
			B	0																		0.5
			A+B	0																		0.4

* Significantly greater than the solvent controls, $p<0.01$.

** Toxic dose level. Very few metaphases on slides. 5/20 and 2/18 metaphases from cultures A and B, respectively, had chromosomal aberrations.

C00321

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TABLE 6
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 44.0 Hours After Treatment

Assay No.: 17073 Trial #: 3 Lab #: CY11275 Metabolic Activation: -S9

Compound: T-6342 Date: 11/28/95

					NUMBER AND TYPE OF ABERRATION																			
						NOT COMPUTED			SIMPLE		COMPLEX								OTHER					
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% POLY-PLOIDY	% MITOTIC INDEX
CONTROLS																								
NEGATIVE:	McCoy's 5a		A	100	2	1		1						2		1			0.04	4.0	0.0	1.0	8.5
			B	100		2			1			1		1	2				0.05	4.0	1.0	2.0	7.5
			A+B	200	2	3		1	1			1		3	2	1			0.05	4.0	0.5	1.5	8.0
SOLVENT:	Water	10.0µl/ml	A	100	3	1								2	1				0.03	3.0	0.0	2.0	9.8
			B	100	1			1											0.01	1.0	0.0	3.0	8.2
			A+B	200	4	1		1						2	1				0.02	2.0	0.0	2.5	9.0
TEST ARTICLE		500µg/ml	A	100	2	3													0.00	0.0	0.0	2.0	9.5
			B	100	3									2	1				0.03	3.0	0.0	1.0	9.7
			A+B	200	5	3								2	1				0.02	1.5	0.0	1.5	9.6
		1250µg/ml	A	100	5	1													0.00	0.0	0.0	1.0	9.7
			B	100	2									1					0.01	1.0	0.0	3.0	9.9
			A+B	200	7	1								1					0.01	0.5	0.0	2.0	9.8
		2490µg/ml	A	100	3	1		1						1					0.02	2.0	0.0	3.0	6.3
			B	100	2			1	1					1					0.03	3.0	0.0	2.0	5.6
			A+B	200	5	1		2	1					2					0.03	2.5	0.0	2.5	6.0
		3740µg/ml	A	100	6			1						2				1	>0.13	4.0	1.0	37.0	4.3
			B	100	6			1	2					5	1			2	>0.29	11.0	2.0	12.0	3.4
			A+B	200	12			2	2					7	1			3	>0.21	7.5**	1.5	24.5*	3.9

* Significantly greater than the solvent controls, $p<0.01$.
** Significantly greater than the solvent controls, $p<0.05$.

C00322

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TABLE 7

CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS

Cells Fixed 20.0 Hours After Treatment

Assay No.:17073 Trial #:1 Lab #: CY9055 Metabolic Activation:+S9

Compound:T-6342 Date:09/06/95

					NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX									OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% MITOTIC INDEX
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																							
NEGATIVE:	McCoy's 5a		A	100	1	4								1					0.01	1.0	0.0	10.0
			B	100	2	1		1	1					1					0.03	2.0	1.0	7.8
			A+B	200	3	5		1	1					2					0.02	1.5	0.5	8.9
SOLVENT:	Water	10.0µl/ml	A	100	2	1		1										1	0.11	2.0	1.0	9.1
			B	100	2	1		1	1		1								0.03	3.0	0.0	8.6
			A+B	200	4	2		2	1		1							1	0.07	2.5	0.5	8.9
POSITIVE:	CP	5.00ng/ml	A	25	9			12	4	1	2	7	1					2	1.88	56.0*	48.0*	2.8
TEST ARTICLE		1250µg/ml	A	100		1		2	1	1									0.04	1.0	1.0	10.5
			B	100	3	1						1		1					0.02	2.0	0.0	9.1
			A+B	200	3	2		2	1	1		1		1					0.03	1.5	0.5	9.8
		2500µg/ml	A	100	2			4		1					1				0.06	4.0	1.0	11.2
			B	100		4	1	2	1		1	2		1					0.07	6.0	1.0	10.6
			A+B	200	2	4	1	6	1	1	1	2		1	1				0.07	5.0	1.0	10.9
		3750µg/ml	A	100	13	4		6		1	3	3	1	1	1	5			0.21	11.0	6.0	10.5
			B	100	5		1	5	2	2	6	11	1	2		2			0.31	18.0	8.0	11.1
			A+B	200	18	4	1	11	2	3	9	14	2	3	1	7			0.26	14.5*	7.0*	10.8
		5000µg/ml	A	94	29	4	2	17	4	2	4	6	4	1	2	4		1	0.57	25.5	12.8	4.3
			B	106	23	2		14	3	4	10	21	4	4	2	11			0.69	36.8	17.0	11.1
			A+B	200	52	6	2	31	7	6	14	27	8	5	4	15		1	0.64	31.5*	15.0*	7.7

* Significantly greater than the solvent controls, $p<0.01$

C00323

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TABLE 8

CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS

Cells Fixed 20.0 Hours After Treatment

Assay No.:17073 Trial #:2 Lab #: CY9155 Metabolic Activation:+S9

Compound:T-6342 Date:09/13/95

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% MITOTIC INDEX
				CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT				
CONTROLS																						
NEGATIVE:	McCoy's 5a		A	100	2									3					0.03	2.0	1.0	17.0
			B	100	5	2													0.00	0.0	0.0	11.2
			A+B	200	7	2								3					0.02	1.0	0.5	14.1
SOLVENT:	Water	10.0µl/ml	A	100	4			1	1						1				0.03	3.0	0.0	13.3
			B	100	6		1												0.00	0.0	0.0	13.3
			A+B	200	10		1	1	1						1				0.02	1.5	0.0	13.3
POSITIVE:	CP	5.00ng/ml	A	25	11	4	3	4	3		1	1	1			2			0.48	36.0*	8.0**	4.7
TEST ARTICLE		1250µg/ml	A	100	6	1								2	1				0.03	2.0	1.0	12.8
			B	100	2		2		2										0.02	2.0	0.0	9.0
			A+B	200	8	1	2		2					2	1				0.03	2.0	0.5	10.9
		2490µg/ml	A	100	2	1								1	1				0.02	2.0	0.0	13.1
			B	100	5										1				0.01	1.0	0.0	15.6
			A+B	200	7	1								1	2				0.02	1.5	0.0	14.4
		3730µg/ml	A	100	9			1	1										0.02	2.0	0.0	13.6
			B	100	9	1	1					1							0.01	1.0	0.0	13.8
			A+B	200	18	1	1	1	1			1							0.02	1.5	0.0	13.7
		4970µg/ml	A	75	29	1	2	17	9	2	9	10	1	2	1	8			0.79	41.3	28.0	8.3
			B	75	32	3		17	2	3	10	19	4	2		5			0.83	44.0	24.0	6.9
			A+B	150	61	4	2	34	11	5	19	29	5	4	1	13			0.81	42.7*	26.0*	7.6

* Significantly greater than the solvent controls, $p<0.01$

** Significantly greater than the solvent controls, $p<0.05$

C00324

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TABLE 9
CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
Cells Fixed 44.1 Hours After Treatment

Assay No.:17073 Trial #:2 Lab #: CY9155 Metabolic Activation:+S9

Compound:T-6342 Date:09/13/95

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH>1 ABERRATIONS	% POLY-PLOIDY	% MITOTIC INDEX
			CELLS SCORED		TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT					
CONTROLS NEGATIVE:	McCoy's 5a		A	100	3		1		1					1					0.01	1.0	0.0	1.0	6.1
			B	100	2														0.01	1.0	0.0	2.0	6.5
			A+B	200	5		1		1					1					0.01	1.0	0.0	1.5	6.3
SOLVENT:	Water	10.0µl/ml	A	100	2	2			1										0.01	1.0	0.0	0.0	5.6
			B	100	2	2		1	1					3					0.05	5.0	0.0	3.0	4.3
			A+B	200	4	4		1	2					3					0.03	3.0	0.0	1.5	5.0
TEST ARTICLE		498µg/ml	A	100	6		1	2	1					1					0.04	3.0	1.0	0.0	4.2
			B	100	4	1								1					0.01	1.0	0.0	2.0	5.0
			A+B	200	10	1	1	2	1					2					0.03	2.0	0.5	1.0	4.6
		1250µg/ml	A	100	3										1				0.00	0.0	0.0	2.0	5.1
			B	100	5	2									1				0.01	1.0	0.0	2.0	4.4
			A+B	200	8	2									1				0.01	0.5	0.0	2.0	4.6
		2490µg/ml	A	100	1	2		1						1					0.02	2.0	0.0	4.0	5.2
			B	100	6	2			1										0.01	1.0	0.0	2.0	5.6
			A+B	200	7	4		1	1					1					0.02	1.5	0.0	3.0	5.4
		3730µg/ml	A	100	2	2		2			1								0.03	2.0	1.0	6.0	6.4
			B	100	3	1		1											0.01	1.0	0.0	4.0	5.8
			A+B	200	5	3		3			1								0.02	1.5	0.5	5.0	6.1
		4970µg/ml**	A	0																		15.0	0.8
			B	0																		26.0	2.1
			A+B	0																		20.5*	1.5

* Significantly greater than the solvent controls, $p<0.01$
** Toxic dose level.

C00321
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TABLE 10

CONTROL DATA OF CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS
6/95 THROUGH 8/95

	Activation		# Of Aberrations Per Cell	% Of Cells With Aberrations	% Of Cells With >1 Aberrations
Negative Control					
	Without	MIN	0.00	0.0	0.0
		MAX	0.06	4.0	0.5
		AVG	0.015	1.19	0.07
		N	35	35	35
Solvent Control					
	Without	MIN	0.00	0.0	0.0
		MAX	0.03	2.0	0.5
		AVG	0.010	0.74	0.04
		N	35	35	35
Positive Control Mitomycin C					
	Without	MIN	0.14	14.0	0.0
		MAX	2.88	68.0	60.0
		AVG	0.553	31.38	11.38
		N	26	26	26
Negative Control					
	With	MIN	0.00	0.0	0.0
		MAX	0.03	3.0	1.0
		AVG	0.014	1.10	0.09
		N	34	34	34
Solvent Control					
	With	MIN	0.00	0.0	0.0
		MAX	0.12	7.0	4.0
		AVG	0.020	1.44	0.29
		N	34	34	34
Positive Control Cyclophosphamide					
	With	MIN	0.36	24.0	8.0
		MAX	4.28	88.0	72.0
		AVG	1.299	51.20	30.40
		N	25	25	25

CONTROL DATA OF POLYPLOIDY IN CHINESE HAMSTER OVARY CELLS 4/95 THROUGH 9/95

		Without Activation	With Activation
Negative Control			
	MIN	0.00	0.0
	MAX	4.00	4.0
	AVG	0.540	0.63
	N	46	46
Solvent Control			
	MIN	0.00	0.0
	MAX	2.00	3.0
	AVG	0.430	0.50
	N	58	58

15.0 DEFINITIONS OF CHROMOSOME ABERRATIONS FOR GIEMSA STAINED CELLS

NOT COMPUTED

TG	Chromatid gap:	("tid gap"). An achromatic (unstained) region in one chromatid, the size of which is equal to or smaller than the width of a chromatid. These are noted but not usually included in final totals of aberrations as they may not all be true breaks.
SG	Chromosome gap:	("isochromatid gap, IG"). Same as chromatid gap but at the same locus in both sister chromatids.
UC	Uncoiled chromosome:	Failure of chromatin packing. Probably not a true aberration.
PP	Polyploid cell:	A cell containing multiple copies of the haploid number (n) of chromosomes. Not counted in the cells scored for aberrations.
E	Endoreduplication:	4n cell in which separation of chromosome pairs has failed. Not counted in the cells scored for aberrations.

SIMPLE

TB	Chromatic break:	An achromatic region in one chromatid, larger than the width of a chromatid. The associated fragment may be partially or completely displaced.
SB	Chromosome break:	Chromosome has a clear break, forming an abnormal (deleted) chromosome with an acentric fragment that is dislocated.
DM	"Double Minute " fragment:	These are small double dots, some of which are terminal deletions and some interstitial deletions and probably small rings. Their origins are not distinguishable.

COMPLEX

ID	Interstitial deletion:	Length of chromatid "cut out" from midregion of a chromatid resulting in a small fragment of ring lying beside a shortened chromatid of a gap in the chromatid.
TR	Triradial:	An exchange between two chromosomes, or one chromosome and an acentric fragment, which results in a three-armed configuration.
QR	Quadri radial:	As triradial, but resulting in a four-armed configuration.
D	Dicentric:	An exchange between two chromosomes which results in a chromosome with two centromeres. This is often associated with an acentric fragment in which case it is classified as DF.
DF		Dicentric with fragment.
TC	Tricentric:	An exchange between three chromosomes which results in a chromosome with three centromeres. Often associated with two to three AF. Such exchanges can involve many chromosomes and are named as follows:
QC	Quadricentric:	four centromeres, up to four AF
PC	Pentacentric:	five centromeres, up to five AF
HC	Hexacentric:	six centromeres, up to six AF
R	Ring	A chromosome which forms a circle containing a centromere. This is often associated with an acentric fragment in which case it is classed as RF.
RC	Ring Chromatid:	Single chromatid ring (acentric).
RF		Ring with associated acentric fragment.

CI	Chromosome Intrachange:	Exchange within a chromosome; e.g., a ring that does not include the entire chromosome.
T	Translocation:	Obvious transfer of material between two chromosomes resulting in two abnormal chromosomes. When identifiable, scored as "T" not "2Ab."
AB		Abnormal monocentric chromosome. This is a chromosome whose morphology is abnormal for the karyotype, and often the result of a translocation, pericentric inversion, etc. Classification used if abnormality cannot be ascribed to; e.g., a reciprocal translocation.
Other		
GT/>		A cell which contains more than 10 aberrations. A heavily damaged cell should be analyzed to identify the types of aberrations and may not actually have >10, e.g., multiple fragments such as those found associated with a tricentric.

MUTAGENICITY TEST ON

T-6342

IN AN *IN VIVO* MOUSE MICRONUCLEUS ASSAY

FINAL REPORT

AUTHOR

Hemalatha Murli, Ph.D.

PERFORMING LABORATORY

Corning Hazleton Inc. (CHV)
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LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17073-0-455

SUBMITTED TO

3M Corporation
Building 220-2E-02, 3M Center
St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

December 14, 1995

QUALITY ASSURANCE STATEMENT

Project Title: *In Vivo* Mouse Micronucleus Assay

Project No.: 20996 Assay No.: 17073

Protocol No.: 455 Edition No.: 17, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Randomization of Animals/09/18/1995	09/18/1995	S. Ballenger
Draft report Review/10/31/1995	10/31/1995	C. Orantes
Final Report Review/12/14/1995	12/14/1995	C. Orantes

Quality Assurance Unit 12/14/95 Date Released

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Food and Drug Administration (FDA), Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

Hemalatha Murli, Ph.D.
Mammalian Cytogenetics
Department of Genetic and Cellular Toxicology

Study Completion Date

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SUMMARY

Mutagenicity Test on T-6342 in an *In Vivo* Mouse Micronucleus Assay

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-6342, to induce micronuclei in bone marrow polychromatic erythrocytes of Crl:CD-1®(ICR) BR mice.

In the dose selection study, the test article was solubilized in deionized water and dosed by oral gavage at 500, 1625, 2750, 3875, and 5000 mg/kg. Six animals (three males and three females) were assigned to each dose group. Animals were observed for three days after dosing for toxic signs and/or mortality .

Based on the results of the dose selection study, the maximum tolerated dose was estimated as >5000 mg/kg. In the micronucleus assay, the test article was solubilized in deionized water and dosed by oral gavage at 1250, 2500, and 5000 mg/kg. Ten animals (five males and five females) were randomly assigned to each dose/harvest time group. Vehicle and positive control groups euthanatized approximately 24 hours after dosing were included in the assay. The animals dosed with the test article were euthanatized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow.

The test material, T-6342, did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes under the conditions of this assay and is considered negative in the mouse bone marrow micronucleus test.

Mutagenicity Test on T-6342 in an *in vivo* Mouse Micronucleus Assay

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (Test Article)

2.1 Client's Identification: T-6342

2.2 Date Received: July 21, 1995

2.3 Physical Description: Clear, colorless liquid

2.4 Genetics Assay No.: 17073

3.0 TYPE OF ASSAY: *In Vivo* Mouse Micronucleus Assay

4.0 PROTOCOL NO.: 455, Edition 17, Modified for 3M Corporation

5.0 STUDY DATES

5.1 Initiation Date: August 15, 1995

5.2 Experimental Start Date: August 29, 1995

5.3 Experimental Termination Date: October 16, 1995

6.0 SUPERVISORY PERSONNEL

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Monica Vegarra, B.S.

7.0 OBJECTIVE

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-6342, to induce micronuclei in bone marrow polychromatic erythrocytes of Crl:CD-1®(ICR) BR mice. This study was conducted using modifications of the procedures suggested by Heddle et al. (1983).

8.0 MATERIALS

Adult male and female mice, strain Crl:CD-1®(ICR) BR, were purchased from Charles River Laboratories, Portage MI.. This healthy, random bred strain was selected to maximize genetic heterogeneity and at the same time assure access to a common source. The protocol for this study was approved by the CHV-ACUC prior to the initiation of dosing.

Animals were housed up to seven per cage during quarantine, and housed up to five per cage at randomization. The temperature and relative humidity were maintained at 72±6°F and 55±15%, respectively. A 12-hour light/12-hour dark cycle was maintained. A commercial diet (Purina® Certified Laboratory Pellets ® # 5002) and water were available ad libitum for the duration of the study. The feed was analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, organophosphates, and specified nutrients. The water was analyzed on a retrospective basis for specified microorganisms, pesticides, alkalinity, heavy metals, and halogens. Sanitized caging was used for housing the animals. Personnel handling animals or working within the animal facilities were required to wear suitable protective garments and equipment.

Animals were quarantined for seven before being placed on study. Animals were randomly assigned to study groups and were individually weighed prior to dosing. All animals were dosed based upon the individual body weights. Animals were uniquely identified by ear tag. Dose or treatment groups were identified by cage card/label.

At the termination of the study all surviving animals were euthanatized by CO_2 inhalation, followed by penetration of the thorax. Any extra animals not used for the study were euthanatized by CO_2 inhalation, followed by penetration of the thorax.

9.0 SOLUBILITY AND STABILITY:

The test article, T-6342, was supplied as a clear colorless liquid. The vehicle selected for this assay was deionized water. The stability of the test material under the dosing conditions of this assay is the responsibility of the sponsor.

10.0 DOSE SELECTION STUDY

10.1 Dose Selection

Dose levels of 500, 1625, 2750, 3875, and 5000 mg/kg were administered by oral gavage for the dose selection study.

10.2 Dosing Information

The animals used in the dose selection assay were dosed on August 29, 1995. The weight range of the animals used in the dose range finding assay was 26.5 - 33.5 and 21.1 - 25.1 grams, for the males and females, respectively. Dosing solutions were prepared just prior to dosing and were prepared by making a 500 mg/ml stock for the high dose (5000 mg/kg). This was prepared by adding 6.6 ml of deionized water (Lot # 17, prepared at CHV) to 6.0007 g of T-6342, resulting in a clear, colorless solution . Dilutions of this stock were prepared for the other dose levels.

Dosing was achieved using a 10 ml/kg dosing volume. All animals were eight weeks and one day old at the time of dosing. An outline of the dosing scheme is found in the following table.

A total of 30 animals was used in this assay.

	DOSE GROUPS	
TREATMENT	M	F
T-6342		
500 mg/kg	3	3
1625 mg/kg	3	3
2750 mg/kg	3	3
3875 mg/kg	3	3
5000 mg/kg	3	3

All doses given were on an acute (one-time only) basis.

10.3 Results and Interpretation

All animals were examined after dosing and daily throughout the duration of the study (three days) for toxic effects and/or mortalities. All animals appeared normal immediately after dosing and remained healthy until the end of the observation period. The mortality data for this assay are summarized in the following table:

Summary of Mortalities Within 3 Days in Mice Dosed Acutely with T-6342

Observations

Treatment	Male	Female
500 mg/kg	0/3	0/3
1625 mg/kg	0/3	0/3
2750 mg/kg	0/3	0/3
3875 mg/kg	0/3	0/3
5000 mg/kg	0/3	0/3

10.4 Conclusion

Based on these results, the maximum tolerated dose was estimated to be >5000 mg/kg.

11.0 MICRONUCLEUS STUDY

11.1 Dose Selection

Based on results from the dose selection study, dose levels of 1250, 2500, and 5000 mg/kg were selected for this study.

11.2 Micronucleus Assay Dosing Information

The animals used in the micronucleus assay were dosed on September 19, 1995. Cyclophosphamide (Sigma, Lot # 43H0269, CAS # 6055-19-2), the positive control, was solubilized in sterile deionized water (Lot #17, prepared at CHV) and was administered by oral gavage at 80 mg/kg. The vehicle control, deionized water (Lot # 17, prepared at CHV), was administered concurrently with the test article at a volume of 10 ml/kg. The weight range of the animals used in the micronucleus assay was 28.7 - 37.6 g and 21.1 - 25.6 g grams for the males and females, respectively. The dosing solutions for the assay were prepared by making a 500 mg/ml stock for the high dose (5000 mg/kg). This was prepared by adding deionized water to 11.0008 g of T-6342 up to a volume of 22.0 ml. A clear, colorless solution was obtained. Dilutions of this stock were prepared for the remaining dose levels.

Ten animals (five males and five females) were randomly assigned to each dose/-harvest time group. Vehicle and positive control groups, euthanatized approximately 24 hours after dosing, were included in the assay. The animals dosed with the test article were euthanatized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow. An outline of the dosing scheme is found in the following table:

Dosing Scheme for Micronucleus Assay

A total of 110 animals was used in this assay

Treatment	Number of Animals Assigned					
	24 Hr		48 Hr		72 Hr	
	M	F	M	F	M	F
T-6342						
1250 mg/kg	5	5	5	5	5	5
2500 mg/kg	5	5	5	5	5	5
5000 mg/kg	5	5	5	5	5	5
Vehicle Control, deionized water 10 ml/kg	5	5	-	-	-	-
Positive Control, Cyclophosphamide, 80 mg/kg	5	5	-	-	-	-

The age of the animals at the time of dosing was eight weeks and one day. Volume dosed was 10 ml/kg and was based upon individual animal weight.

12.0 BONE MARROW HARVEST, SLIDE PREPARATION AND ANALYSIS

At the appropriate harvest time, the animals were euthanatized with CO_2 followed by penetration of the thorax and the adhering soft tissue and epiphyses of both femora were removed. The marrow was flushed from the bone and transferred to centrifuge tubes containing 3 - 5 ml bovine serum (one tube for each animal). Following centrifugation to pellet the tissue, the supernatant was removed by aspiration and portions of the pellet were spread on slides and air dried. The slides were fixed in methanol, and stained in May-Grunwald solution followed by Giemsa (Schmid, 1975). The air-dried slides were coverslipped using Depex® mounting medium.

The slides were coded for analysis, and scored for micronuclei and the polychromatic erythrocyte (PCE) to normochromatic erythrocyte (NCE) cell ratio. Standard forms were

used to record these data. One thousand PCEs per animal were scored. The frequency of micronucleated cells was expressed as percent micronucleated cells based on the total PCEs present in the scored optic field. The normal frequency of micronuclei in this Crl:CD-1®(ICR) BR strain is about 0.0-0.4%.

The frequency of PCEs versus NCEs was determined by scoring the number of PCEs and NCEs observed in the optic fields while scoring the first 1000 erythrocytes.

13.0 EVALUATION CRITERIA:

13.1 General

The criteria for the identification of micronuclei were those of Schmid (1976). Micronuclei were darkly stained and generally round, although almond and ringshaped micronuclei occasionally occurred. Micronuclei had sharp borders and were generally between 1/20 and 1/5 the size of the PCE. The unit of scoring was the micronucleated cell, not the micronucleus; thus the occasional cell with more than one micronucleus was counted as one micronucleated PCE, not two (or more) micronuclei. The staining procedure permitted the differentiation by color of PCEs and NCEs (bluish-grey and red, respectively).

13.2 Data Presentation and Interpretation

Data are summarized by sex and dose groups for the different time points. Individual animal data are also presented. The analysis of these data was performed using an analysis of variance (Winer, 1971) on either untransformed (when variances are homogeneous) and rank transformed (when variances are heterogeneous) proportions of cells with micronuclei per animal. If the analysis of variance was significant ($p<0.05$), a Dunnett's t-test (Dunnett, 1955; 1964) was used to determine which dose groups, if any, were significantly different from the negative control. Analyses were performed separately for each harvest time and sex combination. The criteria for determining a positive response involved a statistically significant dose-related increase in micronucleated PCEs, or the detection of a reproducible and statistically significant positive response for at least one dose level. A test article that induced neither a statistically significant dose response nor a statistically significant and reproducible increase at one dose level was considered negative. In either case, the final decision was based on scientific judgment.

14.0 RESULTS AND INTERPRETATION:

All animals were observed immediately after dosing and periodically throughout the duration of the assay for toxic symptoms and/or mortalities. All animals in the vehicle and positive control groups appeared normal after dosing and remained healthy until the appropriate harvest times. All animals from the 1250 and 2500 mg/kg dose groups appeared normal immediately after dosing and remained healthy until the appropriate harvest times.

Immediately after dosing, all animals in the 5000 mg/kg dose group appeared normal.

Approximately 24 hours after dosing, 2 males (#'s2712, 48 hour harvest group; 2714, 72 hour harvest group) from the 5000 mg/kg dose group were found dead. One male (#2718, 72 hour harvest group) appeared hunched and weak with squinted eyes. All other animals appeared normal at this time.

Approximately 48 hours after dosing, 1 male (#2718, 72 hour harvest group) and 1 female (#2780, 72 hour harvest group) from the 5000 mg/kg dose group were found dead. All other animals appeared normal at this time and remained healthy until the appropriate harvest times.

The test article, T-6342, induced no significant increases in micronucleated polychromatic erythrocytes over the levels observed in the vehicle controls in either sex or at any of the harvest times. Due to toxicity, the PCE/NCE ratios of the males and females from the 5000 mg/kg dose group at the 72 hour harvest group were significantly lower than the vehicle control animals. The positive control, CP, induced significant increases in micronucleated PCEs in both sexes as compared to the vehicle controls, with means and standard errors of 5.44% ± 0.37% and 2.50% ± 0.33% for the males and females, respectively. The data summarized by dose group are presented in Table 1 and individual animal data are found in Tables 2 through 7. Historical control data are presented in Table 8.

15.0 CONCLUSION:

The test material, T-6342, did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes under the conditions of this assay and is considered negative in the mouse micronucleus assay.

16.0 REFERENCES:

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17.0 EXPERIMENT DATA TABLES

TABLE 1
MICRONUCLEUS DATA SUMMARY TABLE

SPONSOR: 3M Corporation

TEST ARTICLE:T-6342

ASSAY:17073

TREATMENT	DOSE	HARVEST TIME (HR)	% MICRONUCLEATED PCEs MEAN OF 1000 PER ANIMAL ± S.E. MALES	FEMALES	TOTAL	RATIO PCE:NCE MEAN ± S.E. MALES	FEMALES
CONTROLS							
VEHICLE	Water	24 hr	0.14 ± 0.02	0.02 ± 0.02	0.08 ± 0.02	0.51 ± 0.06	0.69 ± 0.11
POSITIVE-CP	80.0 mg/kg	24 hr	5.44 ± 0.37*	2.50 ± 0.33*	3.97 ± 0.54*	0.64 ± 0.07	0.63 ± 0.05
TEST ARTICLE	1250 mg/kg	24 hr	0.28 ± 0.05	0.00 ± 0.00	0.14 ± 0.05	0.69 ± 0.09	0.75 ± 0.17
		48 hr	0.00 ± 0.00	0.02 ± 0.02	0.01 ± 0.01	0.68 ± 0.08	0.74 ± 0.06
		72 hr	0.06 ± 0.02	0.02 ± 0.02	0.04 ± 0.02	0.36 ± 0.08	0.59 ± 0.06
	2500 mg/kg	24 hr	0.12 ± 0.04	0.04 ± 0.02	0.08 ± 0.02	0.69 ± 0.07	0.64 ± 0.05
		48 hr	0.02 ± 0.02	0.02 ± 0.02	0.02 ± 0.01	0.79 ± 0.07	0.65 ± 0.01
		72 hr	0.20 ± 0.07	0.06 ± 0.04	0.13 ± 0.04	0.47 ± 0.07	0.64 ± 0.07
	5000 mg/kg	24 hr	0.06 ± 0.04	0.10 ± 0.04	0.08 ± 0.03	0.80 ± 0.08	0.79 ± 0.09
		48 hr	0.15 ± 0.09	0.06 ± 0.02	0.10 ± 0.04	0.56 ± 0.10	0.63 ± 0.06
		72 hr	0.17 ± 0.03	0.03 ± 0.03	0.09 ± 0.03	0.17 ± 0.04*	0.24 ± 0.05*

*Significantly different from the corresponding vehicle control, $p<0.05$.

TABLE 2
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
24 HOUR HARVEST	MALE				
VEHICLE CONTROL	Water		2682	1	0.32
			2689	2	0.54
			2694	1	0.48
			2720	2	0.66
			2721	1	0.52
POSITIVE CONTROL	CP 80.0	mg/kg	2696	46	0.79
			2698	61	0.80
			2715	52	0.53
			2723	65	0.58
			2728	48	0.49
TEST ARTICLE	1250	mg/kg	2683	4	0.67
			2691	1	0.78
			2697	3	0.98
			2703	3	0.45
			2717	3	0.59
	2500	mg/kg	2679	2	0.74
			2685	1	0.47
			2693	0	0.90
			2702	2	0.72
			2724	1	0.60
	5000	mg/kg	2676	0	0.51
			2684	0	0.90
			2709	1	0.81
			2713	0	0.98
			2727	2	0.78

MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 3
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
24 HOUR HARVEST	FEMALE				
VEHICLE CONTROL	Water		2741	0	0.76
			2744	1	0.76
			2773	0	0.70
			2776	0	0.27
			2779	0	0.94
POSITIVE CONTROL	CP 80.0	mg/kg	2734	31	0.78
			2746	17	0.71
			2749	29	0.62
			2760	17	0.54
			2783	31	0.48
TEST ARTICLE	1250	mg/kg	2735	0	1.03
			2742	0	1.25
			2750	0	0.69
			2771	0	0.39
			2781	0	0.39
	2500	mg/kg	2732	0	0.56
			2733	0	0.64
			2738	0	0.81
			2755	1	0.54
			2772	1	0.67
	5000	mg/kg	2743	0	0.92
			2757	0	0.56
			2761	2	0.83
			2763	2	1.04
			2768	1	0.61

MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 4
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
48 HOUR HARVEST	MALE				
TEST ARTICLE	1250	mg/kg	2680	0	0.44
			2681	0	0.54
			2695	0	0.77
			2705	0	0.77
			2710	0	0.89
	2500	mg/kg	2675	1	0.52
			2688	0	0.81
			2707	0	0.96
			2726	0	0.82
			2729	0	0.83
	5000	mg/kg	2677	1	0.32
			2699	1	0.64
			2700	4	0.47
			2708	0	0.79
			2712*		

*Animals found dead
MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 5
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
48 HOUR HARVEST	FEMALE				
TEST ARTICLE	1250	mg/kg	2730	0	0.94
			2736	0	0.62
			2747	1	0.74
			2754	0	0.75
			2775	0	0.64
	2500	mg/kg	2737	0	0.67
			2745	1	0.69
			2758	0	0.62
			2759	0	0.65
			2762	0	0.63
	5000	mg/kg	2739	1	0.43
			2753	0	0.78
			2756	1	0.68
			2767	1	0.67
			2770	0	0.61

MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 6
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
72 HOUR HARVEST	MALE				
TEST ARTICLE	1250	mg/kg	2678	0	0.26
			2687	1	0.30
			2716	1	0.17
			2719	1	0.51
			2722	0	0.56
	2500	mg/kg	2692	0	0.28
			2701	3	0.37
			2704	4	0.52
			2711	2	0.49
			2725	1	0.70
	5000	mg/kg	2686	1	0.11
			2690	2	0.16
			2706	2	0.26
			2714*		
			2718*		

*Animals found dead
MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 7
MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR:3M Corporation

TEST ARTICLE:T-6342

ASSAY NO.:17073

TREATMENT			ANIMAL NUMBER	NO.MN PCEs (1000)	RATIO PCE:NCE
72 HOUR HARVEST	FEMALE				
TEST ARTICLE	1250	mg/kg	2740	0	0.68
			2751	0	0.48
			2766	1	0.68
			2769	0	0.40
			2778	0	0.71
	2500	mg/kg	2748	1	0.68
			2752	0	0.45
			2764	0	0.54
			2774	0	0.85
			2777	2	0.66
	5000	mg/kg	2731	0	0.24
			2765	0	0.38
			2780*		
			2782	1	0.18
			2784	0	0.18

*Animals found dead
MN = Micronucleus
PCE = Polychromatic erythrocyte
No.MN PCEs = Micronucleated PCEs
NCE=Normochromatic erythrocyte

TABLE 8

MOUSE MICRONUCLEUS HISTORICAL CONTROL DATA 2/95 THROUGH 9/95

		% MICRONUCLEATED PCEs per 1000 PCE MEAN OF 1000 PER ANIMAL ± S.E.			RATIO PCE:NCE MEAN ± S.E.	
		MALES	FEMALES	TOTAL	MALES	FEMALES
POOLED VEHICLE CONTROL						
	MIN	0.00	0.00	0.01	0.32	0.34
	MAX	0.26	0.16	0.18	0.82	1.03
	AVG	0.08 ± 0.06	0.06 ± 0.04	0.07 ± 0.04	0.56 ± 0.13	0.61 ± 0.14
	N	49	49	49	49	49
POSITIVE CONTROL Cyclophosphamide, 80 mg/kg						
	MIN	1.72	1.50	1.81	0.44	0.44
	MAX	5.44	6.36	5.38	0.72	0.81
	AVG	3.25 ± 0.94	3.00 ± 1.05	3.13 ± 0.81	0.58 ± 0.09	0.62 ± 0.11
	N	22	22	22	22	22

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MUTAGENICITY TEST WITH

T-6342

IN THE *SALMONELLA - ESCHERICHIA COLI*/MAMMALIAN-MICROSOME REVERSE MUTATION ASSAY

FINAL REPORT

AUTHOR

Timothy E. Lawlor, M.A.

PERFORMING LABORATORY

Corning Hazleton Inc. (CHV)
9200 Leesburg Pike
Vienna, Virginia 22182

LABORATORY PROJECT ID

CHV Study No.: 17073-0-409

SUBMITTED TO

3M Corporation
Building 220-2E-02 3M Center
St. Paul, MN 55144-1000

STUDY COMPLETION DATE

December 14, 1995

000353

QUALITY ASSURANCE STATEMENT

STUDY TITLE: *Salmonella - Escherichia coli/* Mammalian-Microsome Reverse Mutation Assay

ASSAY NO.: 17073-0-409

PROTOCOL NO.: 409, Edition 4, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Plating - 09/19/95	09/19/95	M. Murphy
Draft Report Review - 11/06/95	11/07/95	C. Orantes/ S. Ballenger
Final Report Review - 12/14/95	12/14/95	C. Orantes

Quality Assurance Unit — 12/14/95 Date Released

000354

STUDY COMPLIANCE AND CERTIFICATION

The study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Food and Drug Administration (FDA) Title 21 of the U.S. Code of Federal Regulations Part 58, issued December 22, 1978, (effective June 20, 1979) and with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

Study Director:

Timothy E. Lawlor, M.A.
Bacterial Mutagenesis
Genetic and Cellular Toxicology

12·14·95
Study Completion Date

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SECTION I. SUMMARY

INTRODUCTION AND CONCLUSIONS

SUMMARY

A. Introduction

At the request of 3M Corporation, Corning Hazleton Inc. investigated **T-6342** for mutagenic activity in the *Salmonella-Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay. This assay evaluated the test article and/or its metabolites for their ability to induce reverse mutations at the histidine locus in the genome of specific *Salmonella typhimurium* tester strains and at the tryptophan locus in an *Escherichia coli* tester strain both in the presence and absence of an exogenous metabolic activation system of mammalian microsomal enzymes derived from Aroclor™-induced rat liver (S9).

The doses tested in the mutagenicity assay were selected based on the results of a dose rangefinding study using tester strains TA100 and WP2*uvr*A and ten doses of test article ranging from 5,000 to 6.67 µg per plate, one plate per dose, both in the presence and absence of S9 mix.

The tester strains used in the mutagenicity assay were *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* tester strain WP2*uvr*A. The assay was conducted with five doses of test article in both the presence and absence of S9 mix along with concurrent vehicle and positive controls using three plates per dose. The doses tested were 5,000, 3,330, 1,000, 333, and 100 µg per plate in both the presence and absence of S9 mix.

B. Conclusions

The results of the *Salmonella - Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay indicate that, under the conditions of this study, 3M Corporation's test article, **T-6342**, did not cause a positive increase in the number of revertants per plate of any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor™-induced rat liver (S9).

SECTION II. STUDY INFORMATION

STUDY INFORMATION

A. Sponsor: **3M Corporation**

B. Test Article: **T-6342**

1. Physical Description: **clear colorless liquid**

2. Date Received: **07/21/95**

C. Type of Assay: *Salmonella-Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay

1. Protocol Number: CHV Protocol 409, Edition 4
Modified for 3M Corporation

2. CHV Study Number: 17073-0-409

D. Study Dates

1. Study Initiation Date: **08/28/95**

2. Experimental Start Date: **09/12/95**

3. Experimental Termination Date: **09/22/95**

E. Study Supervisory Personnel

Study Director: Timothy E. Lawlor, M.A.

Laboratory Supervisor: Michael S. Mecchi, B.S.

SECTION III. MATERIALS AND METHODS

MATERIALS AND METHODS

The experimental materials, methods and procedures are based on those described by Ames *et al* (1975) and Green and Muriel (1976).

MATERIALS

A. Tester Strains

1. *Salmonella typhimurium*

The tester strains used were the *Salmonella typhimurium* histidine auxotrophs TA98, TA100, TA1535, and TA1537 as described by Ames *et al* (1975). The specific genotypes of these strains are shown in Table I.

TABLE I. TESTER STRAIN GENOTYPES

Histidine Mutation			Additional Mutations		
*his*G46	*his*C3076	*his*D3052	LPS	Repair	R Factor
TA1535	TA1537		*rfa*	*uvr*B	-
TA100		TA98	*rfa*	*uvr*B	+R

In addition to a mutation in the histidine operon, the tester strains contain two additional mutations which enhance their sensitivity to some mutagenic compounds. The *rfa* wall mutation results in the loss of one of the enzymes responsible for the synthesis of part of the lipopolysaccharide barrier that forms the surface of the bacterial cell wall. The resulting cell wall deficiency increases permeability to certain classes of chemicals such as those containing large ring systems (i.e. benzo(a)pyrene) that would otherwise be excluded by a normal intact cell wall.

The second mutation, a deletion of the *uvr*B gene, results in a deficient DNA excision repair system which greatly enhances the sensitivity of these strains to some mutagens. Since the *uvr*B deletion extends through the *bio* gene, all of the tester strains containing this deletion also require the vitamin biotin for growth.

Strains TA98 and TA100 also contain the R-factor plasmid, pKM101, which further increases the sensitivity of these strains to some mutagens. The mechanism by which this plasmid increases sensitivity to mutagens has been suggested to be by modifying an existing bacterial DNA repair polymerase complex involved with the mismatch-repair process.

Tester strains TA98 and TA1537 are reverted from histidine dependence (auxotrophy) to histidine independence (prototrophy) by frameshift mutagens. TA1535 is reverted by base substitution mutagens and TA100 is reverted by mutagens which cause both frameshifts and base substitutions.

2. *Escherichia coli*

The tester strain used was the tryptophan auxotroph WP2*uvr*A as described by Green and Muriel (1976).

In addition to a mutation in the tryptophan operon, the tester strain contains a *uvr*A DNA repair deficiency which enhances its sensitivity to some mutagenic compounds. This deficiency allows the strain to show enhanced mutability since the *uvr*A repair system would normally act to remove the damaged part of the DNA molecule and accurately repair it afterwards.

Tester strain WP2*uvr*A is reverted from tryptophan dependence (auxotrophy) to tryptophan independence (prototrophy) by base substitution mutagens.

3. Source of Tester Strains

a. *Salmonella typhimurium*

The tester strains in use at CHV were received directly from Dr. Bruce Ames, Department of Biochemistry, University of California, Berkeley.

b. *Escherichia coli*

The tester strain, WP2*uvr*A, in use at CHV was received from the National Collection of Industrial Bacteria, Torrey Research Station, Scotland (United Kingdom).

4. Storage of the Tester Strains

a. Frozen Permanent Stocks

Frozen permanent stocks were prepared by growing fresh overnight cultures, adding DMSO (0.09 ml/ml of culture) and freezing small aliquots (0.5-1.5 ml) at ≤- 70°C.

b. Master Plates

Master plates were prepared by streaking each tester strain from a frozen permanent stock onto minimal agar appropriately supplemented with 1) for *Salmonella typhimurium*, an excess of histidine, and biotin, and for tester strains TA 98 and TA100, ampicillin (25 µg/ml), to ensure the stable maintenance of the pKM101 plasmid; and 2) for *Escherichia coli*, an excess of tryptophan. Tester strain master plates were stored at 5 ± 3 °C.

5. Preparation of Overnight Cultures

a. Inoculation

Overnight cultures for use in all testing procedures were inoculated by transferring a colony from the appropriate master plate to a flask containing culture medium. Inoculated flasks were placed in a shaker/incubator which was programmed to begin operation (shaking, 125 ± 25 rpm; incubation, 37 ± 2 °C) so that the overnight cultures were in log phase or late log phase when turbidity monitoring began.

b. Harvest

To ensure that cultures were harvested in late log phase, the length of incubation was determined by spectrophotometric monitoring of culture turbidity. Cultures were harvested once a predetermined turbidity was reached as determined by a percent transmittance (%T) reading on a spectrophotometer. This target turbidity ensures that cultures have reached a density of at least 0.5 X 10^9 cells per ml and that the cultures have not overgrown. Overgrown (stationary) cultures may exhibit decreased sensitivity to some mutagens. Cultures were removed from incubation when the target %T was reached and were placed at 5 ± 3 °C.

6. Confirmation of Tester Strain Genotypes

Tester strain cultures were checked for the following genetic markers on the day of their use in the mutagenicity assay:

a. *Salmonella typhimurium*

1) *rfa* Wall Mutation

The presence of the *rfa* wall mutation was confirmed by demonstration of the sensitivity of the culture to crystal violet. An aliquot of an overnight

culture of each strain was overlaid onto plates containing selective media and an antibiotic sensitivity disk containing 10 µg of crystal violet was added. Sensitivity was demonstrated by inhibition of bacterial growth in a zone immediately surrounding the disk.

2) pKM101 Plasmid R-factor

The presence of the pKM101 plasmid was confirmed for tester strains TA98 and TA100 by demonstration of resistance to ampicillin. An aliquot of an overnight culture of each strain was overlaid onto plates containing selective media and an antibiotic sensitivity disk containing 10 µg of ampicillin was added. Resistance was demonstrated by bacterial growth in the zone immediately surrounding the disk.

3) Characteristic Number of Spontaneous Revertants

The mean number of spontaneous revertants per plate in the vehicle controls that are characteristic of the respective strains were demonstrated by plating 100 µl aliquots of the culture along with the appropriate vehicle on selective media.

b. *Escherichia coli*

1) Characteristic Number of Spontaneous Revertants

The mean number of spontaneous revertants per plate in the vehicle controls that are characteristic of the respective strains were demonstrated by plating 100 µl aliquots of the WP2*uvr*A culture along with the appropriate vehicle on selective media.

7. Tester Strain Media

a. Culturing Broth

The broth used to grow overnight cultures of the tester strains was Vogel-Bonner salt solution (Vogel and Bonner, 1956) supplemented with 2.5% (w/v) Oxoid Nutrient Broth No. 2 (dry powder).

b. Agar Plates

Bottom agar (25 ml per 15 x 100 mm petri dish) was Vogel-Bonner minimal medium E (Vogel and Bonner, 1956), supplemented with 1.5% (w/v) agar and 0.2% (w/v) glucose.

c. Overlay Agar for Selection of Revertants

Overlay (top) agar was prepared with 0.7% agar (w/v) and 0.5% NaCl (w/v) and was supplemented with 10 ml of 1) 0.5 mM histidine/biotin solution per 100 ml agar for selection of histidine revertants, or 2) 0.5 mM tryptophan solution per 100 ml of agar for selection of tryptophan revertants. When S9 mix was required, 2.0 ml of the supplemented top agar was used in the overlay. However, when S9 mix was not required, water was added to the supplemented top agar (0.5 ml of water per 2 ml of supplemented top agar) and the resulting 2.5 ml of diluted supplemented top agar was used for the overlay. This dilution ensured that the final top agar and amino acid supplement concentrations remained the same both in the presence and absence of S9 mix.

B. Liver Microsomal Enzyme Reaction Mixture (S9 Mix)

1. S9 Homogenate

Liver microsomal enzymes (S9 homogenate) were purchased from Molecular Toxicology, Inc., Annapolis, MD 21401, Batch 0568 (38.8 mg of protein per ml) and Batch 0569 (38.8 mg of protein per ml). The homogenate was prepared from male Sprague-Dawley rats that had been injected (i.p.) with Aroclor™ 1254 (200 mg per ml in corn oil) at 500 mg/kg as described by Ames *et al*, 1975.

2. S9 Mix

The S9 mix was prepared immediately prior to its use in any experimental procedure. The S9 mix contained the components indicated in Table II.

TABLE II. S9 MIX COMPONENTS

H_2O	0.70 ml
1M NaH_2PO_4/Na_2HPO_4, pH7.4	0.10 ml
0.25M Glucose-6-phosphate	0.02 ml
0.10M NADP	0.04 ml
0.825M KCl/0.2M $MgCl_2$	0.04 ml
S9 Homogenate	0.10 ml
	1.00 ml

C. Controls

1. Vehicle Controls

Vehicle controls were plated for all tester strains both in the presence and absence of S9 mix. The vehicle control was plated, using a 50 µl aliquot of vehicle (equal to the maximum aliquot of test article dilution plated), along with a 100 µl aliquot of the appropriate tester strain and a 500 µl aliquot of S9 mix (when necessary), on selective agar.

2. Positive Controls

The combinations of positive controls, activation condition and tester strains plated concurrently with the assay are indicated in Table III.

TABLE III. POSITIVE CONTROLS

Tester Strain	S9 Mix	Positive Control	Conc per plate
TA98	+	2-aminoanthracene	2.5 µg
TA98	-	2-nitrofluorene	1.0 µg
TA100	+	2-aminoanthracene	2.5 µg
TA100	-	sodium azide	2.0 µg
TA1535	+	2-aminoanthracene	2.5 µg
TA1535	-	sodium azide	2.0 µg
TA1537	+	2-aminoanthracene	2.5 µg
TA1537	-	ICR-191	2.0 µg
WP2*uvr*A	+	2-aminoanthracene	25.0 µg
WP2*uvr*A	-	4-nitroquinoline-N-oxide	1.0 µg

a. Source and Grade of Positive Control Articles

2-aminoanthracene (CAS #613-13-8), Sigma Chemical Co., purity ≥ 97.5%; 2-nitrofluorene (CAS #607-57-8), Aldrich Chemical Co., purity 98%; sodium azide (CAS #26628-22-8), Sigma Chemical Co., purity >98%; ICR-191 (CAS #1707-45-0), Polysciences Inc., purity >95%; 4-nitroquinoline-N-oxide (CAS #56-57-5), Sigma Chemical Co., purity >99%.

3. Sterility Controls

a. Test Article

The most concentrated test article dilution was checked for sterility by plating a 50 µl aliquot (the same volume used in the assay) on selective agar.

b. S9 Mix

The S9 mix was checked for sterility by plating 0.5 ml on selective agar.

METHODS

A. Dose Rangefinding Study

The growth inhibitory effect (cytotoxicity) of the test article to the test system was determined in order to allow the selection of appropriate doses to be tested in the mutagenicity assay.

1. Design

The dose rangefinding study was performed using tester strains TA100 and WP2*uvr*A both in the presence and absence of S9 mix. Ten doses of test article were tested at one plate per dose. The test article was checked for cytotoxicity up to a maximum concentration of 5 mg per plate.

a. Rationale

The cytotoxicity of the test article observed on tester strain TA100 is generally representative of that observed on the other tester strains and because of TA100's comparatively high number of spontaneous revertants per plate, gradations of cytotoxicity can be readily discerned from routine experimental variation. The *Escherichia coli* tester strain WP2*uvr*A does not possess the *rfa* wall mutation that the *Salmonella typhimurium* strains have and thus, a different range of cytotoxicity may be observed. Also, the cytotoxicity induced by a test article in the presence of S9 mix may vary greatly from that observed in the absence of S9 mix. Therefore, this would require that different test article dose ranges be tested in the mutagenicity assay based on the presence or absence of the S9 mix.

2. Evaluation of the Dose Rangefinding Study

Cytotoxicity is detectable as a decrease in the number of revertant colonies per plate and/or by a thinning or disappearance of the bacterial background lawn.

3. Selection of the Maximum Dose for the Mutagenicity Assay

a. No Cytotoxicity Observed

Since no cytotoxicity was observed in the dose rangefinding study, the highest dose of test article used in the mutagenicity assay was the same as that tested in the rangefinding study.

B. Mutagenicity Assay

1. Design

The assay was performed using tester strains TA98, TA100, TA1535, TA1537, and WP2*uvr*A both in the presence and absence of S9 mix. Five doses of test article were tested along with the appropriate vehicle and positive controls. The doses of test article were selected based on the results of the dose rangefinding study.

2. Frequency and Route of Administration

The tester strains were exposed to the test article via the plate incorporation methodology originally described by Ames *et al* (1975) and Maron and Ames (1983). This methodology has been shown to detect a wide range of classes of chemical mutagens. In the plate incorporation methodology, the test article, the tester strain and the S9 mix (where appropriate) were combined in molten agar which was overlaid onto a minimal agar plate. Following incubation at 37 ± 2°C for 48 ± 8 hr, revertant colonies were counted. All doses of the test article, the vehicle controls and the positive controls were plated in triplicate.

C. Plating Procedures

These procedures were used in both the dose rangefinding study and the mutagenicity assay.

Each plate was labeled with a code which identified the test article, test phase, tester strain, activation condition and dose. The S9 mix and dilutions of the test article were prepared immediately prior to their use.

When S9 mix was not required, 100 µl of tester strain and 50 µl of vehicle or test article dose was added to 2.5 ml of molten selective top agar (maintained at 45 ± 2°C). When S9 mix was required, 500 µl of S9 mix, 100 µl of tester strain and 50 µl of vehicle or test article dose was added to 2.0 ml of molten selective top agar. After the required components had been added, the mixture was vortexed and overlaid onto the surface of 25 ml of minimal bottom agar contained in a 15 x 100 mm petri dish. After the overlay had solidified, the plates were inverted and incubated for 48 ± 8 hr at 37 ± 2°C. Positive control articles were plated using a 50 µl plating aliquot.

D. Scoring the Plates

Plates which were not evaluated immediately following the incubation period were held at 5 ± 3°C until such time that colony counting and bacterial background lawn evaluation could take place.

1. Bacterial Background Lawn Evaluation

The condition of the bacterial background lawn was evaluated for evidence of cytotoxicity and test article precipitate. Evidence of cytotoxicity was scored relative to the vehicle control plate and was recorded along with the revertant counts for all plates at that dose on the data tables using the code system presented at the end of the Materials and Methods Section.

2. Counting Revertant Colonies

The number of revertant colonies per plate for the vehicle controls and all plates containing test article were counted manually. The number of revertant colonies per plate for the positive controls were counted by automated colony counter.

E. Analysis of Data

For all replicate platings, the mean revertants per plate and the standard deviation were calculated. The results of these calculations are presented in tabular form in the Data Tables Section of this report.

EVALUATION OF TEST RESULTS

Before assay data were evaluated, the criteria for a valid assay had to be met.

A. Criteria For A Valid Assay

The following criteria were used to determine a valid assay:

1. Tester Strain Integrity : *Salmonella typhimurium*

a. *rfa* Wall Mutation

To demonstrate the presence of the *rfa* wall mutation, tester strain cultures exhibited sensitivity to crystal violet.

b. pKM101 Plasmid

To demonstrate the presence of the R-factor plasmid, pKM101, cultures of tester strains TA98 and TA100 exhibited resistance to ampicillin.

c. Characteristic Number of Spontaneous Revertants

To demonstrate the requirement for histidine, the tester strain cultures exhibited a characteristic number of spontaneous revertants per plate when plated along with the vehicle under selective conditions. The acceptable ranges for the vehicle controls were as follows:

TA98	8 - 60
TA100	60 - 240
TA1535	4 - 45
TA1537	2 - 25

2. Tester Strain Integrity : *Escherichia coli*

a. Characteristic Number of Spontaneous Revertants

To demonstrate the requirement for tryptophan, the tester strain culture exhibited a characteristic number of spontaneous revertants per plate when plated along with the vehicle under selective conditions. The acceptable range for WP2*uvr*A was 5 to 40 revertants per plate.

3. Tester Strain Culture Density

To demonstrate that appropriate numbers of bacteria are plated, the density of tester strain cultures were greater than or equal to 0.5×10^9 bacteria per ml and/or had reached

a target level of turbidity demonstrated to produce cultures with a density greater than or equal to 0.5×10^9 bacteria per ml.

4. Positive Control Values

a. Positive Control Values in the Absence of S9 Mix

To demonstrate that the tester strains were capable of identifying a mutagen, the mean value of a positive control for a respective tester strain exhibited at least a 3-fold increase over the mean value of the vehicle control for that strain.

b. Positive Control Values in the Presence of S9 Mix (S9 Mix Integrity)

To demonstrate that the S9 mix was capable of metabolizing a promutagen to its mutagenic form(s), the mean value of the positive control for a respective tester strain in the presence of the S9 mix exhibited at least a 3-fold increase over the mean value of the vehicle control for that strain.

An acceptable positive control in the presence of S9 for a specific strain was evaluated as having demonstrated both the integrity of the S9 mix and the ability of the tester strain to detect a mutagen.

2. Cytotoxicity

A minimum of three non-toxic doses were required to evaluate assay data.

B. Criteria For A Positive Response

Once the criteria for a valid assay had been met, responses observed in the assay were evaluated as follows:

1. Tester Strains TA98 ,TA100, and WP2*uvr*A

For a test article to be considered positive, it had to produce at least a 2-fold increase in the mean revertants per plate of at least one of these tester strains over the mean revertants per plate of the appropriate vehicle control. This increase in the mean number of revertants per plate had to be accompanied by a dose response to increasing concentrations of the test article.

2. Tester Strains TA1535 and TA1537

For a test article to be considered positive, it had to produce at least a 3-fold increase in the mean revertants per plate of at least one of these tester strains over the mean revertants per plate of the appropriate vehicle control. This increase in the mean number of revertants per plate had to be accompanied by a dose response to increasing concentrations of the test article.

RECORDS TO BE MAINTAINED

All raw data, documentation, records, the protocol, and the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc., for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc., for an additional period of time or sent to a storage facility designated by the Sponsor.

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BACTERIAL BACKGROUND LAWN EVALUATION CODE

The condition of the background bacterial lawn is evaluated both macroscopically and microscopically (using a dissecting microscope) for indications of cytotoxicity and test article precipitate as follows:

CODE	DEFINITION	CHARACTERISTICS OF BACKGROUND LAWN
1	Normal	A healthy microcolony lawn.
2	Slightly Reduced	A noticeable thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
3	Moderately Reduced	A marked thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
4	Extremely Reduced	An extreme thinning of the microcolony lawn and an increase in the size of the microcolonies compared to the vehicle control plate.
5	Absent	A complete lack of any microcolony lawn.
6	Obscured by Precipitate	The background bacterial lawn cannot be accurately evaluated due to microscopic and/or macroscopic test article precipitate.

Evidence of macroscopic test article precipitate on the plates is recorded by addition of the following precipitate code to the code number used to evaluate the condition of the background bacterial lawn.

sp	Slight Precipitate	Noticeable macroscopic precipitate on the plate, however, the precipitate does not influence automated counting of the plate.
mp	Moderate Precipitate	The amount of macroscopic precipitate on the plate would interfere with automated counting, thus requiring the plate to be hand counted.
hp	Heavy Precipitate	The large amount of macroscopic precipitate on the plate makes the required hand counting difficult.

Example: 4mp would indicate a plate observed to have an extremely reduced background lawn which had to be counted manually due to the marked amount of macroscopic test article precipitate.

SECTION IV. RESULTS AND CONCLUSIONS

RESULTS

A. Test Article Handling

The test article, **T-6342**, was stored at room temperature. Deionized water (CHV Lot 326) was used as the vehicle. At 100 mg per ml, which was the most concentrated stock dilution prepared, the test article formed a clear, colorless solution. The test article remained a solution in all succeeding dilutions prepared for the mutagenicity assay.

B. Dose Rangefinding Study

Doses to be tested in the mutagenicity assay were selected based on the results of the dose rangefinding study conducted on the test article using tester strains TA100 and WP2*uvr*A in both the presence and absence of S9 mix (one plate per dose). Ten doses of test article, from 5,000 to 6.67 µg per plate, were tested and the results are presented in Tables 1 and 2. These data were generated in Experiment 17073-A1. No cytotoxicity was observed in either the presence or absence of S9 mix as evidenced by a normal background lawn and no decrease in the number of revertants per plate.

C. Mutagenicity Assay

The mutagenicity assay results for **T-6342** are presented in Tables 3 and 4. These data were generated in Experiment 17073-B1. The data are presented as mean revertants per plate ± standard deviation for each treatment and control group (Table 4) and as individual plate counts (Table 3).

The results of the dose rangefinding study were used to select five doses to be tested in the mutagenicity assay. The doses tested were 5,000, 3,330, 1,000, 333, and 100 µg per plate in both the presence and absence of S9 mix.

In Experiment 17073-B1 (Tables 3 and 4), all data were acceptable and no positive increases in the number of revertants per plate were observed with any of the tester strains either in the presence or absence of S9 mix.

All criteria for a valid study were met.

CONCLUSIONS

The results of the *Salmonella-Escherichia coli*/Mammalian-Microsome Reverse Mutation Assay indicate that, under the conditions of this study, 3M Corporation's test article, **T-6342**, did not cause a positive increase in the number of revertants per plate of any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor™-induced rat liver (S9).

SECTION V. DATA TABLES

TABLE 1

DOSE RANGEFINDING STUDY

TEST ARTICLE ID: T-6342

EXPERIMENT ID: 17073-A1 DATE PLATED: 12-Sep-95

VEHICLE: Deionized water DATE COUNTED: 15-Sep-95

µg/PLATE	TA100 REVERTANTS PER PLATE WITH S9		WITHOUT S9	
	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*
0.00 (Vehicle) (50 µl)	127	1	93	1
Test Article				
6.67	103	1	87	1
10.0	100	1	81	1
33.3	85	1	77	1
66.7	120	1	105	1
100	112	1	98	1
333	138		113	1
667	107	1	97	1
1000	119	1	79	1
3330	111	1	107	1
5000	118	1	92	1

* Background Lawn Evaluation Codes:

1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

TABLE 2

DOSE RANGEFINDING STUDY

TEST ARTICLE ID: T-6342

EXPERIMENT ID: 17073-A1 DATE PLATED: 12-Sep-95

VEHICLE: Deionized water DATE COUNTED: 15-Sep-95

µg/PLATE	WP2*uvrA* REVERTANTS PER PLATE WITH S9		WITHOUT S9	
	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*	REVERTANTS PER PLATE	BACKGROUND LAWN EVALUATION*
0.00 (Vehicle) (50 µl)	16	1	20	1
Test Article				
6.67	24	1	11	1
10.0	19	1	16	1
33.3	11	1	11	1
66.7	12	1	12	1
100	23	1	24	1
333	20	1	23	1
667	8	1	15	1
1000	14	1	19	1
3330	20	1	21	1
5000	18	1	18	1

* Background Lawn Evaluation Codes:

1 = normal; 2 = slightly reduced; 3 = moderately reduced

4 = extremely reduced; 5 = absent; 6 = obscured by precipitate

sp = slight precipitate; mp = moderate precipitate (requires hand count); hp = heavy precipitate (requires hand count)

TABLE 3
MUTAGENICITY ASSAY RESULTS
INDIVIDUAL PLATE COUNTS

TEST ARTICLE ID: T-6342

EXPERIMENT ID: 17073-B1

DATE PLATED: 19-Sep-95

DATE COUNTED: 22-Sep-95

VEHICLE: Deionized water

PLATING ALIQUOT: 50 µl

		REVERTANTS PER PLATE															BACKGROUND LAWN*
DOSE/PLATE		TA98			TA100			TA1535			TA1537			WP2uvrA			
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	
MICROSOMES: Rat Liver																	
VEHICLE CONTROL		11	25	24	117	115	118	13	15	7	10	9	7	20	19	19	1
TEST ARTICLE	100 µg	30	36	38	109	115	112	16	13	11	6	12	8	30	14	17	1
	333 µg	30	27	28	121	114	118	8	11	14	7	5	10	15	21	15	1
	1000 µg	29	34	26	118	114	111	13	17	9	10	3	9	12	14	13	1
	3330 µg	38	31	34	128	123	118	15	14	11	10	11	5	15	16	16	1
	5000 µg	23	19	18	119	108	126	15	10	12	10	7	6	20	29	24	1
POSITIVE CONTROL **		848	995	810	926	953	889	110	108	122	107	122	108	201	171	163	1
MICROSOMES: None																	
VEHICLE CONTROL		14	12	13	90	86	86	7	5	6	7	8	1	10	15	18	1
TEST ARTICLE	100 µg	19	19	10	97	88	107	5	8	5	3	7	7	26	11	15	1
	333 µg	11	21	17	103	107	100	13	13	19	10	7	13	18	15	17	1
	1000 µg	12	19	14	104	91	97	8	9	17	5	10	4	27	18	24	1
	3330 µg	10	16	15	82	97	98	6	6	9	4	6	4	9	22	19	1
	5000 µg	20	17	9	92	72	88	9	16	9	12	9	6	10	16	17	1
POSITIVE CONTROL ***		129	154	156	841	817	861	582	599	556	202	224	218	39	45	76	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal
2 = slightly reduced
3 = moderately reduced
4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

TABLE 4
MUTAGENICITY ASSAY RESULTS
SUMMARY

TEST ARTICLE ID: T-6342

EXPERIMENT ID: 17073-B1

DATE PLATED: 19-Sep-95 VEHICLE: Deionized water

DATE COUNTED: 22-Sep-95 PLATING ALIQUOT: 50 µl

		MEAN REVERTANTS PER PLATE WITH STANDARD DEVIATION										BACKGROUND LAWN*
	DOSE/PLATE	TA98		TA100		TA1535		TA1537		WP2uvrA		
		MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	MEAN	S.D.	
MICROSOMES: Rat Liver												
VEHICLE CONTROL		20	8	117	2	12	4	9	2	19	1	1
TEST ARTICLE	100 µg	35	4	112	3	13	3	9	3	20	9	1
	333 µg	28	2	118	4	11	3	7	3	17	3	1
	1000 µg	30	4	114	4	13	4	7	4	13	1	1
	3330 µg	34	4	123	5	13	2	9	3	16	1	1
	5000 µg	20	3	118	9	12	3	8	2	24	5	1
POSITIVE CONTROL **		884	98	923	32	113	8	112	8	178	20	1
MICROSOMES: None												
VEHICLE CONTROL		13	1	87	2	6	1	5	4	14	4	1
TEST ARTICLE	100 µg	16	5	97	10	6	2	6	2	17	8	1
	333 µg	16	5	103	4	15	3	10	3	17	2	1
	1000 µg	15	4	97	7	11	5	6	3	23	5	1
	3330 µg	14	3	92	9	7	2	5	1	17	7	1
	5000 µg	15	6	84	11	11	4	9	3	14	4	1
POSITIVE CONTROL ***		146	15	840	22	579	22	215	11	53	20	1

** TA98 2-aminoanthracene 2.5 µg/plate
TA100 2-aminoanthracene 2.5 µg/plate
TA1535 2-aminoanthracene 2.5 µg/plate
TA1537 2-aminoanthracene 2.5 µg/plate
WP2uvrA 2-aminoanthracene 25.0 µg/plate

*** TA98 2-nitrofluorene 1.0 µg/plate
TA100 sodium azide 2.0 µg/plate
TA1535 sodium azide 2.0 µg/plate
TA1537 ICR-191 2.0 µg/plate
WP2uvrA 4-nitroquinoline-N-oxide 1.0 µg/plate

* Background Lawn Evaluation Codes:
1 = normal
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4 = extremely reduced
5 = absent
6 = obscured by precipitate
sp = slight precipitate
mp = moderate precipitate (requires hand count)
hp = heavy precipitate (requires hand count)

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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
APRIL, 1981 - MAY, 1983

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

000383

STUDY REPORT AMENDMENT NO. 1

EFFECTIVE DATE: NOVEMBER 2, 1987

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

RIKER Experiment No.: 0281CR0012

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

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

Approval:

L.J. Sibinski 11/2/87

L.J. Sibinski
Study Director

Date

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

(RIKER Experiment No. 0281CR0012)

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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.

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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.

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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).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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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)
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 gross lesion

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

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

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

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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

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

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

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

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

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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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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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

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

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

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

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

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

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

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

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

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

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

Leydig cell adenomas (i.e. benign tumors of the testicular interstitial tissue), were found at an incidence of 0%, 14% and 4% in the control, high- and low-dose groups, respectively. The high-dose incidence for this lesion was statistically significant ($p \leq 0.05$) because the incidence in the control group was unusually low (0%). In addition, the spontaneous incidence reported for this neoplasm in this strain of rat was 7.4% for rats 24 to 29 months of age and was 14.6% at 30 to 38 months of age[3]. Based on another set of Sprague-Dawley two year study data compiled by Hazleton Laboratories, the spontaneous incidence of interstitial cell tumors was 28.7%.[5]

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

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

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

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

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

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

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

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

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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.

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CONCLUSIONS

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

1. FC-143-related changes were found more commonly in males than in females of each of the two treatment groups. This finding supports earlier pharmacokinetic studies that demonstrated a increased FC-143 retention by treated males compared to treated female rats.

2. The major dose-related findings were observed in the liver and consisted of megalocytosis and cystoid degeneration with only a minimal proliferative response and related elevations of serum enzyme activities.

3. Other non-neoplastic findings reported in this study were not considered primary test article-related effects, but rather were related to spontaneous changes occurring in aging rats.

4. Based on the incidence, types of tumors, time of tumor appearance, malignancy patterns of tumors and survival rate after 2 years, FC-143 is not considered to be carcinogenic in the rat.

PRINCIPAL PERSONNEL INVOLVED WITH THE CONDUCT AND REPORTING OF RIKER EXPERIMENT NO. 0281CR0012 - TWO YEAR ORAL (DIET) TOXICITY/CARCINOGENICITY STUDY OF FLUOROCHEMICAL FC-143 IN RATS

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SIGNATURE PAGE

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)

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

[a] Commercial Chemicals Division (CCD)

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

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

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Table 2

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

Summary of Mean Body Weights (g) ± % Difference from Control

MALES

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

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Table 2 (concluded)

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

Summary of Mean Body Weights (g) ± % Difference from Control

MALES

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

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Table 3

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

Summary of Mean Body Weights (g) ± % Difference from Control

FEMALES

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

000419

Table 3 (concluded)

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

Summary of Mean Body Weights (g) ± % Difference from Control

FEMALES

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

000420

Table 4

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

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

MALES

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

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

000422

Table 5

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

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

FEMALES

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

000423

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) ± % Difference from Control

FEMALES

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

000424

Table 6

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

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

MALES

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

000425

Table 6

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

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

MALES

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

000426

Table 7

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

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

FEMALES

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

000427

Table 7

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

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

FEMALES

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

000428

TABLE 8

Estimated Mean FC-143 (mg/kg Body Weight)

Consumption Per Day

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

000429

TABLE 8 (Continued)

Estimated Mean FC-143 (mg/kg Body Weight)

Consumption Per Day

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

000430

TABLE 9

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

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

0004431

TABLE 9

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

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

CHI-SQUARE TESTS FOR DOSE GROUP DIFFERENCES FROM CONTROL

DOSE GROUP	MALES CHI-SQUARE	MALES PROB.	FEMALES CHI-SQUARE	FEMALES PROB.
300 PPM	* 4.72	0.028	0.36	0.555
30 PPM	0.05	0.811	0.00	1.000

* Significant difference from control at the 5% level

000432

Table 10

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

Summary of Clinical Observations

	Control			300 ppm			30 ppm		
	M	F	%[a]	M	F	%[a]	M	F	%[a]
Initial number of rats	65	65	100.0	65	65	100.0	50	50	100.0
Survivors at end of study	34	25	45.4	44	29	56.2	36	24	60.0
Mass(es)[b] in various areas	19	38	43.8	10	40	38.5	7	41	48.0
(Mass[es] resolved prior to term)	(11)	(7)	(13.9)	(8)	(7)	(11.5)	(4)	(5)	(9.0)
Alopecia in various areas	6	14	15.4	9	16	19.2	6	16	22.0
Swollen throat[c]	13	10	15.4	2	9	8.5	4	8	12.0
Pale (blanched) eyes and/or appears thin (emaciated)	9	9	13.9	5	8	10.0	9	10	19.0
Excessive lacrimation	8	12	15.4	9	7	12.3	8	5	13.0
Ataxia	4	2	4.6	2	15	13.1	5	9	14.0
Convulsions (clonic)	3	0	2.3	2	0	1.5	4	0	4.0
Occasional urinary incontinence and/or hematuria	5	4	6.9	1	2	2.3	3	4	7.0
Raised ulcerated lesion on hind foot pad(s)	7	0	5.4	1	1	1.5	5	0	5.0
Occasional bloody nares	3	1	3.0	0	6	4.6	0	1	1.0

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

C00433

Table 10

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

Summary of Clinical Observations

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

000434

Table 11

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

Summary of Clinical Ophthalmologic Findings

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

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

000435

Table 11

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

Summary of Clinical Ophthalmologic Findings

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

000436

TABLE 12

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

		ERYTHROCYTES (CELLS X 10**6)		HEMOGLOBIN (G/DL)		HEMATOCRIT (% PACKED CELLS)		MCV (MICRONS**3)		MCH (PICOGRAMS)		MCHC (%)	
	N	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE													
MONTH 3													
0 PPM	15	8.29	0.322	16.4	0.39	45.9	0.96	55	1.9	19.8	0.80	35.6	0.47
300 PPM	15	7.91	0.743	15.5*	0.50	43.3*	1.10	56	4.3	19.7	1.55	35.8	0.45
30 PPM	15	7.87	0.475	16.1	0.67	44.5*	1.92	57	2.5	20.6	0.83	36.2*	0.55
MONTH 6													
0 PPM	15	8.42	0.384	15.1	0.94	44.5	2.70	58	4.3	17.9	1.41	33.9	0.77
300 PPM	15	7.91*	0.350	14.5	1.01	43.1	1.64	56	3.0	18.4	1.34	33.7	1.93
30 PPM	15	7.58*	0.306	14.8	0.83	43.9	2.39	58*	1.9	19.6*	0.79	33.8	1.02
MONTH 12													
0 PPM	14	8.44	0.554	15.9	1.17	46.7	3.69	55	2.2	18.8	0.84	34.0	0.97
300 PPM	15	8.01*	0.473	15.2	0.70	42.7*	1.98	53*	1.7	19.0	0.54	35.7*	0.76
30 PPM	15	8.38	0.354	15.5	0.52	44.5	1.88	53*	1.2	18.5	0.72	34.8*	0.99
MONTH 18													
0 PPM	15	7.48	2.071	15.1	3.12	40.8	9.14	56	6.2	21.0	3.09	37.2	1.53
300 PPM	15	7.55#	0.635	14.8#	1.15	40.6#	3.00	54	2.2	19.6	0.92	36.4	0.69
30 PPM	15	8.62	1.106	15.8	1.52	46.1#	4.41	54	4.6	18.4#	0.93	34.3*	1.40
MONTH 24													
0 PPM	15	7.84	1.083	14.5	1.59	42.3	5.34	54	3.4	18.6	1.27	34.4	0.89
300 PPM	15	7.92	0.670	14.6	1.42	43.3	5.72	55	5.6	18.4	1.10	33.8	1.70
30 PPM	14	7.95	0.869	14.7	1.23	42.5	4.22	54	2.0	18.5	0.91	34.6	0.78

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

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TABLE 12

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

	N	LEUKOCYTES (CELLS X 10**3) MEAN	S.DEV.	NEUTROPHILS (CELLS X 10**3) MEAN	S.DEV.	LYMPHOCYTES (CELLS X 10**3) MEAN	S.DEV.	MONOCYTES (CELLS X 10**3) MEAN	S.DEV.	EOSINOPHILS (CELLS X 10**3) MEAN	S.DEV.
MALE											
MONTH 3											
0 PPM	15	12.73	2.074	1.65	0.656	10.72	1.803	0.18	0.196	0.17	0.136
300 PPM	15	14.93	2.801	1.58	0.936	13.08*	2.206	0.18	0.102	0.16	0.178
30 PPM	15	15.22*	3.052	2.14	0.870	12.83*	2.861	0.17	0.173	0.11	0.157
MONTH 6											
0 PPM	15	10.74	2.423	1.43	0.727	8.85	2.416	0.29	0.180	0.17	0.121
300 PPM	15	12.72	2.160	1.99	0.989	10.06	2.316	0.38	0.154	0.20	0.227
30 PPM	15	14.46*	3.223	1.92	1.146	11.81*	2.978	0.33	0.235	0.31	0.362
MONTH 12											
0 PPM	14	7.94	1.572	1.10	0.612	6.35	1.256	0.48	0.216	0.10	0.107
300 PPM	15	8.14	1.789	2.26*	0.656	5.36	1.246	0.39	0.247	0.14	0.105
30 PPM	15	10.38*	1.747	2.21*	1.396	7.56	2.151	0.44	0.233	0.18	0.117
MONTH 18											
0 PPM	15	11.41	7.325	5.06	6.402	5.61	1.504	0.59	0.405	0.16	0.128
300 PPM	15	9.91	1.479	2.78	1.657	6.30	1.070	0.69	0.294	0.20	0.156
30 PPM	15	11.16	5.157	2.55#	3.353	8.20*	2.568	0.38*	0.190	0.11	0.163
MONTH 24											
0 PPM	15	10.79	7.529	3.72	5.666	6.66	2.140	0.34	0.398	0.08	0.083
300 PPM	15	9.09	2.351	2.41	1.488	6.34	1.619	0.26	0.176	0.08	0.109
30 PPM	14	10.44	3.464	3.24	2.032	6.72	2.171	0.39	0.292	0.09	0.106

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

TABLE 12

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

MONTH=3

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3518	8.10	16.1	45	55.5556	19.8765	35.7778	12.60	1.3860	10.9620	0.000	0.252
0 PPM	A1R3527	7.77	15.5	44	56.6281	19.9485	35.2273	11.00	1.6500	9.0200	0.110	0.220
0 PPM	A1R3532	8.69	16.5	46	52.9344	18.9873	35.8696	10.00	1.0000	8.9000	0.000	0.100
0 PPM	A1R3534	8.15	16.3	45	55.2147	20.0000	36.2222	13.30	1.3300	11.5710	0.266	0.133
0 PPM	A1R3537	7.71	16.3	45	56.3658	21.1414	36.2222	11.30	2.4860	8.8140	0.000	0.000
0 PPM	A1R3540	8.04	16.7	46	57.2139	20.7711	36.3043	12.50	1.8750	9.8750	0.250	0.500
0 PPM	A1R3542	8.70	16.8	47	54.0230	19.3103	35.7447	12.60	1.3860	10.9620	0.252	0.000
0 PPM	A1R3548	8.13	16.5	47	57.8106	20.2952	35.1064	15.50	2.6350	12.0900	0.620	0.155
0 PPM	A1R3552	8.20	16.6	46	56.0976	20.2439	36.0870	14.00	1.9600	11.4800	0.280	0.280
0 PPM	A1R3559	8.63	16.4	46	53.3024	19.0035	35.6522	11.50	1.0350	10.1200	0.000	0.345
0 PPM	A1R3562	8.73	15.6	45	51.5464	17.8694	34.6667	11.90	2.2610	9.4010	0.119	0.119
0 PPM	A1R3564	8.37	16.6	47	56.1529	19.8327	35.3191	12.60	1.3860	10.8360	0.252	0.126
0 PPM	A1R3565	8.41	16.3	46	54.6968	19.3817	35.4348	9.58	0.7664	8.8136	0.000	0.000
0 PPM	A1R3567	8.24	16.8	47	57.0388	20.3883	35.7447	15.50	2.7900	12.5550	0.000	0.155
0 PPM	A1R3569	8.46	16.6	47	55.5556	19.6217	35.3191	17.00	0.8500	15.4700	0.510	0.170
300 PPM	B1R3585	7.33	15.0	42	57.2988	20.4638	35.7143	14.20	1.1360	13.0640	0.000	0.000
300 PPM	B1R3587	7.83	16.0	44	56.1941	20.4342	36.3636	14.30	1.7160	12.4410	0.000	0.143
300 PPM	B1R3589	7.67	15.1	43	56.0626	19.6871	35.1163	13.40	1.0720	11.9260	0.268	0.134
300 PPM	B1R3592	7.73	15.0	43	55.6274	19.4049	34.8837	19.60	2.1560	17.2480	0.000	0.196
300 PPM	B1R3593	6.09	14.7	41	67.3235	24.1379	35.8537	10.70	0.5350	10.0580	0.107	0.000
300 PPM	B1R3595	7.81	15.5	43	55.0576	19.8464	36.0465	13.90	1.2510	12.3710	0.139	0.139
300 PPM	B1R3604	7.77	14.8	42	54.0541	19.0476	35.2381	14.00	0.4200	13.3000	0.000	0.280
300 PPM	B1R3605	7.64	15.4	43	56.2827	20.1571	35.8140	15.20	2.1280	12.9200	0.000	0.152
300 PPM	B1R3610	7.99	15.5	43	53.8173	19.3992	36.0465	21.70	3.6890	17.7940	0.217	0.000
300 PPM	B1R3611	8.27	15.9	44	53.2044	19.2261	36.1364	17.90	1.9690	15.3940	0.000	0.537
300 PPM	B1R3617	7.70	16.0	44	57.1429	20.7792	36.3636	14.40	3.0240	11.0880	0.288	0.000
300 PPM	B1R3623	9.02	16.0	45	49.8891	17.7384	35.5556	13.50	1.3500	11.6100	0.135	0.405
300 PPM	B1R3634	8.15	15.8	44	53.9877	19.3865	35.9091	14.70	0.5880	13.9650	0.147	0.000
300 PPM	B1R3640	8.17	15.5	43	52.6316	18.9718	36.0465	12.20	0.7320	11.3460	0.122	0.000
300 PPM	B1R3643	9.44	16.3	45	47.6695	17.2669	36.2222	14.30	2.0020	11.7260	0.143	0.429
30 PPM	C1R3654	7.10	15.6	43	60.5634	21.9718	36.2791	16.40	2.2960	13.9400	0.164	0.000
30 PPM	C1R3655	7.85	15.7	42	53.5032	20.0000	37.3810	10.40	0.5200	9.8800	0.000	0.000
30 PPM	C1R3665	7.77	15.8	43	55.3411	20.3346	36.7442	12.70	2.1590	10.5410	0.000	0.000
30 PPM	C1R3667	7.88	16.5	45	57.1066	20.9391	36.6667	14.70	2.3520	11.7600	0.441	0.147
30 PPM	C1R3668	8.31	17.0	46	55.3550	20.4573	36.9565	11.50	2.4150	8.7400	0.345	0.000
30 PPM	C1R3673	8.27	16.0	44	53.2044	19.3470	36.3636	15.10	2.5670	12.3820	0.151	0.000
30 PPM	C1R3675	7.30	15.0	42	57.5342	20.5479	35.7143	17.00	3.4000	12.7500	0.510	0.340
30 PPM	C1R3677	8.58	16.5	46	53.6131	19.2308	35.8696	14.50	2.3200	12.0350	0.000	0.145
30 PPM	C1R3679	8.41	16.6	46	54.6968	19.7384	36.0870	20.80	2.2880	18.5120	0.208	0.208
30 PPM	C1R3683	7.83	16.5	46	58.7484	21.0728	35.8696	17.20	1.7200	15.4800	0.000	0.000
30 PPM	C1R3687	8.37	17.6	49	58.5424	21.0275	35.9184	15.70	0.9420	14.6010	0.157	0.000
30 PPM	C1R3690	7.03	15.5	43	61.1664	22.0484	36.0465	14.80	1.3320	13.0240	0.296	0.148
30 PPM	C1R3691	7.90	15.8	45	56.9620	20.0000	35.1111	21.30	3.4080	17.8920	0.000	0.000
30 PPM	C1R3692	7.91	16.0	44	55.6258	20.2276	36.3636	13.40	3.2160	9.6480	0.000	0.536
30 PPM	C1R3695	7.52	15.6	43	57.1809	20.7447	36.2791	12.80	1.1520	11.2640	0.256	0.128

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TABLE 12

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

MONTH=6

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3519	8.24	15.0	46	55.8252	18.2039	32.6087	7.70	1.3090	6.0830	0.2310	0.0770
0 PPM	A1R3524	8.51	14.4	42	49.3537	16.9213	34.2857	8.98	1.2572	7.6330	0.0000	0.0898
0 PPM	A1R3529	8.23	14.6	44	53.4629	17.7400	33.1818	11.70	1.0530	10.4130	0.2340	0.0000
0 PPM	A1R3533	8.30	15.7	45	54.2169	18.9157	34.8889	9.96	1.5936	7.9680	0.0996	0.2988
0 PPM	A1R3537	8.13	15.9	47	57.8106	19.5572	33.8298	9.14	1.6452	7.0378	0.1828	0.2742
0 PPM	A1R3541	8.42	15.9	46	54.6318	18.8836	34.5652	9.83	0.9830	8.3555	0.1966	0.2949
0 PPM	A1R3547	7.40	14.8	44	59.4595	20.0000	33.6364	14.00	1.2600	12.0400	0.4200	0.2800
0 PPM	A1R3550	8.38	15.4	45	53.6993	18.3771	34.2222	7.71	1.6962	5.6263	0.3855	0.0000
0 PPM	A1R3553	8.30	15.6	46	55.4217	18.7952	33.9130	10.90	3.5970	6.6490	0.4360	0.2180
0 PPM	A1R3557	8.95	13.0	37	41.3408	14.5251	35.1351	13.40	1.7420	11.1220	0.2680	0.2680
0 PPM	A1R3559	9.03	16.2	47	52.0487	17.9402	34.4681	8.20	0.5740	7.0520	0.2460	0.3280
0 PPM	A1R3562	8.58	14.8	45	52.4476	17.2494	32.8889	10.70	1.1770	8.8810	0.5350	0.1070
0 PPM	A1R3567	8.69	16.2	47	54.0852	18.6421	34.4681	11.30	0.3390	10.7350	0.0000	0.2260
0 PPM	A1R3573	8.70	15.0	45	51.7241	17.2414	33.3333	11.30	1.5820	9.0400	0.5650	0.1130
0 PPM	A1R3575	8.44	13.5	41	48.5782	15.9953	32.9268	16.30	1.6300	14.1810	0.4890	0.0000
300 PPM	B1R3583	8.16	14.8	43	52.6961	18.1373	34.4186	13.40	1.0720	10.7200	0.1340	0.1340
300 PPM	B1R3584	7.93	14.5	42	52.9634	18.2850	34.5238	11.70	1.1700	10.0620	0.4680	0.0000
300 PPM	B1R3596	7.63	11.7	43	56.3565	15.3342	27.2093	12.70	1.6510	10.5410	0.5080	0.0000
300 PPM	B1R3598	7.71	15.1	43	55.7717	19.5850	35.1163	9.74	3.6038	5.8440	0.2922	0.0974
300 PPM	B1R3600	8.27	15.6	44	53.2044	18.8634	35.4545	15.30	1.9890	13.1580	0.1530	0.0000
300 PPM	B1R3604	7.79	13.8	41	52.6316	17.7150	33.6585	12.80	1.1520	10.7520	0.3840	0.5120
300 PPM	B1R3608	8.08	14.8	43	53.2178	18.3168	34.4186	10.60	3.2860	6.7840	0.4240	0.1060
300 PPM	B1R3609	8.00	15.7	46	57.5000	19.6250	34.1304	12.60	2.0160	10.2060	0.1260	0.2520
300 PPM	B1R3613	8.03	15.0	44	54.7945	18.6800	34.0909	13.80	4.0020	8.4180	0.5520	0.8280
300 PPM	B1R3617	7.01	15.1	45	64.1940	21.5407	33.5556	10.50	1.9950	8.0850	0.2100	0.2100
300 PPM	B1R3628	8.32	14.4	44	52.8846	17.3077	32.7273	12.70	0.8890	11.1760	0.3810	0.2540
300 PPM	B1R3629	8.07	14.2	43	53.2838	17.5960	33.0233	18.70	2.6180	15.3340	0.5610	0.1870
300 PPM	B1R3631	8.03	14.8	43	53.5492	18.4309	34.4186	11.50	0.9200	10.0050	0.4600	0.1150
300 PPM	B1R3633	7.42	13.3	39	52.5606	17.9245	34.1026	12.60	2.0160	9.7020	0.5040	0.3780
300 PPM	B1R3642	8.20	15.2	44	53.6585	18.5366	34.5455	12.10	1.4520	10.1640	0.4840	0.0000
30 PPM	C1R3646	7.48	14.7	44	58.8235	19.6524	33.4091	14.80	1.6280	12.2840	0.7400	0.1480
30 PPM	C1R3650	7.79	14.8	45	57.7664	18.9987	32.8889	15.30	0.4590	12.5460	0.6120	0.1530
30 PPM	C1R3656	7.71	15.7	45	58.3658	20.3632	34.8864	16.90	4.2250	11.9990	0.1690	0.5070
30 PPM	C1R3658	7.60	15.3	42	55.2632	20.1316	36.4286	9.05	3.1675	5.3395	0.1810	0.3620
30 PPM	C1R3660	7.58	14.2	42	55.4090	18.7335	33.8095	14.10	2.9610	10.7160	0.4230	0.0000
30 PPM	C1R3664	7.51	14.8	43	57.2570	19.7071	34.4186	13.40	2.5460	10.3180	0.1340	0.4020
30 PPM	C1R3665	6.95	14.0	41	58.9928	20.1439	34.1463	11.20	1.7920	8.7360	0.5600	0.1120
30 PPM	C1R3667	7.65	15.2	45	58.8235	19.8693	33.7778	14.00	2.2400	11.2000	0.5600	0.0000
30 PPM	C1R3679	7.95	15.8	46	57.8616	19.8742	34.3478	20.50	1.6400	17.0150	0.4100	1.4350
30 PPM	C1R3680	7.31	14.0	41	56.0876	19.1518	34.1463	14.00	1.8200	11.6200	0.2800	0.2800
30 PPM	C1R3682	7.99	14.5	45	56.3204	18.1477	32.2222	19.00	3.2300	15.5800	0.1900	0.0000
30 PPM	C1R3687	7.95	16.7	50	62.8931	21.0063	33.4000	9.11	0.0911	8.7456	0.0000	0.3644
30 PPM	C1R3689	7.05	14.1	42	59.5745	20.0000	33.5714	13.10	0.7860	12.0520	0.1310	0.1310
30 PPM	C1R3691	7.72	15.2	45	58.2902	19.6891	33.7778	17.50	1.0500	15.7500	0.5250	0.1750
30 PPM	C1R3694	7.44	13.6	42	56.4516	18.2796	32.3810	15.00	1.2000	13.2000	0.0000	0.6000

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TABLE 12

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

MONTH=12

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3516	8.33	15.6	48	57.6230	18.7275	32.5000	7.9	1.817	5.293	0.632	0.158
0 PPM	A1R3517	8.07	15.7	45	55.7621	19.4548	34.8889	5.2	0.624	4.420	0.156	0.000
0 PPM	A1R3520	8.49	15.7	45	53.0035	18.4923	34.8889	6.8	0.816	5.440	0.476	0.068
0 PPM	A1R3522	8.47	16.4	47	55.4900	19.3625	34.8936	9.2	0.736	7.728	0.460	0.276
0 PPM	A1R3527	8.84	15.7	46	52.0362	17.7602	34.1304	7.4	0.814	6.068	0.518	0.000
0 PPM	A1R3535	8.47	15.6	45	53.1287	18.4179	34.6667	9.1	2.002	6.097	0.819	0.182
0 PPM	A1R3543	8.97	16.4	48	53.5117	18.2832	34.1667	6.9	0.828	5.796	0.276	0.000
0 PPM	A1R3546	9.47	18.1	55	58.0781	19.1130	32.9091	8.2	0.328	7.298	0.574	0.082
0 PPM	A1R3550	9.12	16.4	51	55.9211	17.9825	32.1569	5.7	0.399	5.073	0.228	0.000
0 PPM	A1R3551	8.48	15.8	47	55.4245	18.6321	33.6170	9.2	1.564	7.268	0.184	0.184
0 PPM	A1R3554	.	.	.	.	.	.	.	.	.	.	.
0 PPM	A1R3568	7.88	15.8	46	58.3756	20.0508	34.3478	8.0	1.520	6.160	0.240	0.080
0 PPM	A1R3570	8.29	16.4	47	56.6948	19.7829	34.8936	7.0	1.260	5.600	0.070	0.070
0 PPM	A1R3575	7.27	12.5	38	52.2696	17.1939	32.8947	9.9	0.495	8.811	0.594	0.000
0 PPM	A1R3580	8.04	15.9	46	57.2139	19.7761	34.5652	10.7	2.140	7.918	0.428	0.321
300 PPM	B1R3584	7.78	15.0	42	53.9846	19.2802	35.7143	7.6	2.660	4.332	0.380	0.228
300 PPM	B1R3588	8.06	15.6	44	54.5906	19.3548	35.4545	5.6	1.232	4.088	0.224	0.056
300 PPM	B1R3589	8.15	14.9	41	50.3067	18.2822	36.3415	6.8	1.836	4.148	0.612	0.204
300 PPM	B1R3592	6.60	13.4	38	57.5758	20.3030	35.2632	6.9	1.932	4.347	0.414	0.207
300 PPM	B1R3598	7.68	14.8	41	53.3854	19.2708	36.0976	8.1	2.511	5.184	0.324	0.081
300 PPM	B1R3604	8.04	14.7	44	54.7264	18.2836	33.4091	8.5	2.380	5.610	0.510	0.000
300 PPM	B1R3613	8.07	15.5	43	53.2838	19.2069	36.0465	9.7	2.522	6.402	0.485	0.291
300 PPM	B1R3617	8.83	16.6	47	53.2276	18.7995	35.3191	4.7	1.175	3.431	0.000	0.094
300 PPM	B1R3620	7.89	14.9	42	53.2319	18.8847	35.4762	8.2	2.214	5.412	0.492	0.082
300 PPM	B1R3622	8.16	15.6	43	52.6961	19.1176	36.2791	9.3	3.069	5.115	1.023	0.093
300 PPM	B1R3626	8.13	15.5	42	51.6605	19.0652	36.9048	9.1	2.639	6.097	0.182	0.182
300 PPM	B1R3627	8.01	15.7	44	54.9313	19.6005	35.6818	9.3	3.162	5.487	0.279	0.372
300 PPM	B1R3638	8.12	15.3	43	52.9557	18.8424	35.5814	6.7	1.206	5.293	0.134	0.134
300 PPM	B1R3642	8.30	15.7	44	53.0120	18.9157	35.6818	10.3	2.369	7.622	0.206	0.103
300 PPM	B1R3643	8.38	15.3	43	51.3126	18.2578	35.5814	11.3	2.938	7.797	0.565	0.000
30 PPM	C1R3649	8.57	16.2	46	53.6756	18.9032	35.2174	11.5	2.185	8.510	0.575	0.230
30 PPM	C1R3650	8.69	15.7	47	54.0852	18.0667	33.4043	7.7	2.233	4.466	0.693	0.308
30 PPM	C1R3652	8.29	14.8	43	51.8697	17.8528	34.4186	9.0	2.160	6.390	0.360	0.090
30 PPM	C1R3663	8.87	15.6	47	52.9876	17.5874	33.1915	8.0	1.120	6.400	0.400	0.080
30 PPM	C1R3668	8.19	15.7	45	54.9451	19.1697	34.8889	8.6	3.354	4.730	0.344	0.172
30 PPM	C1R3670	8.05	15.3	43	53.4161	19.0062	35.5814	10.2	4.692	5.100	0.102	0.306
30 PPM	C1R3672	8.00	14.9	42	52.5000	18.6250	35.4762	12.4	1.364	10.416	0.372	0.248
30 PPM	C1R3676	9.02	16.1	47	51.7052	17.7118	34.2553	13.9	4.170	8.896	0.834	0.000
30 PPM	C1R3679	8.59	16.2	45	52.3865	18.8591	36.0000	12.2	1.586	9.882	0.488	0.244
30 PPM	C1R3680	7.97	14.6	42	52.6976	18.3187	34.7619	10.2	4.590	5.202	0.204	0.204
30 PPM	C1R3681	7.89	15.3	42	53.2319	19.3916	36.4286	11.9	0.238	11.067	0.357	0.238
30 PPM	C1R3683	8.10	16.1	45	55.5556	19.8765	35.7778	10.5	0.840	9.450	0.210	0.000
30 PPM	C1R3685	8.76	15.3	46	52.5114	17.4658	33.2609	9.3	1.488	7.347	0.372	0.093
30 PPM	C1R3691	8.33	15.6	45	54.0216	18.7275	34.6667	10.4	2.184	7.176	0.936	0.104
30 PPM	C1R3694	8.41	15.1	43	51.1296	17.9548	35.1163	9.9	0.891	8.316	0.297	0.396

000441

TABLE 12

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

MONTH=18

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WHC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3519	8.42	15.3	44	52.2565	18.1710	34.7727	10.0	4.400	4.600	1.000	0.000
0 PPM	A1R3521	2.48	7.2	18	72.5806	29.0323	40.0000	35.4	26.196	7.080	1.770	0.354
0 PPM	A1R3528	8.92	16.5	44	49.3274	18.4978	37.5000	8.7	4.176	4.176	0.261	0.087
0 PPM	A1R3531	8.43	16.9	46	54.5670	20.0474	36.7391	9.1	1.729	6.734	0.546	0.091
0 PPM	A1R353A	8.23	15.9	45	54.6780	19.3196	35.3333	6.1	1.769	3.904	0.244	0.183
0 PPM	A1R3539	8.14	16.4	43	52.8256	20.1474	38.1395	7.3	3.139	3.577	0.438	0.146
0 PPM	A1R3542	8.79	16.8	47	53.4699	19.1126	35.7447	7.8	2.418	4.836	0.468	0.078
0 PPM	A1R3552	8.17	16.8	44	53.8556	20.5630	38.1818	9.9	2.574	6.336	0.594	0.396
0 PPM	A1R3553	8.32	16.9	45	54.0865	20.3125	37.5556	6.7	2.211	3.953	0.402	0.134
0 PPM	A1R3555	7.99	15.8	43	53.8173	19.7747	36.7442	8.7	1.218	6.960	0.435	0.087
0 PPM	A1R3561	9.06	17.6	48	52.9801	19.4260	36.6667	9.7	3.977	4.850	0.485	0.388
0 PPM	A1R3565	4.75	12.3	31	65.2632	25.8947	39.6774	10.5	4.725	4.725	0.945	0.105
0 PPM	A1R3567	8.25	16.4	46	55.7576	19.8788	35.6522	12.1	3.872	8.107	0.121	0.000
0 PPM	A1R3574	3.59	8.9	23	64.0669	24.7911	38.6957	19.4	12.028	6.790	0.388	0.194
0 PPM	A1R3577	8.64	16.7	45	52.0833	19.3287	37.1111	9.7	1.455	7.469	0.679	0.097
300 PPM	B1R35A3	6.04	11.8	33	54.6358	19.5364	35.7576	9.6	1.440	7.584	0.480	0.096
300 PPM	B1R3593	6.88	13.8	39	56.6660	20.0581	35.3846	6.7	2.680	4.020	0.000	0.000
300 PPM	B1R3596	7.84	15.6	43	54.8469	19.8980	36.2791	9.0	2.070	6.300	0.450	0.180
300 PPM	B1R3600	7.28	13.9	38	52.1978	19.0934	36.5789	9.6	1.440	7.488	0.384	0.288
300 PPM	B1R3601	7.05	14.6	40	56.7376	20.7092	36.5000	9.8	2.352	6.664	0.490	0.294
300 PPM	B1R3605	7.82	16.0	44	56.2660	20.4604	36.3636	9.3	1.209	7.533	0.465	0.093
300 PPM	B1R360B	7.71	14.2	39	50.5837	18.4176	36.4103	11.4	5.700	4.788	0.684	0.228
300 PPM	B1R3610	7.11	15.5	41	57.6653	21.8003	37.8049	9.5	1.805	6.935	0.760	0.000
300 PPM	B1R3612	7.59	14.7	40	52.7009	19.3676	36.7500	13.6	7.208	4.896	0.952	0.544
300 PPM	B1R3615	8.03	15.6	42	52.3039	19.4271	37.1429	9.2	2.116	5.980	0.828	0.276
300 PPM	B1R3624	8.16	14.9	42	51.4706	18.2598	35.4762	10.5	3.360	5.985	1.155	0.000
300 PPM	B1R3632	8.55	16.6	45	52.6316	19.4152	36.8889	11.2	3.584	6.496	0.784	0.336
300 PPM	B1R3641	7.48	14.3	39	52.1390	19.1176	36.6667	9.3	2.046	5.859	1.023	0.372
300 PPM	B1R3644	8.31	15.5	44	52.9483	18.6522	35.2273	10.0	2.700	6.700	0.500	0.100
300 PPM	B1R3645	7.36	14.6	40	54.3478	19.8370	36.5000	9.9	1.980	7.227	0.495	0.198
30 PPM	C1R3647	6.20	11.7	35	56.4516	18.8710	33.4286	21.9	11.826	9.198	0.657	0.219
30 PPM	C1R3651	8.70	16.3	47	54.0230	18.7356	34.6809	10.5	1.260	8.715	0.420	0.105
30 PPM	C1R3654	8.19	15.6	45	54.9451	19.0476	34.6667	9.5	0.570	8.740	0.095	0.095
30 PPM	C1R365A	8.98	15.9	47	52.3385	17.7060	33.8298	6.5	1.560	4.680	0.130	0.130
30 PPM	C1R3662	11.48	19.1	53	46.1672	16.6376	36.0377	21.5	7.955	12.900	0.645	0.000
30 PPM	C1R3663	9.21	16.1	47	51.0315	17.4810	34.2553	9.3	1.953	6.975	0.372	0.000
30 PPM	C1R3664	9.26	16.5	48	51.8359	17.8186	34.3750	8.7	0.609	7.830	0.261	0.000
30 PPM	C1R3667	7.95	16.5	54	67.9245	20.7547	30.5556	7.6	0.608	6.916	0.076	0.000
30 PPM	C1R3668	8.79	16.2	47	53.4699	18.4300	34.4681	6.7	0.402	5.963	0.335	0.000
30 PPM	C1R3676	8.90	16.2	46	51.6854	18.2022	35.2174	16.1	5.474	9.660	0.322	0.644
30 PPM	C1R3679	8.90	16.5	46	51.6854	18.5393	35.8696	12.5	0.375	11.750	0.250	0.125
30 PPM	C1R3681	7.65	14.8	41	53.5948	19.3464	36.0976	14.5	1.740	12.180	0.435	0.145
30 PPM	C1R3685	8.74	15.9	46	52.6316	18.1922	34.5652	8.6	3.010	5.332	0.258	0.000
30 PPM	C1R3689	8.37	15.2	46	54.9582	18.1601	33.0435	7.1	0.426	6.319	0.284	0.071
30 PPM	C1R3695	8.02	14.7	44	54.8628	18.3292	33.4091	6.4	0.448	5.824	0.000	0.128

000442

TABLE 12

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

MONTH=24

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	A1R3518	7.44	13.1	37	49.7312	17.6075	35.4054	13.2	3.036	9.108	0.924	0.132
0 PPM	A1R3524	8.08	14.4	43	53.2178	17.8218	33.4884	6.8	1.632	4.760	0.340	0.068
0 PPM	A1R3528	8.70	15.5	45	51.7241	17.8161	34.4444	7.2	0.432	6.624	0.000	0.144
0 PPM	A1R3531	8.33	16.0	47	56.4226	19.2077	34.0426	8.4	1.092	6.972	0.336	0.000
0 PPM	A1R3534	7.96	15.3	46	57.7889	19.2211	33.2609	36.3	22.506	12.342	1.452	0.000
0 PPM	A1R3538	8.54	15.1	45	52.6932	17.6815	33.5556	7.2	1.584	5.256	0.288	0.072
0 PPM	A1R3542	8.86	16.0	46	51.9187	18.0587	34.7826	7.1	0.710	6.248	0.071	0.071
0 PPM	A1R3548	8.09	15.6	46	56.8603	19.2831	33.9130	8.5	1.445	6.885	0.170	0.000
0 PPM	A1R3554	6.08	11.8	34	55.9211	19.4079	34.7059	4.4	0.264	4.136	0.000	0.000
0 PPM	A1R3557	9.47	16.7	50	52.7983	17.6346	33.4000	8.0	1.840	6.000	0.080	0.080
0 PPM	A1R3562	7.74	13.2	37	47.8036	17.0543	35.6757	12.6	5.922	6.300	0.378	0.000
0 PPM	A1R3564	7.68	14.4	42	54.6875	18.7500	34.2857	12.4	4.712	6.820	0.620	0.248
0 PPM	A1R3569	5.38	12.0	33	61.3383	22.3048	36.3636	9.7	0.776	8.924	0.000	0.000
0 PPM	A1R3573	8.52	16.1	47	55.1643	18.8967	34.2553	7.4	1.554	5.328	0.296	0.222
0 PPM	A1R3578	6.70	12.7	37	55.2239	18.9552	34.3243	12.7	8.255	4.191	0.127	0.127
300 PPM	B1R3581	8.42	15.5	46	54.6318	18.4086	33.6957	6.2	0.868	4.960	0.372	0.000
300 PPM	B1R3585	7.94	14.8	43	54.1562	18.6398	34.4186	10.5	2.100	8.085	0.210	0.105
300 PPM	B1R3591	7.98	16.0	48	60.1504	20.0501	33.3333	8.4	3.528	4.620	0.252	0.000
300 PPM	B1R3594	8.17	14.4	43	52.6316	17.6255	33.4884	5.7	0.741	4.845	0.114	0.000
300 PPM	B1R3597	8.03	15.3	44	54.7945	19.0535	34.7727	8.7	2.697	5.655	0.261	0.087
300 PPM	B1R3601	6.21	12.0	35	56.3607	19.3237	34.2857	9.6	4.608	4.416	0.384	0.192
300 PPM	B1R3605	8.02	15.8	53	66.0848	19.7007	29.8113	6.3	1.197	5.040	0.000	0.063
300 PPM	B1R3608	8.21	13.6	39	47.5030	16.5652	34.8718	9.8	1.862	7.742	0.196	0.000
300 PPM	B1R3611	8.04	15.2	43	53.4826	18.9055	35.3488	11.0	1.540	8.910	0.330	0.220
300 PPM	B1R3618	8.58	15.3	45	52.4476	17.8322	34.0000	8.2	1.722	6.232	0.246	0.000
300 PPM	B1R3623	8.00	15.6	52	65.0000	19.5000	30.0000	9.5	1.805	7.410	0.190	0.095
300 PPM	B1R3630	8.59	16.3	48	55.8789	18.9756	33.9583	7.5	1.050	6.300	0.075	0.075
300 PPM	B1R3633	6.51	11.6	33	50.6912	17.8187	35.1515	14.2	4.544	9.514	0.142	0.000
300 PPM	B1R3636	8.15	13.4	38	46.6258	16.4417	35.2632	12.6	5.544	5.922	0.756	0.378
300 PPM	B1R3641	7.92	13.8	40	50.5051	17.4242	34.5000	8.2	2.378	5.494	0.328	0.000
30 PPM	C1R3646	.	.	.	.	.	.	.	.	.	.	.
30 PPM	C1R3650	8.35	15.0	45	53.8922	17.9641	33.3333	9.3	5.208	3.813	0.279	0.000
30 PPM	C1R3654	7.90	14.2	41	51.8987	17.9747	34.6341	13.1	3.537	8.908	0.655	0.000
30 PPM	C1R3658	8.96	16.0	47	52.4554	17.8571	34.0426	5.0	1.400	3.450	0.100	0.050
30 PPM	C1R3663	8.34	15.2	44	52.7578	18.2254	34.5455	8.7	2.349	5.829	0.435	0.087
30 PPM	C1R3667	7.34	15.2	43	58.5831	20.7044	35.3488	7.4	1.776	5.254	0.222	0.148
30 PPM	C1R3670	7.21	13.7	39	54.0915	19.0014	35.1282	12.8	4.096	7.808	0.768	0.128
30 PPM	C1R3672	8.87	15.4	46	51.8602	17.3619	33.4783	14.7	7.644	6.468	0.588	0.000
30 PPM	C1R3676	5.93	11.2	31	52.2766	18.8870	36.1290	18.0	6.120	10.800	1.080	0.000
30 PPM	C1R3679	9.14	15.7	46	50.3282	17.1772	34.1304	12.5	2.375	9.750	0.125	0.250
30 PPM	C1R3682	8.37	15.1	44	52.5687	18.0406	34.3182	10.2	4.590	5.202	0.306	0.102
30 PPM	C1R3684	7.73	14.7	42	54.3338	19.0168	35.0000	9.5	1.900	7.410	0.190	0.000
30 PPM	C1R3689	8.14	15.2	45	55.2826	18.6732	33.7778	7.4	1.850	4.958	0.370	0.222
30 PPM	C1R3691	6.97	13.4	38	54.5194	19.2253	35.2632	10.4	1.976	7.904	0.208	0.312
30 PPM	C1R3694	8.02	15.3	44	54.8628	19.0773	34.7727	7.2	0.576	6.552	0.072	0.000

000443

TABLE 13

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

		ERYTHROCYTES (CELLS X 10**6)		HEMOGLOBIN (G/DL)		HEMATOCRIT (% PACKED CELLS)		MCV (MICRONS**3)		MCH (PICOGRAMS)		MCHC (%)	
	N	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE													
MONTH 3													
0 PPM	15	6.91	0.319	15.8	0.48	43.7	1.11	63	2.2	22.9	0.75	36.2	0.44
300 PPM	15	6.67	0.266	15.4	0.56	42.0*	1.85	63	2.3	23.0	0.63	36.6	0.58
30 PPM	15	7.26*	0.505	16.0	0.70	43.9	1.75	61*	3.5	22.1*	1.37	36.3	0.49
MONTH 6													
0 PPM	15	7.32	0.413	15.0	0.55	42.3	1.84	58	2.2	20.5	0.95	35.4	1.01
300 PPM	15	7.37	0.327	15.4	0.64	42.5	1.60	58	2.2	21.0	0.93	36.3	0.83
30 PPM	15	6.92*	0.475	13.7*	0.95	38.7*	3.20	56	4.9	19.9	1.93	35.5	1.65
MONTH 12													
0 PPM	15	7.60	0.300	15.6	0.40	44.3	1.39	58	2.1	20.6	0.71	35.3	0.48
300 PPM	15	6.92#	1.193	14.6#	1.74	40.5#	4.73	60	8.1	21.5	3.19	36.0	1.20
30 PPM	15	7.29	1.212	15.1	1.70	42.5	4.76	59	6.8	21.0	2.47	35.5	0.64
MONTH 18													
0 PPM	15	7.37	0.668	15.4	1.43	42.9	4.13	58	1.7	21.0	0.68	36.0	0.85
300 PPM	15	7.24	0.809	14.9	1.33	41.9	3.86	58	2.6	20.7	0.96	35.6	0.52
30 PPM	15	7.01	0.763	14.8	1.32	41.5	3.85	59	3.0	21.2	1.09	35.8	0.65
MONTH 24													
0 PPM	15	7.06	1.129	14.8	1.80	42.3	5.40	60	3.5	21.2	1.45	35.1	0.87
300 PPM	15	7.14	0.744	14.4	1.26	40.4	3.66	58*	2.1	20.3*	0.74	35.8	0.99
30 PPM	15	7.06	1.097	14.6	2.03	41.7	5.97	59	2.5	20.7	0.91	35.0	0.81

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

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0004444

TABLE 13

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

		LEUKOCYTES (CELLS X 10**3)		NEUTROPHILS (CELLS X 10**3)		LYMPHOCYTES (CELLS X 10**3)		MONOCYTES (CELLS X 10**3)		EOSINOPHILS (CELLS X 10**3)	
	N	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE											
MONTH 3											
0 PPM	15	18.98	2.698	2.57	1.406	15.73	2.970	0.37	0.217	0.31	0.262
300 PPM	15	18.51	3.778	3.24	1.728	14.78	2.834	0.28	0.312	0.22	0.258
30 PPM	15	18.06	3.470	3.33	1.347	14.23	3.105	0.22	0.250	0.30	0.258
MONTH 6											
0 PPM	15	7.52	2.559	1.44	1.586	5.87	2.160	0.18	0.096	0.08	0.067
300 PPM	15	8.60	1.953	1.55	0.705	6.73	1.784	0.20	0.122	0.11	0.102
30 PPM	15	7.18	1.723	1.76	1.023	5.06	1.607	0.28	0.142	0.15	0.119
MONTH 12											
0 PPM	15	5.73	2.120	1.27	1.562	4.13	1.049	0.21	0.108	0.12	0.125
300 PPM	15	5.72	1.818	1.45	1.281	3.95	1.061	0.22	0.165	0.09	0.094
30 PPM	15	5.83	1.135	1.34	0.679	4.13	0.792	0.25	0.098	0.10	0.091
MONTH 18											
0 PPM	15	5.75	2.230	1.01	1.631	4.48	0.973	0.28	0.249	0.03	0.057
300 PPM	15	6.30	2.368	2.21	1.950	3.62	1.305	0.36	0.226	0.10*	0.108
30 PPM	15	6.83	2.608	2.89*	2.240	3.51*	1.061	0.36	0.148	0.07	0.074
MONTH 24											
0 PPM	15	6.73	4.064	2.87	2.959	3.67	1.329	0.11	0.151	0.07	0.074
300 PPM	15	6.39	1.691	2.15	0.962	4.04	1.190	0.10	0.062	0.06	0.057
30 PPM	15	8.57	3.434	3.44	2.915	4.81	1.641	0.24	0.241	0.08	0.094

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

000445

TABLE 13

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

MONTH=3

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4576	6.98	15.6	43	61.6046	22.3496	36.2791	17.5	1.925	14.525	0.700	0.350
0 PPM	N1R4578	7.72	16.1	44	56.9948	20.8549	36.5909	20.1	3.417	16.080	0.402	0.201
0 PPM	N1R4582	6.79	15.7	43	63.3284	23.1222	36.5116	17.0	2.040	14.280	0.510	0.170
0 PPM	N1R4583	6.74	15.6	43	63.7982	23.1454	36.2791	19.4	2.134	17.072	0.000	0.194
0 PPM	N1R4584	6.31	14.9	42	66.5610	23.6133	35.4762	20.5	4.715	14.555	0.410	0.820
0 PPM	N1R4592	7.03	16.2	45	64.0114	23.0441	36.0000	17.3	5.882	11.072	0.173	0.173
0 PPM	N1R4610	6.94	15.6	44	63.4006	22.4784	35.4545	15.4	2.156	12.782	0.154	0.308
0 PPM	N1R4612	6.88	15.7	44	63.9535	22.8198	35.6818	21.0	2.310	18.480	0.210	0.000
0 PPM	N1R4613	6.73	15.0	42	62.4071	22.2883	35.7143	16.1	2.898	12.397	0.322	0.483
0 PPM	N1R4619	7.35	16.5	45	61.2245	22.4490	36.6667	21.0	0.630	19.320	0.420	0.630
0 PPM	N1R4621	6.60	15.5	42	63.6364	23.4848	36.9048	24.3	1.944	21.384	0.243	0.729
0 PPM	N1R4626	6.98	16.0	44	63.0372	22.9226	36.3636	21.1	4.009	16.458	0.211	0.422
0 PPM	N1R4627	6.84	16.4	45	65.7895	23.9766	36.4444	19.6	1.176	18.032	0.392	0.000
0 PPM	N1R4633	6.84	16.0	44	64.3275	23.3918	36.3636	20.4	2.040	17.544	0.816	0.000
0 PPM	N1R4640	6.99	16.4	45	64.3777	23.4621	36.4444	14.0	1.260	12.040	0.560	0.140
300 PPM	O1R4645	6.51	15.3	42	64.5161	23.5023	36.4286	12.4	1.860	10.168	0.124	0.248
300 PPM	O1R4654	6.77	16.2	45	66.4697	23.9291	36.0000	16.7	2.171	14.028	0.167	0.334
300 PPM	O1R4660	6.34	14.6	40	63.0915	23.0284	36.5000	19.2	1.728	17.088	0.384	0.000
300 PPM	O1R4664	6.36	14.8	40	62.8931	23.2704	37.0000	18.3	6.771	11.163	0.366	0.000
300 PPM	O1R4668	7.02	15.8	43	61.2536	22.5071	36.7442	18.6	2.046	15.624	0.372	0.558
300 PPM	O1R4669	6.99	15.5	42	60.0858	22.1745	36.9048	15.3	1.224	13.923	0.153	0.000
300 PPM	O1R4672	6.35	14.8	40	62.9921	23.3071	37.0000	17.8	3.204	13.706	0.712	0.178
300 PPM	O1R4673	6.42	14.8	40	62.3053	23.0530	37.0000	28.4	6.532	21.016	0.284	0.852
300 PPM	O1R4674	6.88	16.1	44	63.9535	23.4012	36.5909	16.3	2.282	13.855	0.163	0.000
300 PPM	O1R4679	6.72	14.7	39	58.0357	21.8750	37.6923	18.0	2.340	15.480	0.000	0.180
300 PPM	O1R4680	6.46	15.4	42	65.0155	23.8390	36.6667	23.7	4.977	17.301	1.185	0.237
300 PPM	O1R4693	6.88	15.2	42	61.0465	22.0930	36.1905	18.3	3.660	14.091	0.000	0.549
300 PPM	O1R4698	6.99	15.9	44	62.9471	22.7468	36.1364	21.6	3.456	18.144	0.000	0.000
300 PPM	O1R4700	6.92	16.1	44	63.5838	23.2659	36.5909	16.9	2.028	14.703	0.169	0.000
300 PPM	O1R4701	6.42	15.1	43	66.9782	23.5202	35.1163	16.1	4.347	11.431	0.161	0.161
30 PPM	P1R4708	7.79	16.7	45	57.7664	21.4377	37.1111	15.3	2.448	12.546	0.153	0.459
30 PPM	P1R4710	6.95	15.5	43	61.8705	22.3022	36.0465	20.4	2.040	18.156	0.204	0.000
30 PPM	P1R4720	6.83	15.7	43	62.9575	22.9868	36.5116	15.5	2.170	12.710	0.155	0.465
30 PPM	P1R4721	6.71	15.7	44	65.5738	23.3979	35.6818	22.0	4.400	16.940	0.000	0.660
30 PPM	P1R4730	7.44	16.4	45	60.4839	22.0430	36.4444	16.6	1.992	14.110	0.166	0.332
30 PPM	P1R4731	6.80	15.9	44	64.7059	23.3824	36.1364	18.1	3.077	14.842	0.181	0.000
30 PPM	P1R4734	6.41	16.0	43	67.0827	24.9610	37.2093	13.2	1.320	11.616	0.000	0.264
30 PPM	P1R4735	7.65	15.8	43	56.2092	20.6536	36.7442	26.8	3.752	21.976	0.804	0.268
30 PPM	P1R4736	7.88	17.1	47	59.6447	21.7005	36.3830	19.4	3.880	15.326	0.000	0.194
30 PPM	P1R4737	7.12	16.6	45	63.2022	23.3146	36.8889	20.6	3.708	16.068	0.618	0.206
30 PPM	P1R4738	7.40	15.8	44	59.4595	21.3514	35.9091	16.0	4.960	10.720	0.160	0.160
30 PPM	P1R4744	7.14	15.8	44	61.6246	22.1289	35.9091	18.0	5.220	11.700	0.360	0.720
30 PPM	P1R4749	7.05	14.9	41	58.1560	21.1348	36.3415	17.3	3.287	14.013	0.000	0.000
30 PPM	P1R4752	8.30	17.0	47	56.6265	20.4819	36.1702	17.9	5.728	10.919	0.537	0.716
30 PPM	P1R4753	7.39	14.6	41	55.4804	19.7564	35.6098	13.8	1.932	11.868	0.000	0.000

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TABLE 13

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

MONTH=6

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4582	7.32	15.0	43	58.7432	20.4918	34.8837	8.59	0.6872	7.5592	0.2577	0.0859
0 PPM	N1R4584	7.85	15.8	46	58.5987	20.1274	34.3478	6.45	0.5160	5.8695	0.0000	0.0645
0 PPM	N1R4586	6.81	13.8	39	57.2687	20.2643	35.3846	6.24	1.9344	4.0560	0.0624	0.1872
0 PPM	N1R4590	7.19	15.3	43	59.8053	21.2796	35.5814	7.95	1.1925	6.5190	0.2385	0.0000
0 PPM	N1R4598	7.31	15.1	42	57.4555	20.6566	35.9524	7.43	0.9659	6.3155	0.0000	0.1486
0 PPM	N1R4603	6.60	14.7	40	60.6061	22.2727	36.7500	7.69	0.4614	7.0748	0.0769	0.0769
0 PPM	N1R4607	7.88	15.8	44	55.8376	20.0508	35.9091	6.43	0.5787	5.7227	0.1286	0.0000
0 PPM	N1R4616	8.03	14.6	44	54.7945	18.1818	33.1818	6.95	0.4170	6.3940	0.1390	0.0000
0 PPM	N1R4619	7.70	15.3	44	57.1429	19.8701	34.7727	5.98	0.5382	5.3222	0.0598	0.0598
0 PPM	N1R4621	6.80	14.3	42	61.7647	21.0294	34.0476	6.61	1.2559	5.2219	0.0661	0.0661
0 PPM	N1R4622	7.23	14.4	41	56.7082	19.9170	35.1220	4.59	0.4131	4.0392	0.0918	0.0459
0 PPM	N1R4629	7.32	15.1	42	57.3770	20.6284	35.9524	14.90	4.7680	9.8340	0.1490	0.1490
0 PPM	N1R4631	7.36	14.8	40	54.3478	20.1087	37.0000	11.00	1.2100	9.2400	0.3300	0.2200
0 PPM	N1R4632	7.28	15.1	42	57.6923	20.7418	35.9524	4.76	1.0948	3.5224	0.0952	0.0476
0 PPM	N1R4639	7.05	15.4	43	60.9929	21.8440	35.8140	7.28	5.6056	1.3832	0.2184	0.0728
300 PPM	O1R4650	6.91	15.1	42	60.7815	21.8524	35.9524	7.98	2.1546	5.7456	0.0000	0.0798
300 PPM	O1R4653	7.47	16.6	43	57.5636	22.2222	38.6047	6.80	2.3120	4.1480	0.1360	0.2040
300 PPM	O1R4657	7.32	15.1	41	56.0109	20.6284	36.8293	12.70	2.9210	9.2710	0.3810	0.1270
300 PPM	O1R4660	7.49	15.3	43	57.4099	20.4272	35.5814	11.30	1.4690	9.6050	0.2260	0.0000
300 PPM	O1R4663	7.72	15.0	42	54.4041	19.4301	35.7143	7.86	1.8078	5.8950	0.1572	0.0000
300 PPM	O1R4670	7.38	16.0	43	58.2656	21.6802	37.2093	8.77	1.4032	7.1914	0.1754	0.0000
300 PPM	O1R4673	6.71	14.6	40	59.6125	21.7586	36.5000	9.73	1.5568	7.4921	0.3892	0.2919
300 PPM	O1R4681	6.87	14.8	41	59.6798	21.5429	36.0976	9.50	0.8550	8.2650	0.2850	0.0950
300 PPM	O1R4682	7.44	15.8	44	59.1398	21.2366	35.9091	9.18	0.5508	8.3538	0.1836	0.0918
300 PPM	O1R4692	7.75	15.0	42	54.1935	19.3548	35.7143	7.29	2.3328	4.7385	0.2187	0.0000
300 PPM	O1R4693	7.65	15.0	42	54.9020	19.6078	35.7143	9.41	2.1643	6.7752	0.1882	0.2823
300 PPM	O1R4694	7.64	16.5	45	58.9005	21.5969	36.6667	9.99	1.0989	8.3916	0.3996	0.0999
300 PPM	O1R4698	7.07	14.9	41	57.9915	21.0750	36.3415	6.55	1.0480	5.2400	0.0000	0.2620
300 PPM	O1R4699	7.56	15.5	43	56.8783	20.5026	36.0465	6.39	0.8946	5.3037	0.1278	0.0639
300 PPM	O1R4700	7.53	16.2	46	61.0890	21.5139	35.2174	5.55	0.7215	4.5510	0.1665	0.1110
30 PPM	P1R4710	6.66	13.8	39	58.5586	20.7207	35.3846	10.80	1.6200	8.9640	0.2160	0.0000
30 PPM	P1R4711	6.85	12.2	35	51.0949	17.8102	34.8571	5.65	1.8080	3.5030	0.1695	0.1695
30 PPM	P1R4717	6.98	13.2	37	53.0086	18.9112	35.6757	8.13	3.4146	4.2276	0.2439	0.2439
30 PPM	P1R4719	7.03	14.8	43	61.1664	21.0526	34.4186	6.99	2.0271	4.6134	0.2097	0.1398
30 PPM	P1R4729	7.00	12.4	35	50.0000	17.7143	35.4286	5.16	1.3932	3.1476	0.4644	0.1548
30 PPM	P1R4731	6.78	12.8	36	53.0973	18.8791	35.5556	7.23	1.3014	5.3502	0.5061	0.0723
30 PPM	P1R4732	6.35	15.0	41	64.5669	23.6220	36.5854	9.28	1.0208	7.7024	0.0928	0.4640
30 PPM	P1R4733	7.30	14.7	42	57.5342	20.1370	35.0000	5.49	0.6588	4.7214	0.0549	0.0549
30 PPM	P1R4737	5.95	14.1	35	58.8235	23.6975	40.2857	6.83	1.2977	4.9859	0.2732	0.2732
30 PPM	P1R4740	7.02	12.6	35	49.8575	17.9487	36.0000	4.06	0.5278	3.3292	0.0812	0.1218
30 PPM	P1R4743	6.80	13.0	36	52.9412	19.1176	36.1111	8.81	4.3169	4.0526	0.4405	0.0000
30 PPM	P1R4745	7.18	14.8	43	59.8886	20.6128	34.4186	6.64	2.0584	4.3160	0.1992	0.0664
30 PPM	P1R4746	7.12	14.1	40	56.1798	19.8034	35.2500	7.07	0.7777	5.8681	0.2121	0.2121
30 PPM	P1R4749	8.13	14.3	41	50.4305	17.5892	34.8780	8.14	1.7094	6.2678	0.0814	0.0814
30 PPM	P1R4750	6.71	13.6	42	62.5931	20.2683	32.3810	7.48	2.3936	4.7872	0.1496	0.1496

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TABLE 13

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

MONTH=12

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4578	7.55	15.7	44	58.2781	20.7947	35.6818	3.5	0.840	2.450	0.140	0.070
0 PPM	N1R4582	7.57	15.7	44	58.1292	20.7398	35.6818	6.9	0.621	5.865	0.207	0.207
0 PPM	N1R4585	7.84	15.9	45	57.3980	20.2806	35.3333	4.1	0.451	3.280	0.287	0.082
0 PPM	N1R4588	7.23	15.2	43	59.4744	21.0235	35.3488	3.9	0.390	3.276	0.156	0.078
0 PPM	N1R4589	7.94	15.1	43	54.1562	19.0176	35.1163	6.8	3.264	3.468	0.068	0.000
0 PPM	N1R4590	7.44	15.8	44	59.1398	21.2366	35.9091	5.4	0.648	4.482	0.162	0.108
0 PPM	N1R4601	7.17	15.2	43	59.9721	21.1994	35.3488	4.6	0.598	3.542	0.276	0.184
0 PPM	N1R4608	8.26	16.3	46	55.6901	19.7337	35.4348	7.1	0.710	5.822	0.355	0.213
0 PPM	N1R4610	7.32	15.1	42	57.3770	20.6284	35.9524	3.8	0.152	3.534	0.038	0.076
0 PPM	N1R4620	7.80	15.3	43	55.1282	19.6154	35.5814	5.2	0.156	4.888	0.156	0.000
0 PPM	N1R4629	7.84	16.0	47	59.9490	20.4082	34.0426	12.1	6.171	5.324	0.121	0.484
0 PPM	N1R4630	7.44	15.6	44	59.1398	20.9677	35.4545	6.5	1.365	4.810	0.325	0.000
0 PPM	N1R4631	7.68	15.8	45	58.5938	20.5729	35.1111	5.9	1.239	4.189	0.413	0.059
0 PPM	N1R4632	7.55	16.3	46	60.9272	21.5894	35.4348	4.9	1.666	2.891	0.294	0.049
0 PPM	N1R4640	7.30	15.6	45	61.6438	21.3699	34.6667	5.2	0.728	4.056	0.208	0.208
300 PPM	O1R4642	7.22	14.2	40	55.4017	19.6676	35.5000	7.0	0.560	6.230	0.140	0.070
300 PPM	O1R4652	7.31	14.8	40	54.7196	20.2462	37.0000	5.1	1.530	3.264	0.153	0.153
300 PPM	O1R4655	6.96	15.3	41	58.9080	21.9828	37.3171	5.3	1.378	3.657	0.159	0.106
300 PPM	O1R4656	7.81	15.4	44	56.3380	19.7183	35.0000	8.1	2.187	5.508	0.162	0.243
300 PPM	O1R4664	7.11	15.0	42	59.0717	21.0970	35.7143	8.1	2.349	4.941	0.486	0.324
300 PPM	O1R4666	6.90	13.9	39	56.5217	20.1449	35.6410	9.2	5.428	3.036	0.644	0.092
300 PPM	O1R4669	7.16	15.3	43	60.0559	21.3687	35.5814	4.4	0.660	3.608	0.088	0.044
300 PPM	O1R4671	6.95	15.0	40	57.5540	21.5827	37.5000	4.9	1.421	3.087	0.294	0.098
300 PPM	O1R4674	7.92	16.0	44	55.5556	20.2020	36.3636	4.8	0.960	3.552	0.240	0.048
300 PPM	O1R4676	6.76	14.8	40	59.1716	21.8935	37.0000	2.4	0.024	2.352	0.024	0.000
300 PPM	O1R4687	6.54	12.4	38	58.1040	18.9602	32.6316	7.1	1.562	5.325	0.213	0.000
300 PPM	O1R4689	2.83	9.2	25	88.3392	32.5088	36.8000	4.4	0.440	3.784	0.132	0.044
300 PPM	O1R4692	7.45	15.3	43	57.7181	20.5369	35.5814	4.3	0.688	3.569	0.043	0.000
300 PPM	O1R4699	7.18	16.0	44	61.2813	22.2841	36.3636	4.9	0.833	3.626	0.294	0.147
300 PPM	O1R4704	7.67	15.7	44	57.3664	20.4694	35.6818	5.8	1.740	3.770	0.290	0.000
30 PPM	P1R4711	8.03	15.5	44	54.7946	19.3026	35.2273	4.9	1.666	2.744	0.343	0.147
30 PPM	P1R4714	7.69	15.3	43	55.9168	19.8960	35.5814	6.0	1.380	4.380	0.120	0.120
30 PPM	P1R4715	7.74	15.6	45	58.1395	20.1550	34.6667	6.9	2.277	4.416	0.207	0.000
30 PPM	P1R4716	7.18	15.2	44	61.2813	21.1699	34.5455	5.2	0.416	4.524	0.104	0.156
30 PPM	P1R4717	8.56	16.7	48	56.0748	19.5093	34.7917	6.7	2.613	3.618	0.335	0.134
30 PPM	P1R4721	7.74	16.1	46	59.4315	20.8010	35.0000	3.3	0.132	2.937	0.198	0.033
30 PPM	P1R4725	3.15	9.3	27	82.5397	29.5238	35.7692	4.3	0.258	3.913	0.129	0.000
30 PPM	P1R4727	7.45	15.0	42	56.3758	20.1342	35.7143	6.0	1.680	3.540	0.420	0.360
30 PPM	P1R4729	7.89	15.8	45	57.0342	20.0253	35.1111	6.2	1.302	4.464	0.372	0.062
30 PPM	P1R4734	7.13	16.0	44	61.7111	22.4404	36.3636	6.7	1.541	4.623	0.335	0.201
30 PPM	P1R4742	6.97	14.0	39	55.9541	20.0861	35.8974	7.2	1.440	5.400	0.288	0.072
30 PPM	P1R4743	7.46	15.2	43	57.6408	20.3753	35.3488	6.8	1.700	4.760	0.272	0.068
30 PPM	P1R4749	7.27	15.0	41	56.3961	20.6327	36.5854	4.5	1.170	3.060	0.180	0.090
30 PPM	P1R4750	7.52	15.5	43	57.1809	20.6117	36.0465	6.5	1.170	5.005	0.260	0.065
30 PPM	P1R4755	7.57	15.6	43	56.8032	20.6077	36.2791	6.2	1.364	4.588	0.186	0.062

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TABLE 13

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

MONTH=18

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4581	6.16	12.3	34	55.1948	19.9675	36.1765	13.2	6.600	5.544	1.056	0.000
0 PPM	N1R4583	7.52	15.6	44	58.5106	20.7447	35.4545	5.2	0.208	4.836	0.156	0.000
0 PPM	N1R4586	7.08	14.5	41	57.9096	20.4802	35.3659	4.7	0.517	3.854	0.188	0.141
0 PPM	N1R4592	8.04	16.8	46	57.2139	20.8955	36.5217	6.5	1.690	4.680	0.130	0.000
0 PPM	N1R4595	7.52	15.3	44	58.5106	20.3457	34.7727	4.3	1.075	2.967	0.129	0.129
0 PPM	N1R4598	7.44	16.4	45	60.4839	22.0430	36.4444	5.0	0.200	4.650	0.150	0.000
0 PPM	N1R4599	7.80	16.1	44	56.4103	20.6410	36.5909	4.8	0.384	4.128	0.144	0.144
0 PPM	N1R4602	7.72	16.6	45	58.2902	21.5026	36.8889	6.5	0.195	6.305	0.065	0.000
0 PPM	N1R4604	7.97	16.4	47	58.9711	20.5772	34.8936	4.9	0.441	4.410	0.049	0.000
0 PPM	N1R4606	5.85	12.4	34	58.1197	21.1966	36.4706	5.1	1.632	3.060	0.408	0.000
0 PPM	N1R4609	7.07	15.5	41	57.9915	21.9236	37.8049	4.9	0.931	3.675	0.294	0.000
0 PPM	N1R4611	6.95	14.7	41	58.9928	21.1511	35.8537	5.3	0.371	4.664	0.265	0.000
0 PPM	N1R4612	8.27	16.5	47	56.8319	19.9516	35.1064	7.0	0.840	5.950	0.210	0.000
0 PPM	N1R4627	7.36	16.2	46	62.5000	22.0109	35.2174	5.0	0.050	4.900	0.050	0.000
0 PPM	N1R4638	7.76	16.4	45	57.9897	21.1340	36.4444	3.8	0.076	3.610	0.114	0.000
300 PPM	O1R4645	7.49	15.4	44	58.7450	20.5607	35.0000	4.5	2.475	1.485	0.405	0.135
300 PPM	O1R4647	7.57	15.2	43	56.8032	20.0793	35.3488	4.5	1.215	2.880	0.315	0.090
300 PPM	O1R4648	5.54	12.0	34	61.3718	21.6606	35.2941	12.6	8.568	3.024	0.882	0.126
300 PPM	O1R4651	7.60	15.3	43	56.5789	20.1316	35.5814	5.3	1.378	3.498	0.371	0.053
300 PPM	O1R4663	7.84	15.7	44	56.1224	20.0255	35.6818	3.7	1.184	2.109	0.370	0.037
300 PPM	O1R4667	5.84	12.2	34	58.2192	20.8904	35.8824	10.1	3.131	6.161	0.808	0.000
300 PPM	O1R4675	8.83	16.8	48	54.3601	19.0260	35.0000	7.8	2.652	4.680	0.390	0.078
300 PPM	O1R4679	7.31	14.4	41	56.0876	19.6990	35.1220	6.3	2.016	4.095	0.189	0.000
300 PPM	O1R4684	6.57	14.3	40	60.8828	21.7656	35.7500	6.3	3.213	2.709	0.315	0.063
300 PPM	O1R4688	7.45	15.7	45	60.4027	21.0738	34.8889	7.1	1.917	4.615	0.426	0.142
300 PPM	O1R4690	7.21	15.3	42	58.2524	21.2205	36.4286	4.2	2.142	1.806	0.168	0.084
300 PPM	O1R4693	7.97	15.4	43	53.9523	19.3225	35.8140	6.1	0.610	4.941	0.183	0.366
300 PPM	O1R4694	7.30	16.4	46	63.0137	22.4658	35.6522	5.4	0.864	4.158	0.324	0.054
300 PPM	O1R4696	6.95	14.4	40	57.5540	20.7194	36.0000	5.3	1.219	3.445	0.318	0.318
300 PPM	O1R4698	7.20	15.4	42	58.3333	21.3889	36.6667	5.3	0.636	4.664	0.000	0.000
30 PPM	P1R4707	6.67	13.5	38	56.9715	20.2399	35.5263	7.7	3.080	4.158	0.462	0.000
30 PPM	P1R4709	6.05	14.4	40	66.1157	23.8017	36.0000	3.7	0.740	2.701	0.259	0.000
30 PPM	P1R4714	7.46	15.3	43	57.6408	20.5094	35.5814	4.9	0.490	4.116	0.245	0.049
30 PPM	P1R4718	6.65	14.7	39	58.6466	22.1053	37.6923	4.9	1.176	3.332	0.343	0.049
30 PPM	P1R4720	6.46	14.1	39	60.3715	21.8266	36.1538	10.3	5.459	4.120	0.618	0.103
30 PPM	P1R4722	5.47	11.8	33	60.3291	21.5722	35.7576	9.2	5.428	3.312	0.460	0.000
30 PPM	P1R4725	7.54	16.8	48	63.6605	22.2812	35.0000	3.9	1.014	2.535	0.195	0.156
30 PPM	P1R4729	7.31	15.2	42	57.4555	20.7934	36.1905	5.1	2.601	2.193	0.306	0.000
30 PPM	P1R4732	6.42	13.7	38	59.1900	21.3396	36.0526	10.8	4.212	6.156	0.216	0.216
30 PPM	P1R4733	8.08	15.7	44	54.4554	19.4307	35.6818	4.1	1.312	2.542	0.205	0.041
30 PPM	P1R4737	6.91	15.2	43	62.2287	21.9971	35.3488	5.8	1.624	3.654	0.348	0.174
30 PPM	P1R4748	7.32	14.7	42	57.3770	20.0820	35.0000	6.6	3.366	2.970	0.198	0.066
30 PPM	P1R4749	7.88	16.2	45	57.1066	20.5584	36.0000	8.2	2.870	4.592	0.574	0.164
30 PPM	P1R4752	8.17	16.9	47	57.5275	20.6854	35.9574	5.9	1.416	4.012	0.413	0.059
30 PPM	P1R4754	6.81	14.5	41	60.2056	21.2922	35.3659	11.4	8.550	2.280	0.570	0.000

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TABLE 13

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

MONTH=24

DOSE	ANIMAL	ERYTH	HEMO	HEMAT	MCV	MCH	MCHC	WBC	PMNAB	LYMAB	MONOAB	EOSAB
0 PPM	N1R4583	7.48	15.3	42	56.1497	20.4545	36.4286	18.7	12.529	5.984	0.187	0.000
0 PPM	N1R4586	7.22	14.3	42	58.1717	19.8061	34.0476	4.1	1.148	2.952	0.000	0.000
0 PPM	N1R4591	7.91	15.7	45	56.8900	19.8483	34.8889	4.9	0.735	4.018	0.000	0.147
0 PPM	N1R4595	7.97	15.9	46	57.7164	19.9498	34.5652	4.6	2.714	1.702	0.092	0.138
0 PPM	N1R4598	7.43	16.4	47	63.2571	22.0727	34.8936	6.2	2.232	3.844	0.062	0.062
0 PPM	N1R4603	7.07	14.9	44	62.2348	21.0750	33.8636	4.2	1.092	3.066	0.000	0.042
0 PPM	N1R4606	7.78	15.9	46	59.1260	20.4370	34.5652	4.7	1.081	3.525	0.094	0.000
0 PPM	N1R4611	4.21	10.3	29	68.8836	24.4656	35.5172	9.2	3.496	5.428	0.184	0.092
0 PPM	N1R4614	7.34	16.0	44	59.9455	21.7984	36.3636	5.1	1.989	3.060	0.051	0.000
0 PPM	N1R4616	7.24	15.2	43	59.3923	20.9945	35.3488	4.5	2.115	2.340	0.000	0.045
0 PPM	N1R4626	7.31	14.5	42	57.4555	19.8358	34.5238	5.4	2.592	2.646	0.108	0.054
0 PPM	N1R4628	6.21	13.4	38	61.1916	21.5781	35.2632	8.6	3.870	4.386	0.086	0.258
0 PPM	N1R4634	4.86	11.7	32	65.8436	24.0741	36.5625	12.2	5.246	6.222	0.610	0.122
0 PPM	N1R4636	7.90	16.1	47	59.4937	20.3797	34.2553	5.0	1.650	3.250	0.100	0.000
0 PPM	N1R4638	7.99	16.8	47	58.8235	21.0263	35.7447	3.5	0.630	2.695	0.140	0.035
300 PPM	O1R4644	7.07	14.0	41	57.9915	19.8020	34.1463	4.8	1.056	3.600	0.096	0.048
300 PPM	O1R4646	6.84	14.2	41	59.9415	20.7602	34.6341	7.9	2.607	5.293	0.000	0.000
300 PPM	O1R4649	7.12	14.6	42	58.9888	20.5056	34.7619	8.3	3.652	4.399	0.083	0.166
300 PPM	O1R4657	6.55	14.0	37	56.4885	21.3740	37.8378	6.0	1.920	3.840	0.180	0.060
300 PPM	O1R4659	5.06	11.0	30	59.2885	21.7391	36.6667	8.6	3.956	4.386	0.172	0.086
300 PPM	O1R4661	7.42	15.0	42	56.6038	20.2156	35.7143	6.5	1.365	5.070	0.065	0.000
300 PPM	O1R4663	8.35	16.6	45	53.8922	19.8802	36.8889	3.8	1.216	2.508	0.000	0.076
300 PPM	O1R4672	6.80	13.9	40	58.8235	20.4412	34.7500	6.5	2.600	2.990	0.130	0.130
300 PPM	O1R4679	7.14	14.6	40	56.0224	20.4482	36.5000	5.9	3.363	2.419	0.118	0.000
300 PPM	O1R4683	7.67	15.1	42	54.7588	19.6871	35.9524	8.0	2.080	5.760	0.160	0.000
300 PPM	O1R4688	7.24	15.2	42	58.0110	20.9945	36.1905	5.4	1.134	4.212	0.054	0.000
300 PPM	O1R4693	7.66	15.1	42	54.8303	19.7128	35.9524	4.6	1.794	2.622	0.046	0.138
300 PPM	O1R4695	6.82	13.0	36	52.7859	19.0616	36.1111	9.3	2.790	6.231	0.186	0.093
300 PPM	O1R4697	7.80	15.1	43	55.1282	19.3590	35.1163	5.8	1.508	4.118	0.116	0.058
300 PPM	O1R4701	7.62	15.2	43	56.4304	19.9475	35.3488	4.4	1.232	3.124	0.044	0.000
30 PPM	P1R4708	7.26	15.1	44	60.6061	20.7989	34.3182	7.8	3.588	3.900	0.078	0.234
30 PPM	P1R4711	6.89	13.7	38	55.1524	19.8839	36.0526	13.7	7.672	5.343	0.548	0.137
30 PPM	P1R4714	7.11	15.0	42	59.0717	21.0970	35.7143	5.8	1.914	3.828	0.058	0.000
30 PPM	P1R4716	7.34	15.0	45	61.3079	20.4360	33.3333	4.4	1.936	2.288	0.132	0.044
30 PPM	P1R4720	6.91	14.9	43	62.2287	21.5630	34.6512	8.6	3.698	4.472	0.258	0.172
30 PPM	P1R4723	6.36	12.8	37	58.1761	20.1258	34.5946	9.9	2.574	7.128	0.198	0.000
30 PPM	P1R4726	7.64	16.3	46	60.2094	21.3351	35.4348	6.4	0.640	5.696	0.064	0.000
30 PPM	P1R4729	7.53	15.2	44	58.4329	20.1859	34.5455	7.4	2.146	4.884	0.074	0.296
30 PPM	P1R4733	8.81	17.0	49	55.6186	19.2963	34.6939	5.2	2.340	2.704	0.156	0.000
30 PPM	P1R4736	7.97	16.4	47	58.9711	20.5772	34.8936	6.2	1.736	4.340	0.062	0.062
30 PPM	P1R4739	4.01	8.9	25	62.3441	22.1945	35.6000	12.0	2.760	8.400	0.720	0.120
30 PPM	P1R4745	7.45	15.4	45	60.4027	20.6711	34.2222	6.2	0.682	5.332	0.124	0.062
30 PPM	P1R4747	7.05	13.5	39	55.3191	19.1489	34.6154	12.6	5.418	6.426	0.756	0.000
30 PPM	P1R4752	7.82	16.4	45	57.5448	20.9719	36.4444	6.6	2.706	3.762	0.066	0.066
30 PPM	P1R4754	5.76	12.8	36	62.5000	22.2222	35.5556	15.7	11.775	3.611	0.314	0.000

000450

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)		BLOOD UREA NITROGEN (MG/DL)		ALT (IU/L)		AST (IU/L)	
	N	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
MALE									
MONTH 3									
0 PPM	15	120.6	13.74	16.3	1.84	21.4	2.67	45.3	7.26
300 PPM	15	129.5*	8.38	19.4*	2.06	31.9#	21.94	58.2	27.23
30 PPM	15	134.6*	8.83	17.1	1.46	24.5#	15.33	59.7	22.47
MONTH 6									
0 PPM	15	119.0	13.29	17.5	1.36	24.1	3.75	49.7	14.98
300 PPM	15	123.7	11.17	20.7*	1.40	54.8#	29.26	87.8#	34.83
30 PPM	15	134.9*	10.33	15.9*	1.44	53.3#	29.34	92.1#	45.60
MONTH 12									
0 PPM	14	154.3	26.17	16.4	2.50	83.5	19.45	79.1	44.61
300 PPM	15	138.7	8.85	17.5	1.73	106.1#	70.00	132.7	76.84
30 PPM	15	131.1#	8.70	16.2	1.15	77.6#	56.59	124.4	94.04
MONTH 18									
0 PPM	15	123.4	26.39	18.1	3.38	84.1	10.68	99.1	68.14
300 PPM	15	139.3	16.14	17.6	1.88	84.3#	55.95	123.3	62.98
30 PPM	15	120.6	27.62	16.5#	6.48	59.7#	33.41	116.4	57.99
MONTH 24									
0 PPM	15	122.5	23.07	16.5	3.16	83.4	8.10	64.9	25.76
300 PPM	15	147.1*	13.26	17.2	5.03	61.8*	20.13	95.7*	29.76
30 PPM	14	121.3	13.72	16.6	6.70	42.5	10.00	68.0	17.64

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

000451

TABLE 14

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

		TOTAL BILIRUBIN (MG/DL)		ALBUMIN (GM/DL)		TOTAL PROTEIN (GM/DL)		ALKALINE PHOSPHATASE (IU/L)		CREATINE PHOSPHOKINASE (IU/L)		CALCIUM (MG/DL)	
	N	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV
MALE													
MONTH 3													
0 PPM	15	0.6	0.16	4.4	0.34	6.8	0.34	91.1	26.22	100.7	26.46	11.1	0.68
300 PPM	15	0.8	0.40	5.1*	0.29	6.5	0.31	153.5*	91.86	67.0*	24.24	10.8	0.50
30 PPM	15	0.7	0.09	4.7*	0.37	6.6	0.34	138.7*	93.14	60.5*	12.65	11.0	0.78
MONTH 6													
0 PPM	15	0.8	0.19	4.6	0.20	7.0	0.36	97.1	40.41	89.9	41.32	11.5	0.40
300 PPM	15	0.7	0.22	5.4*	0.31	6.6*	0.28	147.3*	94.85	81.4	26.66	11.1*	0.22
30 PPM	15	0.5*	0.14	5.0*	0.48	6.7*	0.33	146.9*	97.18	58.3*	31.23	10.9*	0.33
MONTH 12													
0 PPM	14	0.7	0.20	3.7	0.20	6.8	0.27	105.8	43.94	79.7	47.61	10.5	0.30
300 PPM	15	0.6	0.12	4.4*	0.34	6.8	0.31	166.5*	89.28	68.3	23.65	10.6	0.24
30 PPM	15	0.8	0.22	3.9	0.26	6.9	0.33	128.3	41.75	67.6	19.45	10.6	0.29
MONTH 18													
0 PPM	15	0.9	0.35	3.2	0.38	7.1	0.61	85.2	93.78	79.9	74.52	11.1	0.93
300 PPM	15	0.7	0.31	3.7*	0.34	6.9	0.42	184.4*	73.37	82.5	45.87	10.8	1.10
30 PPM	15	0.7	0.25	3.2	0.29	7.2	0.45	112.5	92.61	106.5	69.23	10.4	0.80[a]
MONTH 24													
0 PPM	15	0.4	0.25	2.8	0.23	6.9	0.44	70.1	25.58	111.1	68.04	10.9	0.43
300 PPM	15	0.2#	0.06	3.1*	0.27	6.9	0.50	113.5*	22.86	88.3	37.33	10.8	0.25
30 PPM	14	0.4	0.12	2.8	0.30	6.8	0.39	81.2	26.20	71.1#	20.55	10.5*	0.31

* : P <= .05, TWO TAILED DUNNETT T ON RAW DATA.
# : P <= .05, TWO TAILED DUNNETT T ON RANKED DATA.
[a] N NUMBER IS 14 FOR THIS MEAN.

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TABLE 14

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

MONTH=3

DOSE	ANIMAL	GLU	BUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	A1R3518	112	17	20	38	0.6	4.2	6.8	107	115	11.5
0 PPM	A1R3527	140	21	22	42	0.5	4.4	6.6	106	104	11.3
0 PPM	A1R3532	138	17	20	36	0.9	4.4	7.1	58	69	11.2
0 PPM	A1R3534	112	17	22	50	0.8	5.1	7.8	105	140	12.4
0 PPM	A1R3537	129	15	28	54	0.8	4.4	6.6	100	144	10.8
0 PPM	A1R3540	102	17	21	42	0.5	4.1	6.5	80	120	10.8
0 PPM	A1R3542	111	14	22	43	0.7	4.4	6.7	60	80	10.8
0 PPM	A1R3548	98	14	21	46	0.5	3.9	6.5	125	80	11.2
0 PPM	A1R3552	141	16	18	38	0.5	4.2	6.8	71	74	11.1
0 PPM	A1R3559	108	17	18	44	0.5	4.4	6.6	52	109	11.6
0 PPM	A1R3562	130	16	21	51	0.4	4.1	6.5	73	85	9.3
0 PPM	A1R3564	125	18	24	50	0.8	5.1	6.6	125	72	12.0
0 PPM	A1R3565	129	17	20	47	0.9	4.6	6.8	128	113	11.0
0 PPM	A1R3567	114	15	19	36	0.6	4.2	6.5	69	72	11.2
0 PPM	A1R3569	120	14	25	58	0.7	4.3	7.0	108	134	11.0
300 PPM	B1R3585	135	22	24	48	0.5	4.8	6.3	140	41	11.4
300 PPM	B1R3587	128	20	28	75	0.5	4.6	6.4	124	80	10.3
300 PPM	B1R3589	139	17	23	37	0.5	5.1	6.3	114	47	11.0
300 PPM	B1R3592	128	17	26	48	1.9	4.7	6.5	162	97	11.2
300 PPM	B1R3593	121	18	24	50	0.5	4.9	6.4	183	82	10.9
300 PPM	B1R3595	131	21	25	44	0.7	5.0	6.2	124	60	11.2
300 PPM	B1R3604	141	19	23	42	0.5	5.2	6.8	142	43	11.4
300 PPM	B1R3605	145	19	25	45	0.7	5.0	6.3	143	54	11.1
300 PPM	B1R3610	124	19	110	148	0.6	4.9	6.6	212	72	10.8
300 PPM	B1R3611	120	17	34	65	0.9	5.3	6.5	181	53	10.8
300 PPM	B1R3617	136	24	21	49	0.7	5.0	6.6	160	45	9.8
300 PPM	B1R3623	115	18	33	51	0.9	5.3	6.8	128	72	11.3
300 PPM	B1R3634	124	22	23	47	0.6	5.4	6.2	134	117	10.3
300 PPM	B1R3640	128	19	27	49	0.5	5.3	6.4	138	41	11.1
300 PPM	B1R3643	127	19	30	75	1.4	5.7	7.4	217	101	10.1
30 PPM	C1R3654	120	16	21	43	0.6	4.2	6.3	86	71	10.2
30 PPM	C1R3655	152	20	39	62	0.7	4.6	6.2	148	69	10.0
30 PPM	C1R3665	130	16	30	50	0.7	4.9	6.8	147	73	12.0
30 PPM	C1R3667	136	16	26	56	0.7	4.7	6.4	192	79	11.0
30 PPM	C1R3668	138	16	74	120	0.6	4.6	6.3	156	59	10.4
30 PPM	C1R3673	119	17	28	51	0.6	4.4	6.3	108	67	10.9
30 PPM	C1R3675	139	18	43	82	0.7	4.7	6.9	163	76	12.1
30 PPM	C1R3677	135	16	25	45	0.7	5.1	7.0	188	40	11.1
30 PPM	C1R3679	142	15	23	37	0.8	5.3	7.2	97	53	11.9
30 PPM	C1R3683	144	18	21	40	0.7	5.0	6.7	96	47	12.2
30 PPM	C1R3687	132	19	26	38	0.8	5.3	7.0	168	38	10.0
30 PPM	C1R3690	138	19	56	82	0.5	4.9	6.5	139	66	11.0
30 PPM	C1R3691	125	16	51	78	0.7	4.3	6.1	145	59	10.8
30 PPM	C1R3692	138	18	30	58	0.8	4.1	6.3	109	52	10.1
30 PPM	C1R3695	131	17	25	53	0.6	4.7	6.5	138	58	11.5

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TABLE 14

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

MONTH=6

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	A1R3519	133	19	18	39	0.6	4.3	6.4	123	70	10.6
0 PPM	A1R3524	139	17	21	54	0.8	4.4	7.3	109	82	11.6
0 PPM	A1R3529	130	16	20	25	0.6	4.7	6.7	72	51	11.3
0 PPM	A1R3533	124	19	28	41	0.8	4.8	7.5	85	119	11.7
0 PPM	A1R3537	109	16	27	58	1.1	4.9	7.0	110	204	11.6
0 PPM	A1R3541	124	18	19	35	0.7	4.5	7.2	65	58	11.3
0 PPM	A1R3547	115	19	29	28	1.1	4.8	7.5	114	62	12.2
0 PPM	A1R3550	128	15	25	43	0.6	4.7	7.0	213	57	11.6
0 PPM	A1R3553	99	20	29	53	0.7	4.6	7.1	62	57	11.9
0 PPM	A1R3557	109	17	22	74	1.1	4.7	7.3	120	119	11.6
0 PPM	A1R3559	100	17	21	51	0.9	4.5	6.7	50	85	11.4
0 PPM	A1R3562	133	18	28	55	0.6	4.7	6.6	69	79	10.9
0 PPM	A1R3567	129	18	23	49	0.8	4.6	6.8	69	85	11.4
0 PPM	A1R3573	102	17	26	74	1.0	5.0	7.5	118	144	11.7
0 PPM	A1R3575	111	17	25	67	0.7	4.4	6.7	78	77	11.0
300 PPM	B1R3583	119	21	29	57	0.7	5.7	6.4	162	77	11.0
300 PPM	B1R3584	152	23	84	112	1.2	5.1	6.7	178	76	11.2
300 PPM	B1R3596	119	21	21	47	0.9	5.3	6.6	156	80	11.4
300 PPM	B1R3598	121	21	92	122	0.8	6.0	7.2	183	106	11.5
300 PPM	B1R3600	110	22	27	47	1.1	5.1	6.3	97	75	10.9
300 PPM	B1R3604	144	21	60	86	0.5	5.4	7.0	123	46	11.4
300 PPM	B1R3608	117	19	73	80	0.7	5.3	6.3	160	61	11.2
300 PPM	B1R3609	123	21	37	89	1.0	5.5	6.7	127	142	11.1
300 PPM	B1R3613	112	20	85	174	0.6	5.0	6.5	109	55	11.0
300 PPM	B1R3617	122	23	35	73	0.6	5.5	7.0	162	58	11.2
300 PPM	B1R3628	120	21	73	95	0.6	5.8	6.9	172	110	11.3
300 PPM	B1R3629	122	20	37	79	0.6	4.9	6.3	102	63	10.7
300 PPM	B1R3631	117	19	34	70	0.5	5.5	6.6	166	65	10.9
300 PPM	B1R3633	129	20	111	130	0.6	5.2	6.5	211	115	11.0
300 PPM	B1R3642	128	18	24	56	0.6	5.7	6.6	102	92	11.1
30 PPM	C1R3646	146	19	35	64	0.6	5.0	6.5	94	50	11.0
30 PPM	C1R3650	151	16	53	83	0.4	4.9	6.5	163	91	10.6
30 PPM	C1R3656	149	15	131	212	0.5	4.8	6.5	188	64	10.6
30 PPM	C1R3658	137	15	48	65	0.4	4.7	6.4	165	42	10.9
30 PPM	C1R3660	138	15	25	49	0.4	4.9	6.7	79	43	10.6
30 PPM	C1R3664	138	16	81	118	0.4	4.5	6.5	121	28	10.9
30 PPM	C1R3665	133	16	87	148	0.4	4.9	6.8	185	40	11.2
30 PPM	C1R3667	133	17	39	72	0.4	5.0	6.7	172	41	10.8
30 PPM	C1R3679	144	16	39	77	0.6	5.8	7.6	97	157	11.4
30 PPM	C1R3680	130	15	49	77	0.4	5.6	7.1	135	38	11.3
30 PPM	C1R3682	122	16	75	139	0.4	4.4	6.9	209	58	11.0
30 PPM	C1R3687	112	18	36	74	0.9	5.3	7.1	158	63	11.5
30 PPM	C1R3689	128	13	20	39	0.4	5.2	6.6	156	51	10.7
30 PPM	C1R3691	134	15	53	105	0.3	4.4	6.4	134	45	10.4
30 PPM	C1R3694	129	17	28	59	0.5	5.1	6.7	148	63	10.7

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TABLE 14

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

MONTH=12

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	A1R3516	147	18	22	56	0.9	3.6	6.9	139	72	11.0
0 PPM	A1R3517	150	16	16	40	0.5	3.8	7.1	104	43	10.8
0 PPM	A1R3520	124	16	15	43	0.4	3.8	6.6	49	42	10.5
0 PPM	A1R3522	134	15	65	123	0.6	3.7	6.7	108	61	10.4
0 PPM	A1R3527	155	18	37	67	0.6	3.9	6.8	102	80	10.8
0 PPM	A1R3535	141	17	23	56	0.6	3.8	6.8	113	103	10.6
0 PPM	A1R3543	183	17	33	85	1.0	3.9	7.0	115	88	10.7
0 PPM	A1R3546	178	17	37	118	0.9	4.0	6.9	107	234	10.4
0 PPM	A1R3550	185	18	32	79	1.0	3.9	6.9	225	89	10.5
0 PPM	A1R3551	165	20	41	86	0.6	3.9	6.7	95	65	10.2
0 PPM	A1R3554	214	18	87	212	0.6	3.5	6.3	88	105	10.3
0 PPM	A1R3568	123	14	18	43	0.7	3.3	6.2	48	50	10.4
0 PPM	A1R3570	125	9	23	54	0.5	3.6	6.5	72	39	9.8
0 PPM	A1R3575	143	16	23	63	0.4	3.5	6.9	70	58	10.4
0 PPM	A1R3580	148	17	31	59	0.7	3.9	7.1	152	66	10.9
300 PPM	B1R3584	151	17	133	166	0.6	3.7	6.3	205	50	10.4
300 PPM	B1R3588	130	17	35	69	0.7	4.7	6.9	145	108	10.8
300 PPM	B1R3589	144	18	105	116	0.4	4.7	6.8	153	84	10.7
300 PPM	B1R3592	127	16	30	59	0.5	4.1	6.5	118	67	10.5
300 PPM	B1R3598	142	17	162	171	0.5	4.3	6.8	212	84	10.4
300 PPM	B1R3604	153	15	185	202	0.6	3.9	6.9	208	67	10.5
300 PPM	B1R3613	145	18	64	137	0.7	3.9	6.4	103	78	10.2
300 PPM	B1R3617	127	16	208	236	0.7	4.4	7.2	235	107	10.6
300 PPM	B1R3620	150	19	105	106	0.4	4.5	6.5	117	39	10.3
300 PPM	B1R3622	131	22	76	126	0.7	4.7	7.3	190	56	10.9
300 PPM	B1R3626	136	17	50	53	0.8	4.3	7.0	158	57	10.8
300 PPM	B1R3627	135	17	46	66	0.7	4.2	7.1	101	40	10.7
300 PPM	B1R3638	138	20	48	75	0.7	4.5	6.6	105	38	10.8
300 PPM	B1R3642	142	17	84	82	0.7	4.7	7.1	139	54	10.9
300 PPM	B1R3643	129	17	261	326	0.7	4.7	7.1	309	96	11.0
30 PPM	C1R3649	139	16	39	76	0.8	4.1	7.0	89	91	10.9
30 PPM	C1R3650	132	17	46	93	0.6	4.3	7.1	168	56	10.5
30 PPM	C1R3652	128	16	54	75	0.6	3.7	7.1	177	78	10.8
30 PPM	C1R3663	147	17	75	103	0.6	3.8	6.9	82	54	10.4
30 PPM	C1R3668	123	15	241	436	0.6	3.9	7.0	215	66	10.3
30 PPM	C1R3670	139	17	94	127	0.8	3.8	6.8	154	41	10.6
30 PPM	C1R3672	120	16	105	158	0.7	3.8	6.7	84	110	10.4
30 PPM	C1R3676	130	16	37	64	0.9	3.6	7.4	128	66	11.3
30 PPM	C1R3679	137	16	52	94	0.9	4.6	7.6	93	73	10.6
30 PPM	C1R3680	132	17	159	193	0.6	4.1	6.9	145	49	10.6
30 PPM	C1R3681	129	18	62	121	1.4	4.0	7.2	124	98	10.7
30 PPM	C1R3683	141	16	25	65	1.1	4.0	6.9	67	67	10.7
30 PPM	C1R3685	122	17	53	73	0.7	4.0	6.5	159	55	10.5
30 PPM	C1R3691	132	13	83	126	0.7	3.7	6.4	131	59	10.1
30 PPM	C1R3694	115	16	39	62	0.7	3.7	6.5	109	51	10.3

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TABLE 14

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

MONTH=18

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	A1R3519	151	19	41	94	0.7	3.2	6.8	128	37	10.6
0 PPM	A1R3521	125	29	59	317	0.2	2.1	5.5	164	79	10.5
0 PPM	A1R3528	148	19	24	55	0.6	3.2	7.0	57	39	11.9
0 PPM	A1R3531	143	18	42	98	1.0	3.4	7.4	56	34	12.0
0 PPM	A1R3538	129	15	38	93	0.7	3.3	6.8	113	96	10.9
0 PPM	A1R3539	132	16	24	54	0.9	3.7	8.1	82	35	11.8
0 PPM	A1R3542	107	18	30	61	1.1	3.4	7.2	41	49	11.5
0 PPM	A1R3552	117	21	23	54	1.1	3.3	7.4	55	41	12.0
0 PPM	A1R3553	127	17	44	74	0.9	3.4	7.5	65	83	11.9
0 PPM	A1R3555	140	17	35	84	1.1	3.3	7.3	124	108	11.1
0 PPM	A1R3561	135	17	26	61	0.9	3.4	7.6	90	59	10.2
0 PPM	A1R3565	126	15	23	62	0.9	3.3	6.6	87	41	9.0
0 PPM	A1R3567	134	17	34	133	0.9	3.2	7.7	66	77	10.9
0 PPM	A1R3574	91	17	24	79	0.2	2.6	6.7	82	87	10.1
0 PPM	A1R3577	46	17	45	168	1.6	3.4	7.3	68	334	12.4
300 PPM	B1R3583	135	19	31	42	0.4	3.8	5.8	148	59	11.3
300 PPM	B1R3593	124	17	85	109	0.9	3.8	7.5	214	45	10.9
300 PPM	B1R3596	137	19	39	68	1.0	3.4	7.4	113	67	11.5
300 PPM	B1R3600	140	19	92	139	0.4	4.0	6.9	142	54	11.3
300 PPM	B1R3601	138	14	96	132	0.6	3.8	7.0	213	83	11.5
300 PPM	B1R3605	136	20	51	68	0.6	3.9	7.0	172	57	10.3
300 PPM	B1R3608	124	14	124	163	0.4	3.2	6.5	177	64	7.8
300 PPM	B1R3610	150	19	75	117	0.7	3.9	7.0	202	55	11.7
300 PPM	B1R3612	148	19	118	205	0.8	3.4	6.6	168	212	11.7
300 PPM	B1R3615	117	17	63	101	0.8	4.1	7.4	129	104	11.4
300 PPM	B1R3624	118	18	42	95	0.4	2.9	7.0	106	152	9.9
300 PPM	B1R3632	168	19	91	142	1.1	4.0	7.3	233	53	12.0
300 PPM	B1R3641	145	16	47	78	0.9	3.6	6.9	156	52	9.9
300 PPM	B1R3644	173	18	258	295	1.5	3.7	7.0	413	109	9.8
300 PPM	B1R3645	136	16	53	95	0.7	4.0	6.8	180	71	11.1
30 PPM	C1R3647	116	12	40	117	0.3	2.4	7.8	105	73	10.4
30 PPM	C1R3651	142	13	37	60	0.6	3.4	7.0	138	46	9.3
30 PPM	C1R3654	134	16	43	100	0.8	3.2	7.1	92	86	10.7
30 PPM	C1R3658	156	16	71	106	0.6	3.3	6.7	134	71	9.8
30 PPM	C1R3662	31	39	53	161	0.1	2.9	8.3	100	327	12.5
30 PPM	C1R3663	121	18	58	120	0.7	3.1	7.1	69	186	10.8
30 PPM	C1R3664	125	16	97	153	0.8	3.4	6.9	133	71	9.8
30 PPM	C1R3667	134	15	82	156	0.8	3.4	7.2	124	79	10.6
30 PPM	C1R3668	128	15	160	289	0.7	3.5	7.1	186	115	11.0
30 PPM	C1R3676	110	17	34	60	1.1	3.0	7.6	105	80	9.8
30 PPM	C1R3679	123	13	41	89	1.0	3.5	7.5	68	110	10.5
30 PPM	C1R3681	136	12	45	87	0.7	3.2	7.2	82	89	9.8
30 PPM	C1R3685	113	16	34	64	0.8	3.2	6.9	95	108	.
30 PPM	C1R3689	126	15	62	95	0.7	3.4	6.7	156	56	10.5
30 PPM	C1R3695	114	14	39	87	0.5	3.4	6.7	101	100	9.6

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TABLE 14

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

MONTH=24

DOSE	ANIMAL	GLU	BUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	A1R3518	130	14	26	52	0.2	2.6	6.6	118	87	10.5
0 PPM	A1R3524	138	23	29	42	0.6	2.7	7.1	74	51	11.5
0 PPM	A1R3528	141	15	28	47	0.2	3.0	6.8	39	63	10.8
0 PPM	A1R3531	109	14	36	60	0.3	3.1	7.1	55	72	11.0
0 PPM	A1R3534	67	20	21	142	0.3	2.7	5.9	61	190	11.1
0 PPM	A1R3538	147	12	38	69	0.2	2.8	6.4	66	69	10.5
0 PPM	A1R3542	96	15	35	50	0.6	3.0	7.0	37	54	11.6
0 PPM	A1R3548	122	15	32	48	0.4	2.9	7.0	97	108	10.9
0 PPM	A1R3554	158	17	43	74	0.2	3.0	6.6	29	73	11.0
0 PPM	A1R3557	117	16	42	66	0.6	3.0	7.3	109	90	11.2
0 PPM	A1R3562	134	17	33	53	0.1	2.4	6.8	68	76	10.1
0 PPM	A1R3564	116	19	27	50	0.5	2.5	6.9	77	187	10.5
0 PPM	A1R3569	143	22	29	74	1.0	2.7	7.4	58	299	10.3
0 PPM	A1R3573	105	14	29	50	0.7	3.1	7.7	86	101	11.3
0 PPM	A1R3578	115	15	53	97	0.4	2.6	7.3	77	146	10.9
300 PPM	B1R3581	120	15	41	57	0.2	3.4	6.6	97	82	10.8
300 PPM	B1R3585	155	17	111	133	0.2	3.2	6.8	122	57	10.5
300 PPM	B1R3591	147	17	88	130	0.3	2.9	7.9	132	79	10.5
300 PPM	B1R3594	159	16	75	109	0.3	3.4	7.1	162	176	10.8
300 PPM	B1R3597	143	15	64	117	0.2	2.9	6.4	74	95	10.6
300 PPM	B1R3601	146	16	47	68	0.2	3.0	6.2	127	85	10.7
300 PPM	B1R3605	157	14	43	59	0.1	3.3	7.4	99	83	10.5
300 PPM	B1R3608	136	14	41	75	0.2	2.8	6.5	108	86	10.7
300 PPM	B1R3611	128	19	41	56	0.3	3.5	6.8	133	57	11.2
300 PPM	B1R3618	169	17	82	152	0.2	3.1	6.9	105	54	10.8
300 PPM	B1R3623	142	14	60	95	0.3	3.6	7.3	107	162	10.9
300 PPM	B1R3630	137	17	61	101	0.3	3.4	7.8	111	114	11.3
300 PPM	B1R3633	163	34	62	110	0.2	2.7	6.7	121	51	11.0
300 PPM	B1R3636	153	13	52	91	0.2	3.0	6.4	75	86	10.6
300 PPM	B1R3641	152	20	59	83	0.3	3.0	6.9	129	57	11.0
30 PPM	C1R3646	144	17	47	70	0.4	3.1	6.6	62	64	11.4
30 PPM	C1R3650	147	14	35	51	0.3	2.8	7.1	100	71	10.4
30 PPM	C1R3654	133	13	64	89	0.3	2.8	6.7	102	74	10.2
30 PPM	C1R3658	123	15	43	66	0.3	3.2	6.8	102	47	10.8
30 PPM	C1R3663	115	14	27	43	0.6	2.6	6.8	47	51	10.5
30 PPM	C1R3667	107	15	45	72	0.4	3.0	6.8	103	76	10.5
30 PPM	C1R3670	110	21	46	105	0.3	2.3	6.4	75	44	10.6
30 PPM	C1R3672	107	10	29	44	0.2	2.6	7.7	20	47	10.1
30 PPM	C1R3676	125	39	33	52	0.6	2.2	6.6	91	77	10.7
30 PPM	C1R3679	122	16	41	59	0.4	2.9	7.1	64	57	10.5
30 PPM	C1R3682	116	18	39	64	0.3	3.0	7.0	104	105	10.7
30 PPM	C1R3684	132	12	60	92	0.4	3.1	6.5	77	86	10.4
30 PPM	C1R3689	126	15	43	64	0.2	2.9	6.3	118	114	10.2
30 PPM	C1R3691	99	15	41	74	0.3	3.0	6.3	65	73	10.4
30 PPM	C1R3694	113	15	45	75	0.4	3.1	7.3	88	80	10.6

000457

TABLE 15

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

		GLUCOSE (MG/DL)		BLOOD UREA NITROGEN (MG/DL)		ALT (IU/L)		AST (IU/L)	
	N	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.	MEAN	S.DEV.
FEMALE									
MONTH 3									
0 PPM	15	138.9	9.79	19.7	1.62	22.6	4.87	48.0	9.20
300 PPM	15	132.9	10.96	24.5*	3.91	26.2	6.72	51.6	13.42
30 PPM	15	132.1	12.06	18.5	2.07	19.4	3.18	44.9	5.79
MONTH 6									
0 PPM	15	154.8	14.98	21.6	3.22	83.5	17.20	69.7	38.56
300 PPM	15	133.6*	9.61	20.7	2.96	84.3	20.46	59.2	29.11
30 PPM	15	128.6*	13.41	19.1*	2.00	85.7	14.55	59.9	28.60
MONTH 12									
0 PPM	15	134.9	10.51	19.8	2.14	84.1	15.17	68.1	38.77
300 PPM	15	135.3	8.18	21.2	5.21	88.6	21.59	66.2	30.37
30 PPM	15	135.4	10.85	19.9	2.83	87.1	12.94	72.6	36.65
MONTH 18									
0 PPM	15	123.5	15.51	18.1	2.49	68.7	11.60	70.1	24.40
300 PPM	15	120.0	9.39	18.7	3.37	66.4	6.36	63.5	18.97
30 PPM	15	122.2	15.39	20.1	4.02	89.4	14.31	63.5	25.21
MONTH 24									
0 PPM	15	122.2	13.75	17.9	4.10	40.0	10.11	67.8	30.03
300 PPM	15	115.3	18.72	16.2	3.76	63.1	25.27	67.0	35.26
30 PPM	15	119.4	15.23	15.3	3.35	88.6	9.61	63.5	12.95

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

000458

TABLE 15

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

		TOTAL BILIRUBIN (MG/DL)		ALBUMIN (GM/DL)		TOTAL PROTEIN (GM/DL)		ALKALINE PHOSPHATASE (IU/L)		CREATINE PHOSPHOKINASE (IU/L)		CALCIUM (MG/DL)	
	N	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV	MEAN	S.DEV
FEMALE													
MONTH 3													
0 PPM	15	0.6	0.18	5.3	0.45	7.2	0.41	83.7	32.29	93.9	51.44	11.0	0.55
300 PPM	15	0.5*	0.11	5.0	0.52	6.9*	0.41	89.1	25.36	87.7	37.12	11.1	0.52
30 PPM	15	0.6	0.09	5.0	0.41	7.0	0.32	69.9	25.98	86.7	21.06	10.5*	0.69
MONTH 6													
0 PPM	15	0.6	0.14	5.9	0.65	7.4	0.64	77.8	30.58	56.5	14.79	11.7	0.53
300 PPM	15	0.5	0.09	5.6	0.46	7.4	0.34	82.1	22.06	66.7	21.17	11.7	0.43
30 PPM	15	0.6	0.10	5.5	0.66	7.3	0.57	80.9	25.76	89.2	45.03	11.8	0.45
MONTH 12													
0 PPM	15	0.8	0.38	4.3	0.26	7.3	0.52	76.5	30.01	54.6	20.02	11.2	0.60
300 PPM	15	0.6	0.21	4.2	0.32	7.1	0.46	91.1	42.86	41.3	11.52	11.1	0.33
30 PPM	15	0.8	0.21	4.4	0.26	7.5	0.46	89.4	29.87	78.7	78.42	11.0	0.43
MONTH 18													
0 PPM	15	0.6	0.26	3.9	0.23	7.9	0.57	65.5	32.10	37.3	9.81	11.4	0.53
300 PPM	15	0.6	0.23	3.9	0.28	7.8	0.47	76.1	28.30	35.1	9.64	11.1	0.43
30 PPM	15	0.6	0.24	3.8	0.26	8.3	0.73	39.7*	13.47	27.6	19.18	10.6*	1.01
MONTH 24													
0 PPM	15	0.6	0.31	3.4	0.21	7.6	0.69	68.7	33.39	68.4	32.23	11.5	0.64
300 PPM	15	0.4	0.17	3.4	0.28	7.4	0.56	63.1	19.69	67.7	27.06	11.2	0.46
30 PPM	15	0.5	0.21	3.3	0.38	7.2	0.75	56.7	19.98	71.3	35.73	11.3	0.45

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

000459

TABLE 15

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

MONTH=3

DOSE	ANIMAL	GLU	BUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4576	143	22	20	47	0.5	4.8	6.8	120	71	10.1
0 PPM	N1R4578	150	22	18	49	0.8	5.1	7.0	61	95	10.7
0 PPM	N1R4582	129	20	17	55	0.8	5.9	7.8	152	150	11.7
0 PPM	N1R4583	147	18	19	41	0.5	4.9	7.1	61	58	10.6
0 PPM	N1R4584	129	19	29	66	0.5	4.8	7.1	95	234	11.2
0 PPM	N1R4592	134	17	25	62	0.6	5.2	7.0	128	168	11.3
0 PPM	N1R4610	143	21	32	57	0.7	5.9	7.8	68	60	12.2
0 PPM	N1R4612	147	20	19	39	0.5	4.8	6.6	89	58	10.8
0 PPM	N1R4613	129	19	19	41	0.5	4.9	7.0	61	50	10.6
0 PPM	N1R4619	139	18	22	51	1.0	5.3	6.9	65	94	11.2
0 PPM	N1R4621	131	19	23	49	0.5	4.9	7.1	67	80	10.7
0 PPM	N1R4626	163	20	28	48	0.4	5.3	7.1	120	58	10.6
0 PPM	N1R4627	133	18	16	43	0.5	5.7	7.0	40	66	10.9
0 PPM	N1R4633	134	22	25	32	0.8	5.9	8.0	70	90	11.4
0 PPM	N1R4640	133	21	27	40	0.9	5.9	7.6	58	76	11.7
300 PPM	O1R4645	126	28	29	37	0.4	4.7	6.2	51	72	10.1
300 PPM	O1R4654	129	19	35	47	0.5	5.3	7.2	65	63	10.8
300 PPM	O1R4660	119	29	32	45	0.5	3.6	6.2	73	57	10.5
300 PPM	O1R4664	122	26	25	59	0.4	5.1	7.1	125	90	10.9
300 PPM	O1R4668	130	20	32	70	0.6	5.5	7.3	54	136	11.2
300 PPM	O1R4669	138	27	20	39	0.5	5.1	7.0	86	84	10.6
300 PPM	O1R4672	136	19	21	40	0.5	5.3	7.1	118	46	11.3
300 PPM	O1R4673	129	26	38	77	0.3	5.0	6.8	106	123	11.1
300 PPM	O1R4674	124	25	31	72	0.4	5.0	7.1	111	186	11.9
300 PPM	O1R4679	154	23	26	49	0.3	5.0	7.0	82	90	11.5
300 PPM	O1R4680	139	25	15	33	0.4	4.8	6.8	55	56	11.6
300 PPM	O1R4693	145	28	19	49	0.6	5.1	6.8	95	100	10.8
300 PPM	O1R4698	130	31	20	56	0.5	5.0	6.7	124	68	11.8
300 PPM	O1R4700	152	20	21	43	0.7	6.1	7.4	93	57	11.6
300 PPM	O1R4701	120	21	29	58	0.5	4.7	6.1	99	88	11.4
30 PPM	P1R4708	148	20	19	44	0.6	5.3	6.6	75	74	11.8
30 PPM	P1R4710	121	19	19	32	0.5	4.9	7.0	104	65	9.8
30 PPM	P1R4720	135	18	26	50	0.7	5.7	7.5	45	99	9.6
30 PPM	P1R4721	142	18	22	47	0.6	4.9	7.0	97	89	10.7
30 PPM	P1R4730	140	16	18	39	0.6	5.1	7.3	53	63	10.9
30 PPM	P1R4731	145	21	22	40	0.7	4.4	6.7	99	84	10.8
30 PPM	P1R4734	137	18	21	50	0.7	5.5	7.4	61	114	11.5
30 PPM	P1R4735	117	21	14	42	0.6	5.2	7.0	47	109	11.1
30 PPM	P1R4736	106	22	20	53	0.6	5.3	7.1	33	111	11.0
30 PPM	P1R4737	125	16	15	50	0.6	4.6	6.9	33	69	9.8
30 PPM	P1R4738	141	16	17	45	0.6	4.6	6.7	55	83	9.9
30 PPM	P1R4744	118	18	23	46	0.6	5.4	7.3	99	98	10.6
30 PPM	P1R4749	133	21	16	38	0.6	4.9	6.9	58	58	9.8
30 PPM	P1R4752	140	18	20	46	0.8	5.2	7.4	91	121	10.7
30 PPM	P1R4753	133	16	19	51	0.4	4.3	6.4	98	63	9.9

000460

TABLE 15

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

MONTH=6

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4582	178	21	21	37	0.9	7.2	7.7	137	71	12.9
0 PPM	N1R4584	172	22	55	118	0.6	5.8	8.9	125	55	11.2
0 PPM	N1R4586	159	23	88	183	0.5	6.5	7.9	85	41	12.2
0 PPM	N1R4590	183	22	26	48	0.6	5.6	7.2	101	69	11.8
0 PPM	N1R4598	141	20	20	48	0.6	5.8	7.2	51	33	11.6
0 PPM	N1R4603	161	22	32	71	0.4	6.1	7.5	39	85	11.6
0 PPM	N1R4607	147	23	35	96	0.5	5.5	7.0	61	49	11.4
0 PPM	N1R4616	150	18	25	56	0.4	5.2	6.9	55	52	11.0
0 PPM	N1R4619	140	18	26	57	0.6	6.0	7.2	57	66	11.8
0 PPM	N1R4621	154	20	26	47	0.7	6.9	8.1	51	73	12.2
0 PPM	N1R4622	160	18	34	79	0.5	5.6	7.2	108	50	11.0
0 PPM	N1R4629	130	20	33	58	0.4	4.9	6.3	98	55	11.4
0 PPM	N1R4631	137	22	25	55	0.4	5.2	6.7	90	32	11.3
0 PPM	N1R4632	154	24	27	30	0.7	6.4	8.0	50	59	12.3
0 PPM	N1R4639	156	31	30	62	0.6	6.4	7.6	59	57	11.8
300 PPM	O1R4650	133	18	76	122	0.6	6.2	7.4	59	52	12.3
300 PPM	O1R4653	128	19	30	50	0.6	6.2	7.6	111	63	11.7
300 PPM	O1R4657	123	19	75	115	0.5	5.2	7.5	76	60	11.5
300 PPM	O1R4660	136	25	22	61	0.6	5.1	7.3	78	126	11.4
300 PPM	O1R4663	125	17	16	43	0.4	4.9	7.0	88	84	11.0
300 PPM	O1R4670	151	19	14	30	0.6	6.0	7.9	41	80	12.3
300 PPM	O1R4673	125	24	66	100	0.4	5.7	7.5	97	54	11.9
300 PPM	O1R4681	125	21	34	40	0.5	5.4	7.5	81	51	11.9
300 PPM	O1R4682	118	22	26	44	0.5	5.8	7.7	56	51	12.1
300 PPM	O1R4692	142	22	23	42	0.4	5.1	7.4	57	53	11.6
300 PPM	O1R4693	137	24	23	41	0.6	5.1	7.0	97	40	11.5
300 PPM	O1R4694	144	17	23	38	0.6	5.2	6.8	73	83	11.3
300 PPM	O1R4698	135	26	29	53	0.6	5.6	7.3	100	69	11.4
300 PPM	O1R4699	147	18	27	45	0.5	5.5	7.0	116	58	11.5
300 PPM	O1R4700	135	20	31	64	0.7	6.3	8.0	101	77	12.5
30 PPM	P1R4710	109	19	25	54	0.5	4.6	6.7	110	134	11.6
30 PPM	P1R4711	152	22	41	70	0.6	6.0	8.1	140	52	12.1
30 PPM	P1R4717	144	17	32	33	0.7	6.1	7.8	95	49	11.8
30 PPM	P1R4719	116	20	40	63	0.7	6.0	7.7	78	117	12.1
30 PPM	P1R4729	144	18	59	61	0.7	6.3	8.0	93	103	12.3
30 PPM	P1R4731	140	19	27	42	0.5	4.4	6.3	100	38	11.1
30 PPM	P1R4732	122	20	26	38	0.6	5.7	7.3	68	74	12.3
30 PPM	P1R4733	127	18	22	40	0.7	5.0	6.6	57	78	11.3
30 PPM	P1R4737	140	18	25	40	0.5	5.3	7.4	74	45	11.9
30 PPM	P1R4740	133	21	28	53	0.6	5.4	7.0	99	51	12.0
30 PPM	P1R4743	112	19	27	41	0.5	4.6	7.1	42	133	11.6
30 PPM	P1R4745	133	14	23	75	0.5	4.8	6.7	50	205	10.8
30 PPM	P1R4746	117	21	58	102	0.5	6.1	7.9	81	107	12.3
30 PPM	P1R4749	125	21	35	47	0.8	6.2	7.7	61	80	12.0
30 PPM	P1R4750	115	20	67	140	0.7	5.8	7.6	65	72	11.8

000461

TABLE 15

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

MONTH=12

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4578	146	24	27	48	1.2	4.1	7.3	71	62	11.7
0 PPM	N1R4582	124	18	22	42	1.5	4.7	8.6	134	82	12.5
0 PPM	N1R4585	132	24	33	60	0.8	4.5	7.6	84	42	11.5
0 PPM	N1R4588	137	20	23	47	0.5	4.4	7.0	44	56	10.8
0 PPM	N1R4589	132	19	67	183	0.7	4.6	7.7	104	50	11.7
0 PPM	N1R4590	136	19	24	46	0.6	4.5	7.3	84	38	11.3
0 PPM	N1R4601	143	20	40	59	0.6	4.1	7.3	127	41	10.8
0 PPM	N1R4608	131	18	24	51	1.1	4.2	7.2	39	60	11.1
0 PPM	N1R4610	127	21	25	62	1.0	4.1	7.1	72	104	10.7
0 PPM	N1R4620	146	19	31	51	0.6	4.1	7.0	71	55	10.9
0 PPM	N1R4629	136	18	67	119	0.4	3.9	6.7	80	40	10.9
0 PPM	N1R4630	157	22	42	79	0.5	3.8	6.6	54	37	10.5
0 PPM	N1R4631	128	20	41	94	0.5	4.4	7.4	99	29	10.8
0 PPM	N1R4632	113	18	19	33	1.4	4.3	8.2	43	76	12.4
0 PPM	N1R4640	135	17	26	47	0.2	4.4	7.2	42	47	11.1
300 PPM	O1R4642	137	18	28	51	0.5	4.5	7.7	39	31	11.1
300 PPM	O1R4652	128	20	112	163	0.6	4.6	7.8	115	42	11.7
300 PPM	O1R4655	132	24	28	51	0.7	4.6	7.5	137	36	11.5
300 PPM	O1R4656	136	22	32	56	0.6	4.6	7.4	46	41	11.4
300 PPM	O1R4664	127	25	29	54	0.6	4.3	7.0	99	40	11.2
300 PPM	O1R4666	125	15	26	57	0.4	3.7	6.6	44	51	10.7
300 PPM	O1R4669	129	23	23	48	0.6	4.3	7.0	101	37	10.9
300 PPM	O1R4671	139	18	38	59	1.0	4.3	7.1	56	67	11.5
300 PPM	O1R4674	125	22	40	79	0.4	4.0	6.7	155	58	10.7
300 PPM	O1R4676	134	17	41	65	0.9	4.3	7.0	132	40	10.9
300 PPM	O1R4687	132	37	26	52	0.3	3.5	6.6	124	41	10.5
300 PPM	O1R4689	148	22	35	52	0.4	4.2	6.9	96	16	11.1
300 PPM	O1R4692	146	18	32	50	0.6	4.2	7.2	39	44	11.2
300 PPM	O1R4699	149	19	38	53	0.9	4.5	7.8	142	38	11.2
300 PPM	O1R4704	143	18	51	103	0.4	4.1	6.3	41	38	11.0
30 PPM	P1R4711	141	17	38	62	1.2	4.7	8.1	121	52	12.1
30 PPM	P1R4714	121	17	29	57	0.6	4.7	8.3	94	38	11.3
30 PPM	P1R4715	142	19	49	85	0.8	4.1	7.2	86	271	10.9
30 PPM	P1R4716	128	19	36	55	0.6	4.0	6.9	102	35	10.5
30 PPM	P1R4717	134	22	31	51	0.8	4.2	7.7	131	42	10.5
30 PPM	P1R4721	124	19	39	72	1.0	4.7	7.9	122	248	11.1
30 PPM	P1R4725	159	19	76	94	0.4	4.1	6.9	102	42	10.4
30 PPM	P1R4727	149	19	33	48	0.5	4.7	7.7	108	26	11.0
30 PPM	P1R4729	131	18	37	58	0.7	4.4	7.4	85	48	11.2
30 PPM	P1R4734	135	19	36	58	0.7	4.3	7.3	76	39	10.9
30 PPM	P1R4742	135	25	30	55	0.8	4.0	6.9	87	59	10.8
30 PPM	P1R4743	125	21	26	194	1.0	4.5	8.2	22	46	11.5
30 PPM	P1R4749	146	27	42	83	0.9	4.6	7.5	53	45	11.1
30 PPM	P1R4750	130	18	36	74	0.8	4.4	7.5	48	145	11.2
30 PPM	P1R4755	131	19	18	43	0.9	4.4	7.6	104	44	11.2

C004662

TABLE 15

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

MONTH=18

DOSE	ANIMAL	GLU	BUN	ALT	AST	TBILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4581	128	22	37	50	0.3	3.3	6.4	88	33	11.8
0 PPM	N1R4583	120	17	40	64	0.8	3.9	8.4	51	39	11.7
0 PPM	N1R4586	98	19	59	93	0.3	3.7	7.8	152	27	11.3
0 PPM	N1R4592	107	23	35	53	0.6	4.2	8.4	91	42	11.7
0 PPM	N1R4595	116	18	71	132	0.4	4.0	8.6	63	37	11.5
0 PPM	N1R4598	123	17	55	79	0.5	4.0	7.8	40	32	11.7
0 PPM	N1R4599	133	16	69	106	0.5	4.0	7.7	53	47	11.3
0 PPM	N1R4602	103	21	43	58	0.8	4.0	8.2	55	37	12.1
0 PPM	N1R4604	150	14	38	44	0.5	3.8	7.4	62	27	11.0
0 PPM	N1R4606	126	18	58	79	0.7	3.8	7.8	88	27	11.6
0 PPM	N1R4609	110	15	48	65	1.0	4.2	8.6	56	33	11.3
0 PPM	N1R4611	143	19	40	49	0.6	4.0	7.5	17	36	11.2
0 PPM	N1R4612	138	18	42	49	1.2	3.8	7.9	60	66	10.0
0 PPM	N1R4627	116	16	42	65	0.6	3.7	7.8	27	41	12.2
0 PPM	N1R4638	141	18	54	65	0.9	4.0	8.3	79	35	11.0
300 PPM	O1R4645	119	21	50	65	0.5	3.7	7.2	36	31	11.0
300 PPM	O1R4647	117	19	56	49	1.2	4.1	8.5	68	35	9.9
300 PPM	O1R4648	121	21	51	61	0.3	3.4	6.6	59	18	10.6
300 PPM	O1R4651	130	20	33	48	0.5	4.0	7.4	105	37	11.3
300 PPM	O1R4663	134	13	49	57	0.7	4.3	8.2	74	26	11.3
300 PPM	O1R4667	121	19	54	112	0.3	3.4	7.6	149	43	10.9
300 PPM	O1R4675	116	24	52	81	0.8	3.6	8.2	78	54	10.9
300 PPM	O1R4679	118	18	42	52	0.6	3.8	8.1	65	26	11.3
300 PPM	O1R4684	109	15	49	47	0.5	4.0	8.1	63	32	11.2
300 PPM	O1R4688	128	18	45	65	0.5	4.0	7.9	90	26	11.5
300 PPM	O1R4690	124	13	49	66	0.5	4.2	7.9	79	29	11.4
300 PPM	O1R4693	118	20	44	95	0.5	4.2	7.8	91	38	11.6
300 PPM	O1R4694	134	15	44	47	0.6	4.0	8.0	65	40	11.0
300 PPM	O1R4696	112	21	37	51	0.3	3.8	7.7	30	49	11.5
300 PPM	O1R4698	99	23	41	57	0.5	3.9	7.9	89	42	11.3
30 PPM	P1R4707	102	20	18	62	0.4	3.9	7.7	53	30	12.1
30 PPM	P1R4709	118	22	51	60	0.7	3.6	8.7	53	16	8.8
30 PPM	P1R4714	123	20	36	42	0.7	3.9	9.4	53	24	11.1
30 PPM	P1R4718	122	24	45	51	0.9	3.9	8.9	30	18	9.5
30 PPM	P1R4720	98	20	28	56	0.6	3.6	8.0	49	41	10.2
30 PPM	P1R4722	126	16	24	65	0.3	3.3	6.7	31	37	11.5
30 PPM	P1R4725	148	14	21	51	0.3	3.6	7.6	47	25	11.0
30 PPM	P1R4729	127	27	57	48	0.8	3.8	8.8	42	11	9.5
30 PPM	P1R4732	120	19	39	59	0.6	3.8	8.0	40	16	10.5
30 PPM	P1R4733	143	21	60	76	0.7	4.2	8.6	41	22	9.8
30 PPM	P1R4737	136	23	48	60	0.8	3.6	8.0	57	18	11.1
30 PPM	P1R4748	94	13	24	48	0.5	3.6	8.0	21	17	11.3
30 PPM	P1R4749	116	16	42	148	0.6	4.3	9.0	13	89	11.6
30 PPM	P1R4752	127	22	61	52	1.2	3.9	9.3	44	35	9.3
30 PPM	P1R4754	133	25	37	74	0.5	4.0	8.0	22	15	11.6

000463

TABLE 15

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

MONTH=24

DOSE	ANIMAL	GLU	BUN	ALT	AST	THILI	ALB	TPROT	ALKPHOS	CPK	CA
0 PPM	N1R4583	135	17	36	52	1.0	3.3	8.1	49	76	12.4
0 PPM	N1R4586	121	18	52	88	0.3	3.4	7.3	149	45	11.2
0 PPM	N1R4591	118	20	32	58	1.2	3.5	7.8	127	109	12.4
0 PPM	N1R4595	123	17	66	158	0.5	3.6	8.5	53	57	12.0
0 PPM	N1R4598	140	16	37	52	0.4	3.4	7.2	38	34	11.5
0 PPM	N1R4603	138	26	34	56	0.4	3.4	7.2	35	59	11.0
0 PPM	N1R4606	120	17	36	52	0.7	3.3	7.9	78	119	11.4
0 PPM	N1R4611	148	21	42	81	0.5	3.2	6.5	70	50	11.3
0 PPM	N1R4614	115	17	37	42	0.6	3.7	7.6	76	36	11.3
0 PPM	N1R4616	118	16	42	73	0.4	3.3	7.5	46	80	11.0
0 PPM	N1R4626	112	10	27	52	0.2	3.7	8.6	39	52	11.1
0 PPM	N1R4628	107	15	36	48	0.4	3.2	7.5	39	75	11.0
0 PPM	N1R4634	97	26	42	98	0.2	2.9	6.1	87	35	10.5
0 PPM	N1R4636	130	15	29	42	0.6	3.4	7.5	61	58	11.6
0 PPM	N1R4638	111	17	52	65	1.1	3.5	8.4	84	141	12.8
300 PPM	01R4644	154	19	30	41	0.4	3.4	7.0	77	48	11.1
300 PPM	01R4646	113	15	41	51	0.5	3.5	7.0	93	78	11.2
300 PPM	01R4649	100	17	28	50	0.2	2.8	6.5	47	39	10.3
300 PPM	01R4657	117	15	33	52	0.4	3.4	7.2	51	59	10.9
300 PPM	01R4659	108	13	32	58	0.3	3.0	7.9	60	110	10.8
300 PPM	01R4661	148	26	37	54	0.4	3.4	7.2	91	62	10.9
300 PPM	01R4663	121	12	36	49	0.8	3.8	7.5	73	86	11.5
300 PPM	01R4672	100	11	29	52	0.4	3.5	7.2	67	38	11.5
300 PPM	01R4679	114	19	37	59	0.6	3.2	7.8	46	117	11.9
300 PPM	01R4683	105	14	46	100	0.5	3.2	8.8	27	111	11.1
300 PPM	01R4688	109	13	131	183	0.2	3.4	7.4	64	57	10.9
300 PPM	01R4693	129	19	36	61	0.7	3.7	7.9	75	71	11.7
300 PPM	01R4695	81	18	33	53	0.3	3.8	6.8	30	42	12.0
300 PPM	01R4697	104	17	45	83	0.3	3.6	7.5	72	53	11.0
300 PPM	01R4701	127	15	53	59	0.5	3.6	7.0	74	45	11.6
30 PPM	P1R4708	108	17	33	50	0.5	3.3	6.4	56	35	11.2
30 PPM	P1R4711	106	16	37	56	1.0	3.4	7.8	76	83	11.3
30 PPM	P1R4714	114	12	27	41	0.4	3.5	7.7	33	37	11.5
30 PPM	P1R4716	117	17	34	63	0.2	3.3	6.8	70	37	10.4
30 PPM	P1R4720	115	14	40	53	0.4	3.2	8.1	65	70	11.1
30 PPM	P1R4723	141	17	36	80	0.3	3.3	7.2	35	42	11.3
30 PPM	P1R4726	103	19	58	86	0.6	3.3	7.5	72	58	11.4
30 PPM	P1R4729	119	14	38	54	0.6	3.2	6.9	63	63	11.5
30 PPM	P1R4733	127	15	61	78	0.6	3.8	7.9	57	107	11.7
30 PPM	P1R4736	137	12	38	62	0.4	3.6	7.4	29	75	11.4
30 PPM	P1R4739	101	15	32	71	0.2	2.2	5.5	104	59	11.5
30 PPM	P1R4745	121	10	30	55	0.3	3.1	6.6	46	93	10.4
30 PPM	P1R4747	116	13	31	67	0.3	3.0	6.2	36	171	10.7
30 PPM	P1R4752	110	15	39	58	0.6	3.7	8.0	60	93	12.0
30 PPM	P1R4754	156	24	45	79	0.4	3.6	7.3	49	46	11.6

0004464

TABLE 16

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

Ranges of Urinalysis Values at 3 and 6 Months

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

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

000465

TABLE 16

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

Ranges of Urinalysis Values at 12 and 18 Months

Dose Group	Specific Gravity	pH	Albumin	Bilirubin	Glucose	Occult Blood	Ketones
12 Mo. Male							
Control	1.040-1.093	7.0-8.5	N-4+	N-N	N-N	N-3+	N-Tr
300 PPM	1.015-1.054	7.0-8.5	N-3+	N-N	N-N	N-Tr	N-Tr
30 PPM	1.029-1.063	7.5-8.5	N-4+	N-N	N-N	N-3+	N-N
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	N-N	N-N	N-N
30 PPM	1.022-1.066	6.5-8.0	N-4+	N-N	N-N	N-3+	N-N
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 marked; 4+ - marked

000466

TABLE 16

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

Ranges of Urinalysis Values at 24 Months

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

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

C004627

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)

	0 PPM		300 PPM	
MALE	N = 15		N = 15	
ORGAN	WT	SD	WT	SD
BODY	625.5	+-65.905	580.8	+-51.153
LIVER	19.15	+- 3.212	21.33	+- 2.497
HEART	1.629	+- 0.157	1.452	+- 0.053*
SPLEEN	0.894	+- 0.144	0.800	+- 0.109
KIDNEYS	3.854	+- 0.507	4.047	+- 0.419
ADRENALS	.0679	+- 0.013	.0553	+- 0.008*
TESTES	3.553	+- 0.419	3.459	+- 0.325
BRAIN	2.113	+- 0.111	2.064	+- 0.067
PITUITARY	.0205	+- 0.006	.0115	+- 0.004*
FEMALE	N = 15		N = 15	
ORGAN	WT	SD	WT	SD
BODY	401.1	+-77.172	403.1	+-66.702
LIVER	12.28	+- 1.904	12.90	+- 1.781
HEART	1.117	+- 0.134	1.086	+- 0.121
SPLEEN	0.663	+- 0.123	0.613	+- 0.120
KIDNEYS	2.533	+- 0.383	2.599	+- 0.283 A
ADRENALS	.0761	+- 0.012	.0796	+- 0.019
UTERUS	0.775	+- 0.247	0.702	+- 0.221
BRAIN	1.963	+- 0.128	1.970	+- 0.119
PITUITARY	.0227	+- 0.006	.0195	+- 0.007

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

000468

TABLE 17

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

ORGAN WEIGHT/BODY WEIGHT (%)

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

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

C004469

TABLE 17

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

ORGAN WEIGHT/BRAIN WEIGHT (GRAMS)

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

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

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TABLE 17

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

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS[a]	TESTES	BRAIN	PITUITARY[a]
0 PPM	A1R-3516	720	23.88	1.786	1.079	3.970	94	3.727	2.330	9
0 PPM	A1R-3517	651	21.74	1.565	0.874	4.043	66	4.147	2.111	14
0 PPM	A1R-3520	655	20.87	1.719	0.772	4.352	62	3.967	2.204	19
0 PPM	A1R-3522	627	16.18	1.675	0.776	4.281	67	3.794	2.227	20
0 PPM	A1R-3527	634	16.71	1.517	0.658	3.356	57	3.316	2.088	33
0 PPM	A1R-3535	594	18.12	1.654	0.895	3.474	87	3.238	1.953	27
0 PPM	A1R-3543	747	24.96	1.783	0.904	4.365	59	3.704	2.194	16
0 PPM	A1R-3546	656	17.61	2.018	0.905	3.958	77	3.460	2.079	24
0 PPM	A1R-3550	566	15.19	1.476	0.704	3.656	41	3.911	2.150	15
0 PPM	A1R-3551	494	13.96	1.361	0.751	2.657	59	2.581	1.920	24
0 PPM	A1R-3559	627	19.53	1.536	0.872	3.548	78	3.331	2.074	23
0 PPM	A1R-3568	688	22.31	1.629	1.091	4.679	64	3.870	2.207	18
0 PPM	A1R-3570	575	16.55	1.526	0.991	3.525	64	3.503	2.114	25
0 PPM	A1R-3575	551	19.88	1.636	1.113	3.781	67	2.944	1.971	15
0 PPM	A1R-3580	598	19.77	1.556	1.028	4.170	76	3.805	2.071	15
300 PPM	B1R-3584	547	18.56	1.487	0.603	3.845	53	3.226	1.981	6
300 PPM	B1R-3588	564	25.31	1.516	0.593	4.584	63	3.995	2.147	15
300 PPM	B1R-3589	552	24.34	1.506	0.794	3.852	55	3.700	2.076	11
300 PPM	B1R-3592	657	18.67	1.402	0.820	3.659	65	3.839	2.165	20
300 PPM	B1R-3598	565	22.98	1.448	0.742	4.396	61	3.264	2.059	10
300 PPM	B1R-3604	554	21.43	1.503	0.854	4.826	62	3.228	1.987	10
300 PPM	B1R-3613	686	18.07	1.368	0.963	3.593	70	3.376	2.046	9
300 PPM	B1R-3617	552	20.50	1.485	0.875	3.915	48	3.604	2.033	10
300 PPM	B1R-3620	641	22.91	1.499	0.859	4.096	59	3.484	2.109	11
300 PPM	B1R-3622	487	17.88	1.357	0.780	3.442	61	2.700	1.999	16
300 PPM	B1R-3626	603	25.32	1.395	0.813	4.592	47	3.205	2.066	12
300 PPM	B1R-3627	595	20.94	1.481	0.715	3.783	47	3.381	2.124	11
300 PPM	B1R-3638	559	20.30	1.412	0.746	3.793	47	3.822	2.124	6
300 PPM	B1R-3642	543	20.35	1.439	0.887	3.886	49	3.649	2.101	14
300 PPM	B1R-3643	607	22.38	1.489	0.958	4.446	43	3.418	1.938	11

NOTES: Body weights and organ weights in grams.

[a] indicates organ weights in mg.

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TABLE 17

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

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS [a]	UTERUS	BRAIN	PITUITARY [a]
0 PPM	N1R-4578	540	15.34	1.390	0.751	3.279	80	0.696	2.044	22
0 PPM	N1R-4582	385	12.26	1.185	0.418	2.405	81	0.870	1.674	27
0 PPM	N1R-4585	353	12.90	1.035	0.626	2.223	56	0.674	1.912	18
0 PPM	N1R-4588	386	11.99	1.117	0.679	2.535	87	0.654	2.073	18
0 PPM	N1R-4589	375	13.19	1.095	0.651	3.106	78	1.032	1.963	24
0 PPM	N1R-4590	373	10.52	1.037	0.571	2.308	78	0.933	1.875	17
0 PPM	N1R-4601	470	13.39	1.164	0.868	3.115	62	0.407	1.928	25
0 PPM	N1R-4608	429	13.00	1.021	0.648	2.356	85	0.963	2.124	19
0 PPM	N1R-4610	345	11.31	0.982	0.681	2.435	87	1.371	1.969	30
0 PPM	N1R-4620	320	11.45	1.176	0.789	2.470	89	0.846	2.135	18
0 PPM	N1R-4629	401	11.33	1.084	0.663	2.176	65	0.523	1.967	19
0 PPM	N1R-4630	466	13.83	1.280	0.725	2.616	80	0.520	2.154	17
0 PPM	N1R-4631	248	7.37	0.830	0.414	1.844	62	0.520	1.883	20
0 PPM	N1R-4632	531	14.70	1.128	0.723	2.620	59	0.890	1.846	40
0 PPM	N1R-4640	395	11.69	1.238	0.731	2.512	92	0.833	1.893	25
300 PPM	O1R-4642	323	10.85	0.920	0.732	2.679	76	1.150	1.945	25
300 PPM	O1R-4652	383	13.12	1.119	0.609	2.972	64	0.766	2.265	25
300 PPM	O1R-4655	372	12.16	1.045	0.603	2.527	71	0.543	1.740	6
300 PPM	O1R-4656	447	13.49	1.160	0.605	3.020	78	0.888	2.011	6
300 PPM	O1R-4664	399	14.26	1.156	0.685	2.384	75	0.557	1.948	21
300 PPM	O1R-4666	339	12.28	1.066	0.618	2.788	106	0.863	1.966	22
300 PPM	O1R-4669	385	12.10	0.952	0.470	2.396	59	0.756	1.856	16
300 PPM	O1R-4671	497	17.67	1.181	0.663	2.852	114	0.835	2.008	17
300 PPM	O1R-4674	355	13.59	0.927	0.594	2.290	64	0.448	2.009	25
300 PPM	O1R-4676	519	14.36	1.206	0.630	2.888	90	0.704	2.098	30
300 PPM	O1R-4687	329	12.56	1.108	0.437	. [b]	88	0.924	2.047	17
300 PPM	O1R-4689	363	11.72	1.312	0.798	2.647	115	0.668	1.837	21
300 PPM	O1R-4692	531	13.54	1.210	0.468	2.488	60	0.355	1.941	22
300 PPM	O1R-4699	395	11.59	0.982	0.561	2.384	70	0.708	1.830	20
300 PPM	O1R-4704	409	10.18	0.943	0.527	2.067	64	0.358	1.948	19

NOTES: Body weights and organ weights in grams.

[a] Indicates organ weights in mg.

[b] Kidney weights not recorded due to marked hydronephrosis.

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TABLE 18

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

ABSOLUTE ORGAN WEIGHT (GRAMS)

	0 PPM		300 PPM		30 PPM	
MALE	N = 15		N = 15		N = 15	
ORGAN	WT	SD	WT	SD	WT	SD
BODY	666.7	+-99.761	632.6	+-91.947	648.2	+-106.96
LIVER	18.15	+- 3.074	19.12	+- 3.037	18.81	+- 3.427
HEART	1.720	+- 0.225	1.665	+- 0.295	1.806	+- 0.313
SPLEEN	1.217	+- 0.339	1.158	+- 0.310	1.105	+- 0.206
KIDNEYS	4.404	+- 0.746	4.590	+- 0.525	5.185	+- 1.782
ADRENALS	.0801	+- 0.018	.0866	+- 0.018	.0900	+- 0.027
TESTES	3.478	+- 0.702	3.626	+- 0.643	3.696	+- 0.727
BRAIN	2.105	+- 0.133	2.185	+- 0.072	2.203	+- 0.130*
FEMALE	N = 15		N = 15		N = 15	
ORGAN	WT	SD	WT	SD	WT	SD
BODY	512.5	+-82.585	451.2	+-68.116	533.3	+-82.486
LIVER	15.11	+- 3.752	14.05	+- 2.735A	17.06	+- 3.847
HEART	1.306	+- 0.199	1.310	+- 0.170	1.489	+- 0.192
SPLEEN	0.797	+- 0.140	0.698	+- 0.195	1.153	+- 0.681#
KIDNEYS	3.129	+- 0.287	3.195	+- 0.465	3.475	+- 0.446*
ADRENALS	.1030	+- 0.046A	.1126	+- 0.039	.1365	+- 0.044
UTERUS	0.814	+- 0.290	0.819	+- 0.391	0.858	+- 0.487
BRAIN	2.034	+- 0.102	2.049	+- 0.111	2.030	+- 0.131

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

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TABLE 18

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

ORGAN WEIGHT/BODY WEIGHT (%)

	0 PPM		300 PPM		30 PPM	
MALE	N = 15		N = 15		N = 15	
ORGAN	%	SD	%	SD	%	SD
LIVER	2.733+-0.339		3.043+-0.408		2.934+-0.531	
HEART	0.261+-0.037		0.267+-0.054		0.283+-0.055	
SPLEEN	0.187+-0.059		0.184+-0.047		0.174+-0.042	
KIDNEYS	0.686+-0.101		0.736+-0.105		0.821+-0.350	
ADRENALS	0.012+-0.003		0.014+-0.003		0.014+-0.005	
TESTES	0.536+-0.144		0.578+-0.100		0.574+-0.093	
BRAIN	0.322+-0.049		0.353+-0.054		0.347+-0.056	
FEMALE	N = 15		N = 15		N = 15	
ORGAN	%	SD	%	SD	%	SD
LIVER	2.941+-0.465		3.125+-0.417A		3.196+-0.550	
HEART	0.269+-0.036		0.296+-0.056		0.283+-0.046	
SPLEEN	0.158+-0.033		0.197+-0.046		0.210+-0.078*	
KIDNEYS	0.621+-0.080		0.709+-0.120*		0.662+-0.102	
ADRENALS	0.020+-0.008A		0.025+-0.010		0.026+-0.007	
UTERUS	0.161+-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.

000474

TABLE 18

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

ORGAN WEIGHT/BRAIN WEIGHT (GRAMS)

	0 PPM		300 PPM		30 PPM	
MALE	N = 15		N = 15		N = 15	
ORGAN	RATIO	SD	RATIO	SD	RATIO	SD
LIVER	8.648	+-1.587	8.756	+-1.424	8.544	+-1.485
HEART	0.819	+-0.103	0.760	+-0.119	0.821	+-0.141
SPLEEN	0.578	+-0.155	0.531	+-0.149	0.501	+-0.086
KIDNEYS	2.099	+-0.377	2.101	+-0.232	2.360	+-0.827
ADRENALS	0.038	+-0.010	0.040	+-0.008	0.041	+-0.013
TESTES	1.658	+-0.336	1.699	+-0.287	1.675	+-0.297
FEMALE	N = 15		N = 15		N = 15	
ORGAN	RATIO	SD	RATIO	SD	RATIO	SD
LIVER	7.456	+-1.918	6.883	+-1.508A	8.460	+-2.162
HEART	0.673	+-0.100	0.642	+-0.097	0.738	+-0.117
SPLEEN	0.394	+-0.078	0.343	+-0.100	0.568	+-0.325#
KIDNEYS	1.543	+-0.166	1.545	+-0.259	1.716	+-0.231
ADRENALS	0.050	+-0.022A	0.055	+-0.019	0.068	+-0.023
UTERUS	0.404	+-0.156	0.400	+-0.173	0.419	+-0.226

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

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TABLE 18

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

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS[a]	TESTES	BRAIN
0 PPM	A1R3518	556	15.12	1.623	1.318	3.913	60	4.523	2.154
0 PPM	A1R3524	638	23.45	1.511	1.415	4.845	57	3.919	2.046
0 PPM	A1R3528	812	19.67	1.784	1.111	4.924	87	4.082	2.076
0 PPM	A1R3531	733	17.52	1.871	0.870	3.842	75	3.574	2.127
0 PPM	A1R3533	765	18.07	1.575	0.941	4.128	100	2.996	2.040
0 PPM	A1R3538	788	21.72	2.251	1.893	4.535	94	3.778	2.143
0 PPM	A1R3542	733	17.60	1.556	0.728	4.233	54	1.438	2.200
0 PPM	A1R3548	706	18.44	1.667	1.148	4.670	73	3.526	2.329
0 PPM	A1R3554	517	14.19	1.547	1.135	3.461	88	3.628	1.990
0 PPM	A1R3557	612	17.71	1.786	1.106	4.718	70	4.123	2.252
0 PPM	A1R3562	588	15.14	1.616	1.754	3.988	61	3.475	2.061
0 PPM	A1R3564	576	16.20	1.679	1.396	3.745	93	3.328	2.223
0 PPM	A1R3569	696	21.44	2.172	1.586	6.410	100	3.203	2.046
0 PPM	A1R3573	759	22.41	1.625	0.907	5.011	113	3.561	1.861
0 PPM	A1R3578	521	13.52	1.538	0.900	3.641	77	3.015	1.950
300 PPM	B1R3581	734	18.42	1.786	1.227	4.472	92	4.177	2.280
300 PPM	B1R3585	656	21.42	1.465	1.447	4.641	84	3.948	2.074
300 PPM	B1R3591	440	14.04	1.427	0.662	3.831	62	2.631	2.091
300 PPM	B1R3594	774	23.83	1.486	1.237	5.013	76	3.967	2.210
300 PPM	B1R3597	634	14.99	1.582	0.992	4.032	97	4.056	2.134
300 PPM	B1R3601	643	21.09	2.530	1.023	5.680	89	3.983	2.272
300 PPM	B1R3605	626	20.04	1.523	0.995	4.160	92	2.867	2.141
300 PPM	B1R3608	606	18.66	1.385	1.640	4.787	84	3.254	2.095
300 PPM	B1R3611	641	18.83	1.682	1.320	4.271	107	3.777	2.282
300 PPM	B1R3618	801	18.91	1.574	0.790	4.342	77	3.849	2.123
300 PPM	B1R3623	622	20.26	1.803	1.217	5.057	91	3.993	2.212
300 PPM	B1R3630	507	15.62	1.443	0.824	4.081	78	3.886	2.210
300 PPM	B1R3633	632	24.81	1.666	1.800	5.125	135	3.436	2.130
300 PPM	B1R3636	564	16.44	1.585	1.067	4.222	68	2.118	2.247
300 PPM	B1R3641	609	19.45	2.032	1.129	5.133	67	4.444	2.231
30 PPM	C1R3646	680	18.71	1.409	1.042	3.748	66	3.199	2.218
30 PPM	C1R3650	586	18.17	1.605	1.417	4.367	94	4.083	2.473
30 PPM	C1R3654	704	21.84	2.020	1.108	5.309	83	5.371	2.317
30 PPM	C1R3658	628	16.67	1.293	0.837	4.197	60	4.001	2.164
30 PPM	C1R3663	713	25.66	2.172	1.178	5.023	99	3.794	2.220
30 PPM	C1R3667	583	17.03	1.472	0.979	4.562	78	3.305	2.111
30 PPM	C1R3670	653	19.03	2.010	1.417	7.178	124	3.205	2.286
30 PPM	C1R3672	616	16.77	1.825	1.082	4.468	73	2.452	2.060
30 PPM	C1R3676	539	24.00	2.326	1.414	10.404	143	3.209	2.150
30 PPM	C1R3679	921	23.86	2.120	0.962	5.664	90	4.544	2.304
30 PPM	C1R3682	545	16.02	1.464	0.905	4.147	64	3.080	1.938
30 PPM	C1R3684	772	16.98	2.022	1.151	5.550	91	4.109	2.148
30 PPM	C1R3689	491	13.94	1.416	0.773	4.170	62	3.068	2.312
30 PPM	C1R3691	595	16.89	1.707	1.277	3.988	81	3.832	2.248
30 PPM	C1R3694	697	16.58	1.631	1.033	4.626	142	4.179	2.040

NOTES: Body weights and organ weights in grams.

[a] Indicates adrenal weight in mg.

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TABLE 18

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

DOSE	ANIMAL	BODY	LIVER	HEART	SPLEEN	KIDNEYS	ADRENALS [a]	UTERUS	BRAIN
0 PPM	N1R4583	494	15.99	1.174	1.032	3.368	98	0.843	2.045
0 PPM	N1R4586	480	11.86	1.215	0.983	2.824	63	1.065	2.069
0 PPM	N1R4591	516	14.21	1.322	0.749	3.161	84	0.884	1.960
0 PPM	N1R4595	455	11.98	1.415	0.740	2.768	108	0.729	2.089
0 PPM	N1R4598	471	13.45	1.538	0.983	3.466	. [b]	1.155	1.928
0 PPM	N1R4603	481	14.37	1.465	0.657	3.218	84	0.725	2.174
0 PPM	N1R4606	592	14.99	1.601	0.757	3.374	114	1.591	1.927
0 PPM	N1R4611	604	24.88	1.567	0.721	3.318	253	0.566	2.115
0 PPM	N1R4614	518	14.40	1.498	0.697	3.356	91	0.570	2.055
0 PPM	N1R4616	387	11.77	1.254	0.717	3.012	122	0.803	2.140
0 PPM	N1R4626	353	10.28	0.949	0.581	2.464	78	0.354	2.032
0 PPM	N1R4628	535	13.34	1.182	0.938	3.082	79	0.812	1.971
0 PPM	N1R4634	567	19.23	1.523	0.665	2.878	108	0.738	1.919
0 PPM	N1R4636	560	19.57	1.180	0.933	3.261	85	0.746	1.874
0 PPM	N1R4638	675	16.28	1.612	0.798	3.390	75	0.636	2.218
300 PPM	O1R4644	468	14.35	1.208	0.608	2.832	76	0.466	1.968
300 PPM	O1R4646	539	17.04	1.258	0.946	3.688	89	0.767	2.236
300 PPM	O1R4649	378	11.32	1.056	0.495	2.806	38	0.588	2.195
300 PPM	O1R4657	418	14.58	1.179	0.677	2.844	131	0.596	2.043
300 PPM	O1R4659	519	15.84	1.308	1.134	3.293	102	1.465	2.016
300 PPM	O1R4661	459	12.22	1.153	0.630	2.398	64	0.424	2.085
300 PPM	O1R4663	480	14.01	1.452	0.688	3.275	138	1.076	2.024
300 PPM	O1R4672	380	10.92	1.403	0.944	2.930	100	0.665	1.934
300 PPM	O1R4679	551	21.39	1.521	0.717	4.125	128	0.926	1.897
300 PPM	O1R4683	376	13.96	1.575	0.841	3.490	183	0.438	2.065
300 PPM	O1R4688	375	13.32	1.334	0.454	3.183	137	1.083	2.264
300 PPM	O1R4693	480	12.13	1.187	0.557	2.592	129	0.926	2.086
300 PPM	O1R4695	449	. [c]	1.610	0.471	3.737	175	1.532	2.031
300 PPM	O1R4697	354	11.60	1.122	0.722	2.937	87	0.803	1.933
300 PPM	O1R4701	542	13.98	1.288	0.589	3.194	112	0.529	1.958
30 PPM	P1R4708	526	17.63	1.375	0.857	3.809	173	0.949	1.975
30 PPM	P1R4711	559	22.66	1.456	1.016	3.085	123	0.517	1.927
30 PPM	P1R4714	545	23.62	1.693	1.027	3.904	202	0.612	1.859
30 PPM	P1R4716	404	10.49	1.594	0.989	2.722	105	0.408	1.890
30 PPM	P1R4720	539	19.79	1.411	1.296	3.788	185	0.610	2.010
30 PPM	P1R4723	542	16.73	1.432	1.089	4.066	118	2.450	2.127
30 PPM	P1R4726	606	16.96	1.864	1.057	3.878	103	1.064	2.117
30 PPM	P1R4729	502	19.16	1.693	0.947	3.608	169	1.035	1.841
30 PPM	P1R4733	452	12.22	1.217	0.707	2.997	94	0.811	2.103
30 PPM	P1R4736	533	13.87	1.399	0.920	3.216	73	0.590	2.001
30 PPM	P1R4739	756	22.13	1.708	3.561	3.113	210	0.522	2.085
30 PPM	P1R4745	428	14.03	1.464	0.824	3.670	111	0.974	2.097
30 PPM	P1R4747	545	16.57	1.274	0.993	3.407	125	0.846	2.351
30 PPM	P1R4752	575	15.09	1.538	0.854	4.012	168	0.864	2.106
30 PPM	P1R4754	487	14.88	1.210	1.157	2.858	89	0.614	1.967

NOTES: Body weights and organ weights in grams.
[a] Indicates adrenal weights in mg.
[b] Indicates adrenal weight not recorded; left adrenal greatly enlarged.
[c] Indicates liver weight not recorded due to mass.

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TABLE 19

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

Summary of Major Microscopic Findings - Percent Incidence at 2 Years

NEOPLASTIC LESIONS

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

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

* = Significantly different (= 0.05) from controls

000478

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

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

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

* = Significantly different (= 0.05) from controls

000479

FIGURE 1

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

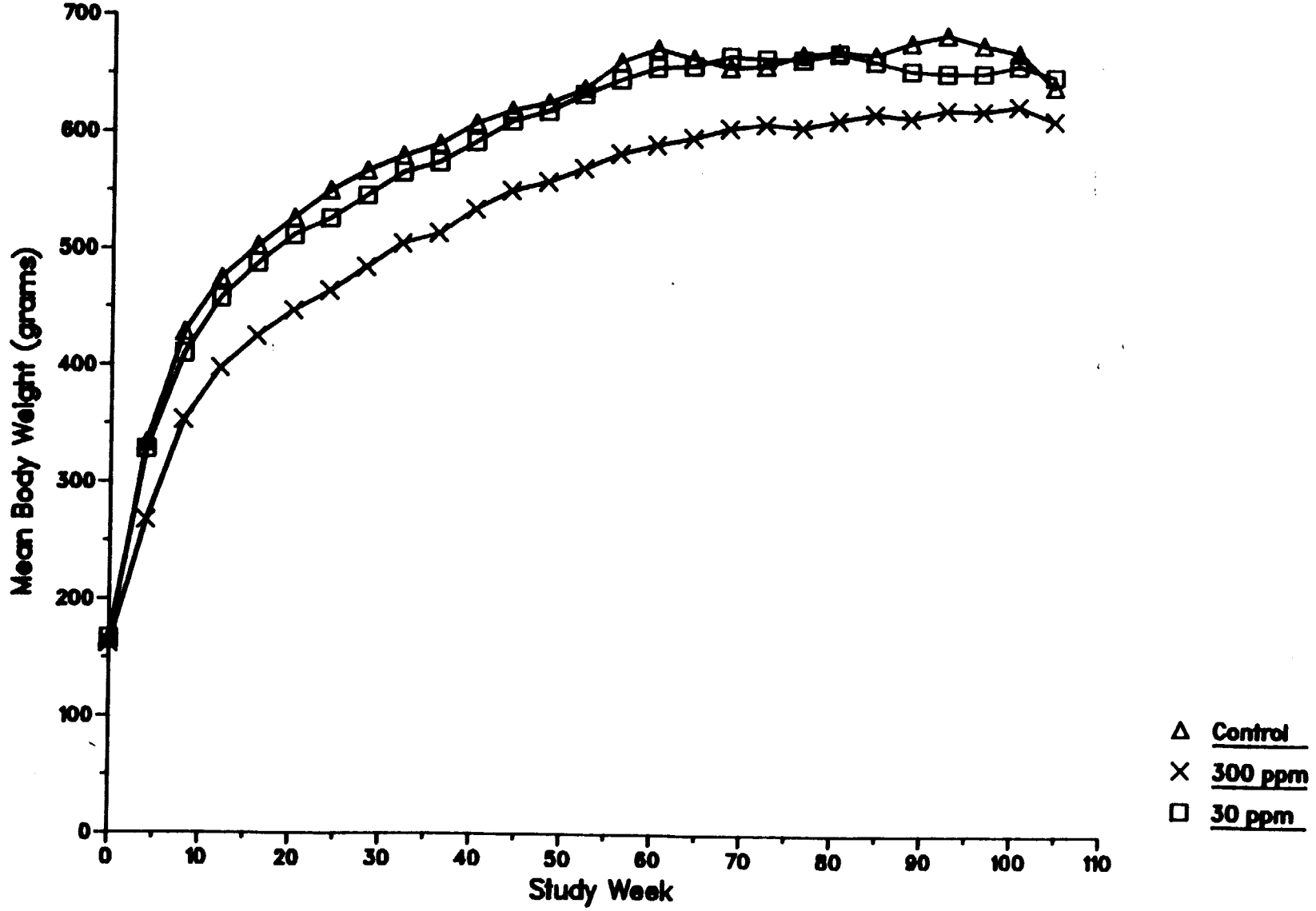
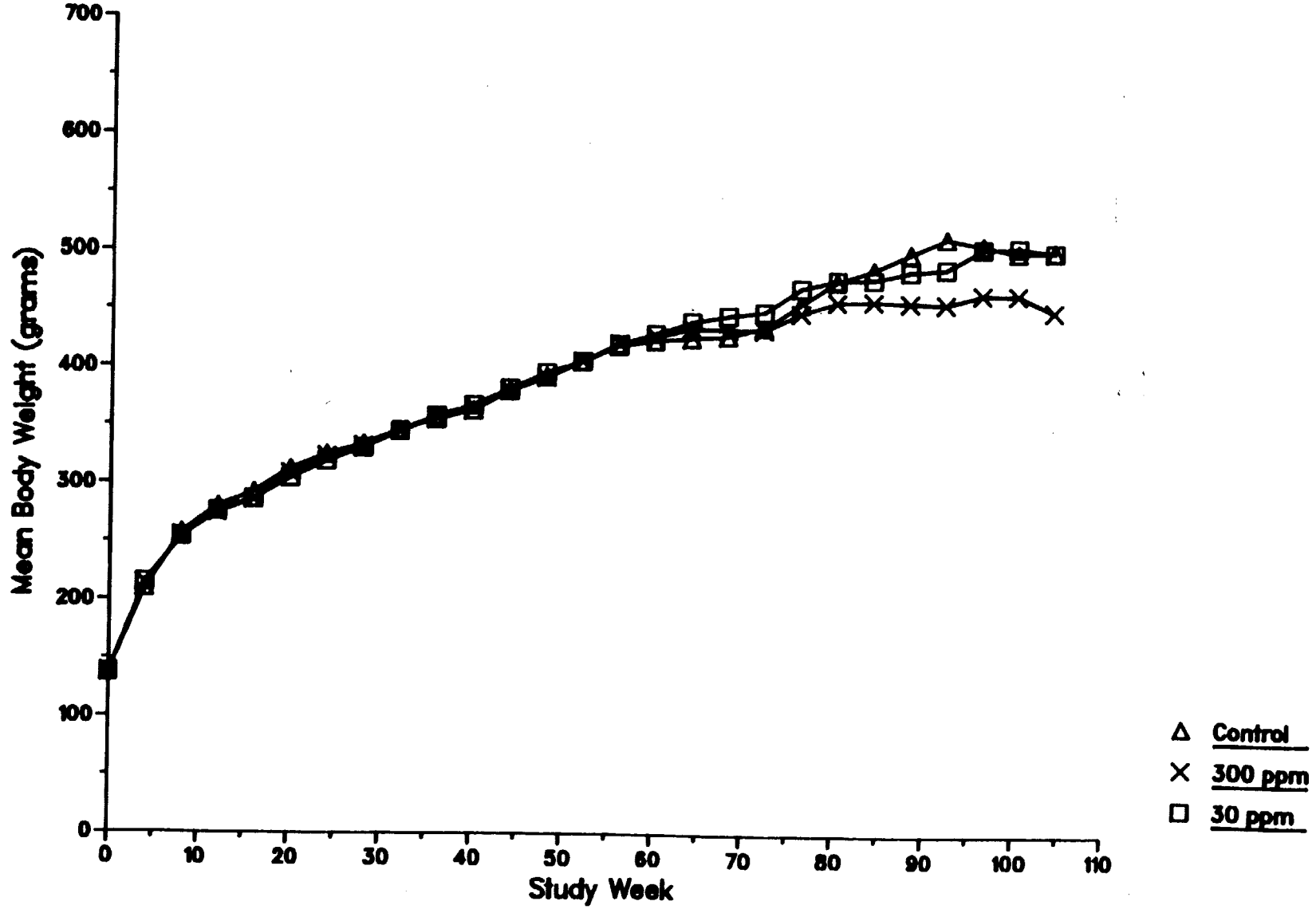


FIGURE 2

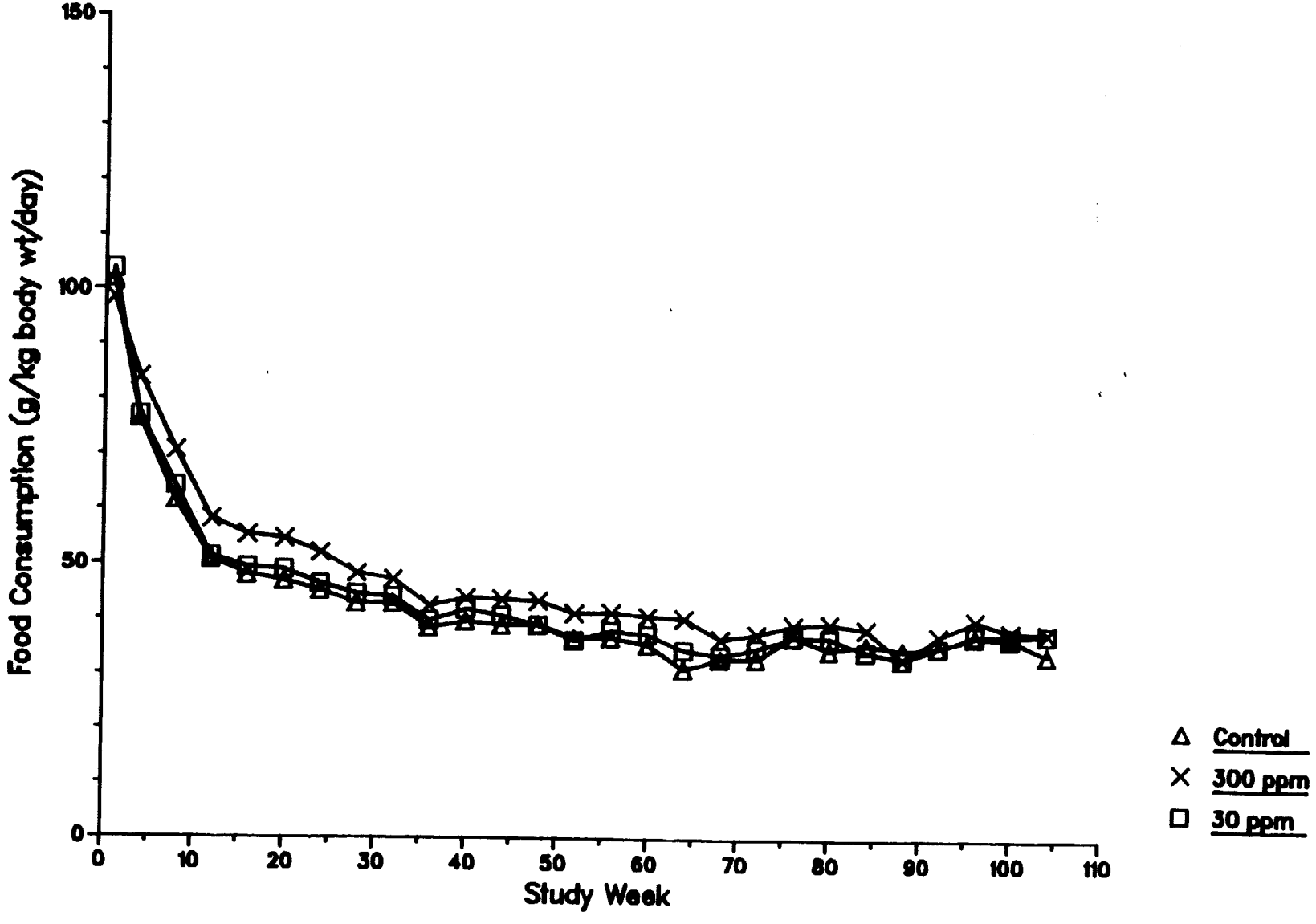
TWO YEAR ORAL (DIET) TOXICITY–ONCOGENICITY STUDY OF FLUOROCARBON FC–143 IN RATS
MEAN BODY WEIGHTS (G) OF FEMALES



94
C004481

FIGURE 3

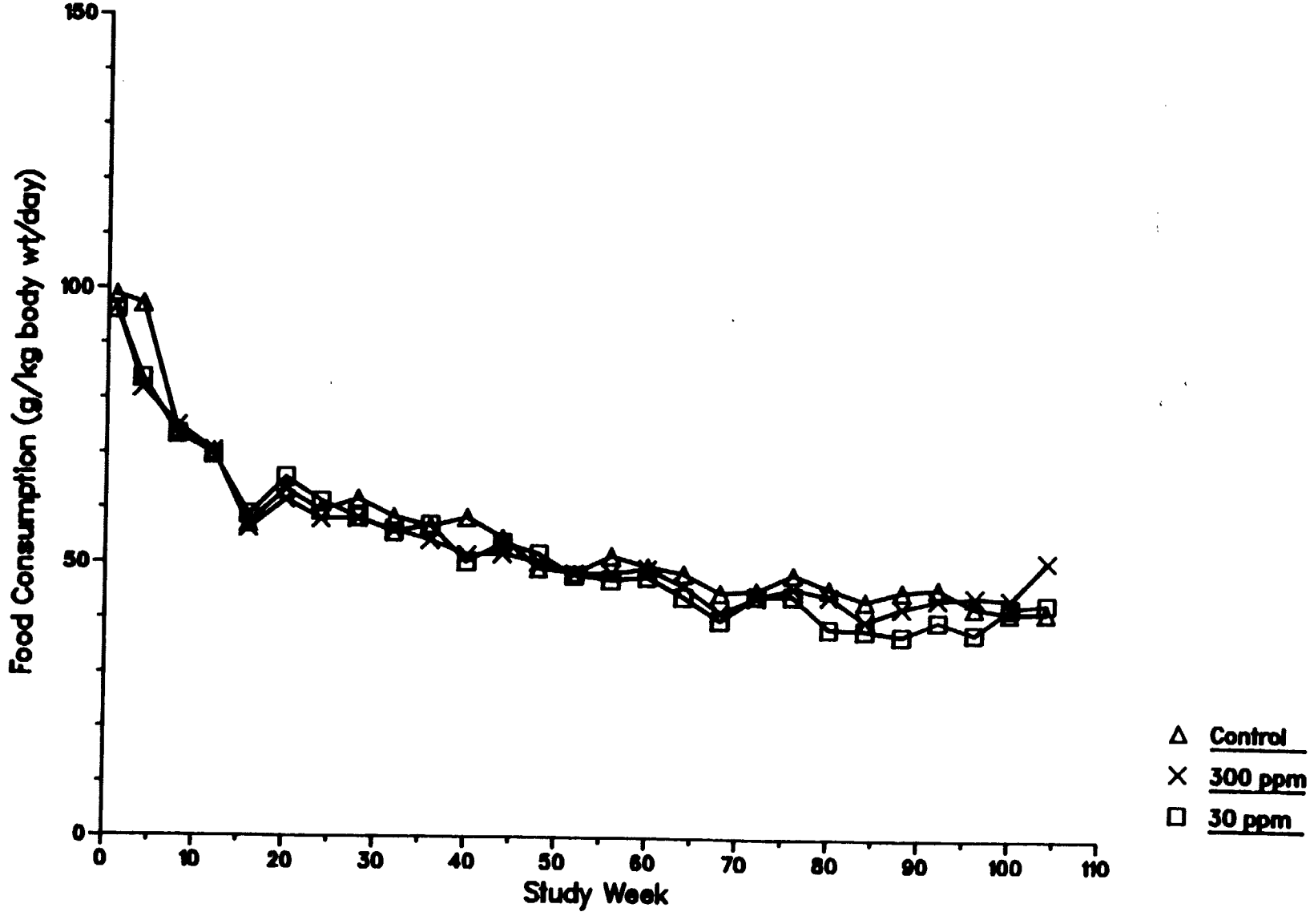
TWO YEAR ORAL (DIET) TOXICITY–ONCOGENICITY STUDY OF FLUOROCARBON FC–143 IN RATS
MEAN FOOD CONSUMPTION (G/KG OF MEAN BODY WEIGHT) OF MALES



000482

FIGURE 4

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



000483

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

APPENDIX ITEMS

000484

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Internal Correspondence

Appendix Item A

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

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

To: M. T. CASE - RIKER LABORATORIES - 218-3S

From: S. D. SORENSON - MEDICAL, IND. HYG. SERV. - 220-2E-02

Subject: Air Monitoring, Project 8900?107

Date: August 27, 1981

3M

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.

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Appendix Item A

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.

S. D. Arenson

SDS:cr

APPENDIX ITEM A

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	< 0.001
CCL81-24	Same as CCL81-22, duplicate sample using silica gel tube.	931-1228	FC-143	< 0.002

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

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

ANALYTICAL REQUEST: #A80248.

Internal Correspondence

APPENDIX ITEM A

To: L. J. Sibinski

From: J. D. Johnson

Subject: Analysis of Plasma Samples from Sentinal Rats Housed in Room with Two Year Tox Study-Rats (Riker Study No. 0281CR0012)

Date: October 7, 1985

3M

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

James D. Johnson
Research Specialist
Riker Laboratories, Inc.

Appendix Item A

Internal Correspondence

cc: M.T. Case
F.D. Griffith
R.E. Ober
W.H. Pearlson
R.A. Prokop
[redacted] 218-3

To: V. Pothapragada

From: J.D. Johnson

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

Date: July 15, 1981

3M

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

The numbers for these rats are as follows:

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

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

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

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

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

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

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

James D. Johnson

J.D. Johnson/mho

Appendix Item B

To [redacted]

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:

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

APPENDIX ITEM B

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

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

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

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

APPENDIX ITEM B

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

LJS/mao

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

APPENDIX ITEM B

Internal Correspondence

Commercial Chemicals
Analytical Report
#229

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

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:

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

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

Paul J Colbert

PJC:da

Internal Correspondence

APPENDIX ITEM B

Commercial Chemicals
Analytical Report #250

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

From: P. J. Colbert - 236-2B

Subject: GLC Analysis of FC-143 (T-2993CoC) Blended into Ground Lab Chow (Riker Study #0281CR0012)

Date: August 20, 1981

3M

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

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

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

PJC/mao Paul J. Colbert

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- 236-2B
R. M. Payfer - 236-2B
G. W. Kirsch - 236-3A

Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #289

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

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

Subject: GLC ANALYSIS OF FC-143 (T-2998 CoC)BLENDED INTO GROUND LAB CHOW (RIKER STUDY #2081cR0012)

Date: November 30, 1981

3M

References: Commercial Chemicals Analytical Laboratory Request #17779

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

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

RMP/hc

Richard M Payfer

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

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APPENDIX ITEM B

Internal Correspondence

dc: M.T. Case - 21[illegible] 2
G.W. Kirsch - [illegible]36-[illegible]
E.G. Lamprech[illegible] - 2[illegible]-3
J.D. LaZerte - 236-[illegible]
W.C. McCormick - 22[illegible]-2E-02
V. Pothapragada - 236-3A
L.D. Winter - 236-2B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #319

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

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

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

Date: MARCH 5, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18069

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

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

incorrect values due to faulty doctor in our conversation with R.M. Payfer on 3/16/82 [illegible]

Re analyze [illegible] done
Samples [illegible]

Richard M. Payfer
RMP:df

Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALYTICAL REPORT #328

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

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

Subject: GLC RE-ANALYSIS OF FC-143 (T-2998 COC) BLENDED INTO GROUND LAB CHOW (RIKER STUDY #2081 CR0012)

Date: March 31, 1982

3M

Reference: Commercial CHemicals Analytical Laboratory Request #18100

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

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

R. M. Payfer

RMP/hc

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

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Internal Correspondence

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALTYICAL REPORT #340

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

From R. M. PAYFER - 236-2B

Subject GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND LAB CHOW (RIKER STUDY #0281 CR0012)

Date May 28, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18320

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

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

Richard M. Payfer

RMP/hc

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

APPENDIX ITEM B

COMMERCIAL CHEMICALS
ANALTYICAL REPORT #366

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

From R. M. PAYFER - 236-2B

Subject GLC ANALYSIS OF FC-143 (T-2998 Coc) BLENDED INTO GROUND LAB CHOW (RIKER STUDY #0281 CR0012)

Date Sept. 13, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18609

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

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

Richard Payfer

RMP/hc

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

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Internal Correspondence

APPENDIX ITEM B

To: L. L. Sibinski - 218-3

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

Commercial Chemicals
Analytical Report #384

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

Date: December 8, 1982

3M

Reference: Commercial Chemicals Analytical Laboratory Request #18855.

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

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

GWK:ch

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

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Internal Correspondence

APPENDIX ITEM B

Commercial Chemicals
Analytical Report #395

To: L. J. SIBINSKI - 218-3

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

Subject: GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND RODENT CHOW (RIKER STUDY #0281-CR0012)

Date: MARCH 7, 1983

3M

Reference: Commercial Chemicals Analytical Laboratory Request #19121

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

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 G.Kirsch

dc: M. T. Case - 218-2
E. G. Lamprechts - 218-3
J. D. LaZerte - 236-1
W. C. McCormick - 220-2E
R. M. Payfer - 236-2B
W. H. Pearlson - 223-6SE
L. D. Winter - 236-2B

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Internal Correspondence

APPENDIX ITEM B

Commercial Chemicals
Analytical Report #404

To L. J. SIBINSKI - 218-3

From G. W. KIRSCH - 236-2B

Subject GLC ANALYSIS OF FC-143 (T-2998 CoC) BLENDED INTO GROUND RODENT CHOW (RIKER STUDY #0281-CR0012)

Date MAY 2, 1983

3M

Reference: Commercial Chemicals Analytical Laboratory Request #19333

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

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

GWK/hc G. Kirsch

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

Appendix Item C

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

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

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

Appendix Item C

Methods Used for Hematology On Bleedings at 3 and 6 Months

Parameters	Units	Methods
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, Model MB International Equipment Co.
Differential	%/100 WBC	Microscope slide

APPENDIX ITEM C

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

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

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

APPENDIX ITEM D

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

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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.

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

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

Histopathology

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

to the cell membrane. The nucleus:cytoplasm ratio was decreased by the increase in cytoplasm in affected cells. In affected livers, most or all lobules were involved and the centrilobular cells were more severely affected. At the 1 year interim, megalocytosis occurred to a minimal to moderate degree in 12/15 males from the 300 ppm group. No females were affected at the 1 year interim. In TS/DOS rats, megalocytosis to a minimal to moderate degree occurred in 40/50 males at the 300 ppm level and to a minimal to mild degree in 8/50 females at the same level. At the 30 ppm level in TS/DOS rats, megalocytosis to a 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

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

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

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

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

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

Date 9/27/81

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

Table: 1

Project Number: 82C1CR0012 Species: Rat

Site/ Description	Group 1	Group 5
No visible lesions	3	9
Eye		
opacity		1
Pituitary		
mass		1
Liver		
pale/tan color	2	3
Mesentery		
fat necrosis	1	
Kidney		
hydronephrosis	1	
cystic lesion	1	
depressed area		1
Testis		
small		1
Skin		
nodule		1
Soft Tissue (leg)		
swollen foot	1	

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

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

Project Number: 0261CR0012 Species: Rat

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

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

* includes "possibly"

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

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

* includes "possibly"

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

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

* includes "possibly"

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

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

* includes "possibly"

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

Project Number: 02-1CR0C12 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
No visible lesions	4	3	3
Eye			
opacity/cloudy	3		
inflammation	1		
atrophy	1		
Pituitary			
mass/enlarged/raised lesion	25	25	25
hemorrhagic/dark lesion		2	3
Adrenal			
enlarged	8	3	7
mass/raised lesion			1
pale	1		
small		1	
Lung			
mottled	1		
consolidation	2	1	1
nodule	1		1
pale	1		
Lymph Node (bronchial)			
enlarged	1		
Heart			
enlarged*		1	1
Abdomen (internal)			
gas, gastrointestinal tract			1
bloody fluid filled			2
nodular tissue, omentum, mesentery			1
Stomach			
ulcerations/erosions	1		
red mucosal areas/reddened	2		
Small Intestine			
inflamed	1		
ulceration/ulcerated outpouching			2
Large Intestine			
impaction	1		
Pancreas			
mass/nodule	1		1
Liver			
pale*	13	3	6
mass/nodule/raised lesion	2	2	
mottled	4	1	1
circular lesion/pale foci/ pale lesion/yellowish lesion		1	2
enlarged*	2	1	2

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

* includes "possibly"

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

Project Number: 0251CR0012 Species: Rat

Site/ Description	Group 1	Group 5	Group 6
Liver (continued)			
dark red area/lobe	1		
rough/irregular surface	1		
Spleen			
enlarged*	5		2
Lymph node (mesenteric/abdominal)			
enlarged	2	1	1
reddened	1		
cystic		1	
Kidney			
enlarged, pale, pitted	2		
enlarged*	1		
pale, pitted	1	2	1
pitted	2		
pale*			1
cyst	3		1
Urinary Bladder			
enlarged	1		
calculi	1		
thickened walls	1	1	
Ovary			
mass	1		
Uterus			
enlarged			1
filled with dark/bloody fluid			1
mass	1		1
dark area/lesion	2		1
hemorrhagic lesion			1
Mammary Gland			
mass/nodule	27	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"

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

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Project Number: 0231CR0012 Species: Rat

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

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

() = Total Examined

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Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

Project Number: 0231CR3012 Species: Rat

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

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

() = Total Examined

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Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

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

Table: 7

Project Number: 0231CR3012 Species: Rat

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

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

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

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

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Esophagus	(15)	(33)	(6)	(41)	(13)	(32)
Within normal limits	15	33	6	41	13	32
Eye	(12)	(33)	(6)	(44)	(2)	(3)
Within normal limits	12	32	4	41	1	0
Cataract	0	0	0	0	1	2
Keratitis, acute	0	0	1	0	0	0
marked	0	0	1	0	0	0
Keratitis, chronic	0	0	0	1	0	1
mild	0	0	0	0	0	1
moderate	0	0	0	1	0	0
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

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

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

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

Table: 7

Project Number: 0221CR0012 Species: Rat

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

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

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

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

Table: 7

Project Number: 0281CR0012 Species: Rat

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

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

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

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Table: 7

Project Number: 0201CR3012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1 DOS	Group 1 SAC	Group 5 DOS	Group 5 SAC	Group 6 DOS	Group 6 SAC
Lung (continued)						
Granuloma	0	3	1	1	0	0
Hemorrhage	6	4	2	20	3	1
mild	2	1	0	5	0	0
moderate	1	2	1	13	0	2
marked	3	1	1	2	0	0
Medial hypertrophy, arteries	0	0	1	1	0	0
moderate	0	0	1	0	0	0
Necrosis	1	0	0	0	0	0
marked	1	0	0	0	0	0
Peribronchial lymphoid hyperplasia	0	1	0	0	0	0
mild	0	1	0	0	0	0
Perivascular mononuclear infiltrate	7	19	0	7	0	3
minimal	0	2	0	0	0	0
mild	2	14	0	2	0	3
moderate	0	3	0	1	0	0
Pneumonia, interstitial, acute	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Pneumonia, interstitial, chronic	2	14	1	6	0	5
mild	1	11	1	6	0	5
moderate	1	3	0	0	0	0
Thrombus	1	0	1	0	0	0
Vascular mineralization	10	33	4	43	11	32
minimal	0	2	0	0	0	0
mild	10	31	4	41	11	32
moderate	0	0	0	2	0	0
Lymph Node (mesenteric)	(12)	(33)	(6)	(44)	(0)	(1)
Within normal limits	10	29	5	38	0	1
Granuloma	0	0	0	1	0	0
moderate	0	0	0	1	0	0
Hemorrhage	2	4	0	4	0	0
minimal	1	2	0	1	0	0
mild	1	1	0	3	0	0
Sinusoidal ectasia	0	0	0	1	0	0
mild	0	0	0	1	0	0
Mammary Gland	(0)	(0)	(0)	(0)	(1)	(0)
Within normal limits	0	0	0	0	1	0
Mesentery	(0)	(2)	(0)	(0)	(1)	(1)
Polyarteritis	0	2	0	0	1	1
marked	0	2	0	0	1	1

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

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

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Pancreas	(13)	(33)	(6)	(43)	(12)	(34)
Within normal limits	10	24	4	27	10	21
Acinar atrophy	2	4	0	11	1	8
minimal	0	0	0	1	1	1
mild	1	2	0	6	0	5
moderate	1	1	0	4	0	2
marked	0	1	0	0	0	0
Hyperplasia, acinar cell	0	0	1	1	0	2
mild	0	0	0	1	0	1
moderate	0	0	1	0	0	1
Hyperplasia, islet cell	0	2	1	3	1	1
mild	0	0	0	0	1	1
moderate	0	2	1	3	0	0
Polyarteritis	0	4	0	2	0	3
minimal	0	0	0	0	0	1
moderate	0	2	0	2	0	2
marked	0	2	0	0	0	0
Parathyroid	(6)	(16)	(5)	(31)	(7)	(26)
Within normal limits	6	16	5	29	7	26
Pituitary	(15)	(33)	(5)	(41)	(13)	(34)
Within normal limits	7	18	3	28	3	20
Cyst	2	2	0	2	1	4
Hyperplasia	0	2	0	0	0	2
mild	0	2	0	0	0	1
Prostate	(13)	(33)	(6)	(43)	(13)	(35)
Within normal limits	10	27	5	40	11	35
Edema	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Prostatitis, acute	3	6	1	3	2	1
minimal	0	0	0	1	0	0
mild	1	2	0	0	1	1
moderate	1	3	0	1	0	0
marked	1	1	1	1	1	0
Salivary Gland	(12)	(32)	(5)	(41)	(10)	(34)
Within normal limits	12	31	4	25	10	21
Sialadenitis, acute	0	0	0	1	0	1
moderate	0	0	0	1	0	0
marked	0	0	0	0	0	1
Sialadenitis, chronic	0	1	0	14	0	12
minimal	0	1	0	0	0	0
mild	0	0	0	0	0	1
moderate	0	0	0	7	0	6

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

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

Table: 7

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Salivary Gland (continued)						
Sialadenitis, chronic						
marked	0	0	0	7	0	5
Skin	(8)	(7)	(0)	(2)	(5)	(4)
Abscess	0	0	0	0	1	0
Pododermatitis, ulcerative	3	5	0	1	2	2
marked	3	5	0	1	2	2
Ulcer	1	0	0	0	0	1
marked	1	0	0	0	0	1
Small Intestine	(14)	(34)	(6)	(44)	(1)	(0)
Within normal limits	13	32	5	44	1	0
Polyarteritis	0	2	0	0	0	0
moderate	0	1	0	0	0	0
marked	0	1	0	0	0	0
Spinal Cord	(15)	(32)	(6)	(42)	(0)	(0)
Within normal limits	15	32	6	42	0	0
Spleen	(16)	(34)	(6)	(44)	(14)	(36)
Within normal limits	6	20	1	25	8	35
Atrophy	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Fibrosis	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Hematopoiesis, extramedullary, increased	4	0	1	1	1	0
mild	2	0	0	1	0	0
moderate	1	0	1	0	0	0
marked	1	0	0	0	1	0
Hemosiderosis	5	11	3	19	4	0
mild	5	11	3	19	4	0
Necrosis	0	1	0	0	0	0
moderate	0	1	0	0	0	0
Polyarteritis	0	0	0	0	0	1
moderate	0	0	0	0	0	1
Stomach	(16)	(33)	(6)	(44)	(14)	(36)
Within normal limits	11	33	5	43	11	36
Edema	3	0	0	0	0	0
moderate	2	0	0	0	0	0
marked	1	0	0	0	0	0
Gastritis, acute	0	0	1	0	0	0
mild	0	0	1	0	0	0
Ulcer	1	0	0	0	3	0
marked	1	0	0	0	3	0

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

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

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

Table: 7

Project Number: C281CR0012 Species: Rat

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

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

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

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

Table: 7

Project Number: 0231CR0012 Species: Rat

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

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

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

000536

Project Number: 0291CR0012 Species: Rat

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

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

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

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Table: 8

Project Number: 0281CR0012 Species: Rat

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

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

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

Table: 3

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Kidney (continued)						
Pelvic mineralization						
marked	1	0	1	1	2	1
Pigment, conv. tub. epithelium	0	0	0	1	0	2
minimal	0	0	0	1	0	0
moderate	0	0	0	0	0	2
Polyarteritis	0	0	0	0	0	1
minimal	0	0	0	0	0	1
Protein resorption droplets	0	0	1	0	1	1
mild	0	0	0	0	0	1
marked	0	0	1	0	1	0
Pyelitis, acute	0	0	2	0	0	0
mild	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Pyelonephritis, acute	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Vacuolation, conv. tub. epitheium	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Large Intestine	(24)	(23)	(17)	(29)	(0)	(0)
Within normal limits	22	22	17	27	0	0
Nematodiasis	1	1	0	2	0	0
Liver	(25)	(25)	(21)	(29)	(26)	(24)
Within normal limits	1	0	4	4	7	7
Atrophy	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Cystoid degeneration	0	0	0	1	1	0
minimal	0	0	0	1	0	0
mild	0	0	0	0	1	0
Hematopoiesis, extramedullary	3	0	1	0	5	2
minimal	0	0	0	0	3	1
mild	3	0	0	0	2	1
moderate	0	0	1	0	0	0
Hepatocyte alteration, basophilic	1	7	0	2	5	3
minimal	0	0	0	1	0	0
mild	1	5	0	1	5	3
moderate	0	2	0	0	0	0
Hepatocyte alteration, eosinophilic	1	2	0	0	0	0
mild	0	2	0	0	0	0
moderate	1	0	0	0	0	0
Hepatocyte alteration, vacuolated	2	11	2	4	1	5
minimal	0	0	1	0	0	1
mild	2	11	1	4	0	4

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

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

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

Table: 8

Project Number: 0281CR0012 Species: Rat

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

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

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

000540

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

Table: 3

Project Number: 0281CR0012 Species: Rat

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

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

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

000541

Table: 8

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Lymph Node (mesenteric) (continued)						
Pigment, brown	0	0	0	5	0	0
minimal	0	0	0	1	0	0
mild	0	0	0	2	0	0
moderate	0	0	0	2	0	0
Sinusoidal ectasia	1	0	0	2	0	0
moderate	1	0	0	1	0	0
marked	0	0	0	1	0	0
Mammary Gland	(23)	(23)	(17)	(27)	(23)	(22)
Within normal limits	4	9	7	9	4	7
Fibrosis	0	0	0	1	0	0
mild	0	0	0	1	0	0
Galactocele	5	4	2	1	7	2
Lobular hyperplasia	4	3	2	1	2	1
moderate	1	0	2	0	0	0
Ovary	(25)	(23)	(18)	(29)	(26)	(24)
Within normal limits	19	17	11	16	23	11
Cyst	3	3	0	5	2	7
Tubular hyperplasia	0	0	7	8	0	7
mild	0	0	0	2	0	1
moderate	0	0	6	6	0	6
marked	0	0	1	0	0	0
Pancreas	(24)	(25)	(19)	(28)	(22)	(21)
Within normal limits	22	16	15	24	18	17
Acinar atrophy	0	6	2	2	3	2
minimal	0	1	0	1	1	1
mild	0	2	2	1	1	0
moderate	0	3	0	0	0	1
marked	0	0	0	0	1	0
Cyst	0	1	0	0	0	0
Edema	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Hyperplasia, islet cell	0	0	0	1	0	1
mild	0	0	0	1	0	1
Pancreatitis, chronic	0	0	1	0	0	0
moderate	0	0	1	0	0	0
Polyarteritis	0	0	0	0	0	1
minimal	0	0	0	0	0	1
Parathyroid	(5)	(0)	(9)	(14)	(15)	(15)
Within normal limits	5	0	9	14	15	15

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

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

Table: 3

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Pituitary	(22)	(24)	(21)	(29)	(23)	(24)
Within normal limits	5	7	7	7	3	4
Cyst	0	0	0	0	0	1
Hemorrhage	1	0	0	0	0	0
marked	1	0	0	0	0	0
Necrosis	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Salivary Gland	(19)	(24)	(15)	(25)	(22)	(24)
Within normal limits	13	24	15	23	22	23
Sialadenitis, chronic	1	0	0	2	0	1
mild	0	0	0	0	0	1
moderate	1	0	0	2	0	0
Skin	(3)	(3)	(2)	(0)	(6)	(4)
Within normal limits	0	0	0	0	2	2
Acanthosis	0	1	0	0	0	0
mild	0	1	0	0	0	0
Pododermatitis, ulcerative	0	0	1	0	0	0
marked	0	0	1	0	0	0
Ulcer	2	0	0	0	0	0
moderate	1	0	0	0	0	0
marked	1	0	0	0	0	0
Small Intestine	(24)	(25)	(18)	(29)	(1)	(1)
Within normal limits	24	25	17	28	0	0
Edema	0	0	1	0	0	0
mild	0	0	1	0	0	0
Granuloma	0	0	0	1	0	0
Ulcer	0	0	0	0	1	0
marked	0	0	0	0	1	0
Spinal Cord	(25)	(23)	(21)	(29)	(0)	(0)
Within normal limits	23	23	21	29	0	0
Malacia	1	0	0	0	0	0
moderate	1	0	0	0	0	0
Spleen	(25)	(25)	(21)	(29)	(24)	(23)
Within normal limits	4	11	12	23	10	17
Hematopoiesis, extramedullary, increased	7	2	2	1	11	5
mild	1	1	1	0	5	2
moderate	4	1	1	0	4	2
marked	2	0	0	1	2	1
Hemosiderosis	12	13	7	5	2	1
minimal	0	0	0	1	0	0
mild	8	13	6	3	0	1
moderate	4	0	1	1	1	0

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

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

Project Number: 0231CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Spleen (continued)						
Hemosiderosis						
marked	0	0	0	0	1	0
Stomach	(25)	(25)	(20)	(29)	(25)	(24)
Within normal limits	20	25	18	29	20	24
Edema	0	0	2	0	0	0
moderate	0	0	2	0	0	0
Hemorrhage	1	0	0	0	1	0
mild	0	0	0	0	1	0
moderate	1	0	0	0	0	0
Mineralization	1	0	0	0	0	0
mild	1	0	0	0	0	0
Necrosis	2	0	0	0	1	0
mild	1	0	0	0	1	0
moderate	1	0	0	0	0	0
Ulcer	1	0	0	0	4	0
mild	0	0	0	0	2	0
Thyroid	(25)	(25)	(15)	(26)	(23)	(22)
Within normal limits	20	23	14	22	22	21
Follicular hyperplasia, cystic	1	0	0	0	0	0
mild	1	0	0	0	0	0
Hyperplasia, C cell	0	0	1	2	1	0
mild	0	0	1	2	1	0
Ultimobranchial cyst	2	1	0	2	0	1
Trachea	(25)	(25)	(20)	(25)	(24)	(23)
Within normal limits	25	25	20	25	24	23
Urinary Bladder	(25)	(25)	(16)	(26)	(25)	(22)
Within normal limits	17	25	15	25	22	22
Calculus	1	0	0	0	0	0
Epithelial hyperplasia, papillary	1	0	0	0	0	0
marked	1	0	0	0	0	0
Epithelial hyperplasia, simple	7	0	0	1	2	0
mild	6	0	0	1	2	0
moderate	1	0	0	0	0	0
Hypertrophy	0	0	0	1	0	0
mild	0	0	0	1	0	0
Uterus	(25)	(25)	(19)	(29)	(26)	(23)
Within normal limits	21	17	17	24	17	17
Cystic glands	2	5	1	4	7	5
minimal	0	0	0	1	0	0
mild	0	1	1	2	1	1
moderate	2	1	0	1	2	1

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

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

Table: 8

Project Number: 0281CR0012 Species: Rat

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

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

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

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

Table: 9

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

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

Table: 10

Project Number: 0281CR0012 Species: Rat

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

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

() = Total Examined

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Table: 11

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Adrenal	(15)	(34)	(6)	(44)	(14)	(36)
Carcinoma, cortical	0	1	0	0	0	0
Ganglioneuroma	0	0	0	1	0	0
Pheochromocytoma, benign	1	1	0	4	0	4
Pheochromocytoma, malignant	0	0	0	0	0	1
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Bone Marrow	(15)	(32)	(6)	(42)	(0)	(0)
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Brain	(16)	(34)	(6)	(44)	(0)	(1)
Astrocytoma, benign	0	1	0	0	0	1
Oligodendroglioma, benign	1	0	0	0	0	0
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Eye	(12)	(33)	(6)	(44)	(2)	(3)
Hemolymphoreticular neoplasm present	0	0	1	0	0	0
Heart	(15)	(34)	(6)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Kidney	(16)	(34)	(6)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	1	0	1	0	1	0
Liver	(15)	(34)	(6)	(44)	(14)	(36)
Hepatocellular carcinoma	2	1	1	4	1	0
Hemolymphoreticular neoplasm present	2	1	1	1	1	0
Lung	(16)	(34)	(6)	(44)	(14)	(36)
Hemolymphoreticular neoplasm present	3	1	1	0	1	0
Lymph Node (abdominal)	(0)	(0)	(1)	(0)	(1)	(0)
Hemolymphoreticular neoplasm present	0	0	1	0	1	0
Lymph Node (mesenteric)	(12)	(33)	(6)	(44)	(0)	(1)
Hemangiosarcoma	0	0	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Pancreas	(13)	(33)	(6)	(43)	(12)	(34)
Adenocarcinoma	0	0	0	1	0	1
Islet cell adenoma	0	1	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Parathyroid	(6)	(16)	(5)	(31)	(7)	(23)
Adenoma	0	0	0	2	0	0
Pituitary	(15)	(33)	(5)	(41)	(13)	(34)
Adenoma	6	11	2	11	9	8
Salivary Gland	(12)	(32)	(5)	(41)	(10)	(34)
Carcinoma	0	0	1	0	0	0
Skin	(8)	(7)	(0)	(2)	(5)	(4)
Fibroma	1	0	0	0	0	0
Fibrosarcoma	1	0	0	0	2	1

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

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

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

Table: 11

Project Number: 0281CR0012 Species: Rat

Tissue/ Diagnosis/ Modifier	Group 1		Group 5		Group 6	
	DOS	SAC	DOS	SAC	DOS	SAC
Skin (continued)						
Keratoacanthoma	1	2	0	1	0	0
Liposarcoma	1	0	0	0	0	0
Papilloma	0	1	0	0	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Small Intestine	(14)	(34)	(6)	(44)	(1)	(0)
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Soft Tissues (abdomen)	(0)	(0)	(0)	(0)	(0)	(1)
Fibroma	0	0	0	0	0	1
Soft Tissues (thorax)	(0)	(0)	(0)	(1)	(0)	(0)
Histiocytoma, malignant	0	0	0	1	0	0
Spleen	(16)	(34)	(6)	(44)	(14)	(36)
Hemangiosarcoma	0	1	0	0	0	0
Hemolymphoreticular neoplasm present	1	1	1	0	1	0
Stomach	(16)	(33)	(6)	(44)	(14)	(36)
Adenocarcinoma	0	0	0	1	0	0
Hemolymphoreticular neoplasm present	1	0	0	0	0	0
Testis/Epididymis	(16)	(33)	(6)	(44)	(14)	(36)
Leydig cell adenoma	0	0	0	7	0	2
Thymus	(1)	(0)	(1)	(1)	(1)	(0)
Hemolymphoreticular neoplasm present	1	0	1	0	1	0
Thyroid	(12)	(31)	(5)	(42)	(12)	(35)
C cell adenoma	0	0	0	4	0	2
C cell carcinoma	0	2	0	0	0	0
Follicular adenoma	0	0	0	0	0	1
Urinary Bladder	(13)	(33)	(6)	(44)	(14)	(35)
Hemolymphoreticular neoplasm present	1	0	1	0	0	0
Hemolymphoreticular System [# affected]	[3]	[1]	[1]	[1]	[1]	[0]
Malignant lymphoma, lymphocytic	0	0	1	1	0	0
Malignant lymphoma, histiocytic	3	1	1	0	0	0
Leukemia, myeloid	0	0	0	0	1	0

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

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

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

Table: 12

Project Number: 0281CR0012 Species: Rat

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

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

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

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Table: 12

Project Number: 0281CR0012 Species: Rat

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

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

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, minimal
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, missing
Small Intestine	-Within normal limits Fewer than protocol number
Thyroid	-Not examined, missing

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, bilateral, moderate
Kidney	-Chronic progressive nephropathy, minimal

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

Microscopic Observations (continued):

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

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

Animal Number: 1R-3522 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:

Liver	-Light (pale) tan in color.

Microscopic Observations:

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

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,

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

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

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

Macroscopic Observations:

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

Microscopic Observations:

Lung	-Alveolar macrophages, multifocal, mild
	-Atellectasis, focal, mild
Mesentary	-Necrosis, fat, marked
	Steatitis, chronic, moderate
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, focal, minimal
Lung	-Vascular mineralization, minimal

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Nodular hyperplasia, cortex, unilateral, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, multifocal, mild
Lung	-Perivascular mononuclear infiltrate, mild
Stomach	-Not examined, missing

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

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

Macroscopic Observations:	
Kidney	-Bilateral hydronephrosis
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, focal, mild
Kidney	-Hydronephrosis, bilateral, moderate Calculus, pelvic
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, focal, moderate Pancreatitis, chronic, focal, mild

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

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

Macroscopic Observations:	
Liver	-Pale tan
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Pneumonia, interstitial, chronic, focal, mild Hemorrhage, multifocal, mild Hyperplasia, septal cell, focal, mild

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Pyelitis, acute, bilateral, minimal Nephritis, interstitial, chronic, focal, unilateral, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Hemorrhage, multifocal, mild

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Pancreas	-Pancreatitis, chronic, focal, mild Acinar atrophy, focal, mild
Parathyroid	-Not examined, not in plane of section

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

Microscopic Observations (continued):

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

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

Macroscopic Observations:
-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, focal, minimal
	Hemorrhage, multifocal, mild
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:

Soft Tissues (leg)	-Swollen left hind foot at the hock joint.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Lung	-Vascular mineralization, minimal
	Alveolar macrophages, multifocal, mild
	Hemorrhage, focal, mild
Pituitary	-Cyst, pars distalis

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

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

Macroscopic Observations:	
Kidney	-Dark cystic lesion, 0.4 cm dia., left.
Microscopic Observations:	
Bone Marrow	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Cyst, cortical, unilateral
Lung	-Alveolar macrophages, multifocal, mild Pneumonia, interstitial, chronic, multifocal, mild
Pancreas	-Pancreatitis, chronic, focal, mild
Parathyroid	-Not examined, not in plane of section
Spinal Cord	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spleen, Liver, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Pelvic mineralization, minimal
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:	
Mesentary	-Yellow nodular mass, 1 x 0.5 cm.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Calculus, pelvic, unilateral

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

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

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

Macroscopic Observations:	
Skin	-Hair loss, neck.
Adrenal	-Left enlarged
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, unilateral, marked Cortical degeneration, unilateral, mild
Kidney	-Hyperplasia, pelvic epithelium, mild Calculus, pelvic, unilateral Cyst, medullary, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, diffuse, moderate
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild

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

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

Macroscopic Observations:	
Pituitary	-Slightly enlarged
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Lung	-Hemorrhage, local areas, moderate

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

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

Macroscopic Observations:	
Kidney	-Hydronephrosis, unilateral
Microscopic Observations:	
Kidney	-Hydronephrosis, unilateral, moderate Calculus, unilateral, mild
Liver	-Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, multifocal, mild

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

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

Macroscopic Observations:	
Uterus	-Left horn cystic looking lesion, 1 x 0.6 cm.
Microscopic Observations:	
Liver	-Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Not examined, missing
Uterus	-Cystic glands, focal, marked

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

Animal Number: 1R-4610 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:	
Pituitary	-Slightly enlarged
Uterus	-Slightly enlarged
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Large Intestine	-Nematodiasis
Lung	-Alveolar macrophages, multifocal, mild
Pancreas	-Pancreatitis, chronic, focal, mild
Parathyroid	-Not examined, not in plane of section
Uterus	-Hyperplasia, glandular epithelium, mild Metaplasia, squamous, glandular, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, 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 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:	
Eye	-Atrophy, right eye.
Microscopic Observations:	
Eye	-Panophthalmitis, unilateral, marked Atrophy, unilateral, marked
Kidney	-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 0 ppm
Fate: (Week= 53) 1 Year Interim Sacrifice

Macroscopic Observations:	
Skin	-Hair loss, head, neck, face.
Microscopic Observations:	
Adrenal	-Cortical degeneration, focal, unilateral, mild

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

Liver	-Possibly slightly pale in color.

Microscopic Observations:

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

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Small Intestine,

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

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

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

Macroscopic Observations:

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

Microscopic Observations:

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

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

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

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

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

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Megalocytosis, mild
	Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild
Spleen	-Hemosiderosis, mild

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Aorta	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild
	Megalocytosis, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, missing
Thyroid	-Not examined, missing

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

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

Macroscopic Observations:	
Pituitary	-Small dark red mass, 0.3 cm dia.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, minimal
	Hepatocyte vacuolation, multifocal, mild
	Pigment, Kupfer cell, multifocal, brown, mild
Lung	-Vascular mineralization, mild
	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 Interim Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, minimal

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

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

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

Macroscopic Observations:	
Liver	-Pale tan color.
Kidney	-Small depressed area, 0.2 cm dia., right kidney.
Microscopic Observations:	
Eye	-Retinal atrophy, focal, minimal
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

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

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

Macroscopic Observations:	
Skin	-Ulcerated nodule in the dorsal area, 1.5 cm dia.
Microscopic Observations:	
Kidney	-Mineralization, multifocal, cortical Pyelitis, acute, unilateral, mild
Liver	-Megalocytosis, minimal
Lung	-Alveolar macrophages, multifocal, mild
Lymph Node (mesenteric)	-Hemorrhage, minimal
Skin	-Keratoacanthoma

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Aorta	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, minimal Megalocytosis, minimal
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:	
Eye	-Ocular opacity, bilateral.
Testis	-Left testis small.
Microscopic Observations:	
Eye	-Cataract, bilateral
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, minimal Megalocytosis, minimal Pigment, Kupfer cell, brown, minimal
Lung	-Vascular mineralization, minimal Pneumonia, interstitial, chronic, multifocal, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Parathyroid	-Not examined, not in plane of section
Prostate	-Not examined, missing
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Alveolar macrophages, multifocal, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Prostate	-Prostatitis, chronic, focal, intersititial, minimal

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

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

Macroscopic Observations:	
Liver	-Slightly pale tan in color.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, minimal Necrosis, multifocal, mild
Lung	-Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Not examined, missing

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

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

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

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

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

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

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Species: Rat
Project Number: 02B1CR0012

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

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:

Eye	-Atrophy, right eye.
Uterus	-Both horns enlarged, filled with clear fluid.

Microscopic Observations:

Eye	-Panophthalmitis, unilateral, marked Atrophy, unilateral, marked
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis
Liver	-Hepatocyte vacuolation, multifocal, mild
Parathyroid	-Not examined, not in plane of section
Uterus	-Hydrometra, moderate Endometritis, chronic, mild

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Parathyroid	-Not examined, not in plane of section

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

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

Macroscopic Observations:
-No visible lesions.

Microscopic Observations:

Aorta	-Not examined, missing
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, local areas, mild
Pituitary	-Not examined, missing

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

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

Macroscopic Observations:
-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild Mineralization, multifocal, cortical, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Not examined, missing

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

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

Macroscopic Observations:

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

Microscopic Observations:

Liver	-Hepatocyte vacuolation, multifocal, mild
Mammary Gland	-Fibroadenoma

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Adrenal, Thyroid,

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

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Not examined, missing

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

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

Macroscopic Observations:	
Mammary Gland	-Subcutaneous mass, 5 cm dia., behind left shoulder.
Microscopic Observations:	
Kidney	-Pelvic mineralization, mild
	Calculus, pelvic, mild

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

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

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

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

Macroscopic Observations:

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

Microscopic Observations:

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

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

Microscopic Observations (continued):

Lung	-Alveolar macrophages, multifocal, mild
Mammary Gland	-Galactocele
	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 bladder.
Kidney	-Bilateral marked hydronephrosis with numerous calculi in the pelvic area.

Microscopic Observations:

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

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

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

Macroscopic Observations:	
Eye	-Right eye atrophied.
Liver	-Pale tan in color.
Lymph Node (mesenteric)	-Hemorrhagic
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Eye	-Atrophy, unilateral, marked
	Panophthalmitis, chronic, unilateral, marked
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, local areas, mild
Lymph Node (mesenteric)	-Hemorrhage, marked
Parathyroid	-Not examined, not in plane of section
Thyroid	-No diagnosis, inadequate section

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Esophagus, Pancreas, Salivary Gland.

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Lung	-Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Not examined, missing

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Large Intestine	-Nematodiasis
Liver	-Hepatocyte vacuolation, multifocal, mild

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

Microscopic Observations (continued):

Lung	-Hemorrhage, local areas, moderate

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

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

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

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

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

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

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

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

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, multifocal, mild Cortical vacuolation, multifocal, mild
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, multifocal, mild

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

Skin	-Both hind footpads ulcerated.
Liver	-Pale
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, mild Medullary cell hyperplasia, multifocal, mild
Heart	-Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Hepatocyte vacuolation, centrilobular, moderate
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, local areas, mild Edema, local areas, mild Fibrosis, pleural, mild Thrombus
Parathyroid	-Not examined, missing
Skin	-Pododermatitis, ulcerative, hindleg, marked
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Stomach	-Edema, submucosal, marked

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

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

Macroscopic Observations:	
Soft Tissues (thorax)	-Mass, 10 x 9 x 4 cm in left axilla involving muscle and rib, extending into left thoracic cavity, collapsing left lung. Mass soft and fatty.
Stomach	-Wall edematous with possible ulceration in cardia.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Sinusoidal ectasia, cortex, diffuse, mild
Heart	-Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild Hemorrhage, focal, mild Alveolar macrophages, mild
Prostate	-Prostatitis, acute, suppurative, marked
Skin	-Fibrosarcoma, thorax Well differentiated, highly cellular with moderate collagen formation.
Stomach	-Ulcer, marked

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

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

Macroscopic Observations:	
Pituitary	-Small red lesion.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, mild
Large Intestine	-Nematodiasis, colon
Liver	-Hepatocyte alteration, vacuolated, moderate Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild

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

Microscopic Observations (continued):

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

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

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

Macroscopic Observations:

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

Microscopic Observations:

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

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder,

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Table: 2

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

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Aorta, Prostate, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

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

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Cystoid degeneration, focal, mild
	Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild

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

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

Macroscopic Observations:	
Kidney	-Hydronephrosis
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild
Kidney	-Chronic progressive nephropathy, moderate
	Hydronephrosis, unilateral, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
Pituitary	-Hyperplasia, focal, pars distalis, mild

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

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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 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Skin	-Areas of dermatitis with hair loss, some scabbed; back, side, abdomen.
Liver	-Raised pale mass, 1.2 cm dia. in left lateral lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocellular carcinoma Trabecular pattern, fairly well differentiated.
Lung	-Vascular mineralization, mild Edema, subpleural, moderate
Parathyroid	-Not examined, not in plane of section
Prostate	-Not examined, missing
Salivary Gland	-Not examined, missing
Skin	-Ulcer, back, abdomen, marked
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

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

Animal Number: 1R-3530 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, moderate Hepatocyte alteration, vacuolated, mild

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Animal Number: 1R-3530 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Lung	-Vascular mineralization, mild
	Peribronchial lymphoid hyperplasia, mild
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3531 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
	Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, local areas, moderate

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

Animal Number: 1R-3532 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised red mass, 0.4 cm dia.
Kidney	-Fluid filled cyst, 1 cm dia., in right kidney
Microscopic Observations:	
Eye	-Retinal atrophy, focal, mild
Heart	-Myocardial fibrosis, focal, mild
Kidney	-Chronic progressive nephropathy, moderate
	Cyst, cortical, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Hemorrhage, local areas, mild
	Perivascular mononuclear infiltrate, mild

Animal Number: 1R-3532 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lymph Node (mesenteric)	-Hemorrhage, mild
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3533 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Spleen	-Pale circular depressed area, 0.4 cm dia.

Microscopic Observations:

Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Perivascular mononuclear infiltrate, mild
Prostate	-Prostatitis, acute, suppurative, mild
Spleen	-Hemosiderosis, mild Fibrosis, local areas, moderate

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

Animal Number: 1R-3534 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations:

Thymus	-Enlarged
Pancreas	-Massive beige colored mass, 7.5 x 3 cm in area of pancreas completely surrounding spleen and adhering to posterior areas of right and left lateral

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Animal Number: 1R-3534 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Sacrificed in extremis

Macroscopic Observations (continued):

Pancreas (continued)	-liver lobes.
Kidney	-Pale and pitted.
Testis/Epididymis	-Right testis small.
Liver	-Pale with yellowish circular lesion 0.3 cm diameter in right anterior lobe

Microscopic Observations:

Adrenal	-Cortical vacuolation, diffuse, moderate Medullary cell hyperplasia, local areas, moderate
Kidney	-Chronic progressive nephropathy, moderate Malignant lymphoma, histiocytic
Liver	-Hepatocyte vacuolation, diffuse, marked
Lung	-Hemorrhage, diffuse, marked Malignant lymphoma, histiocytic
Lymph Node (mesenteric)	-Hemorrhage, mild Malignant lymphoma, histiocytic
Pancreas	-Malignant lymphoma, histiocytic
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Small Intestine	-Malignant lymphoma, histiocytic
Spleen	-Malignant lymphoma, histiocytic
Stomach	-Malignant lymphoma, histiocytic
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
Thymus	-Malignant lymphoma, histiocytic Multiple sections of tumor from thymic and mediastinal areas.
Thyroid	-Not examined, missing
Urinary Bladder	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Trachea, Esophagus, Salivary Gland, Eye, Large Intestine, Aorta, Prostate.

Animal Number: 1R-3536 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Raised lesion, 1.5 cm dia., appears to be abscess.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, focal, moderate
Kidney	-Chronic progressive nephropathy, minimal
Large Intestine	-Nematodiasis, colon
Liver	-Portal bile duct proliferation, multifocal, mild Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, minimal
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Skin	-Keratoacanthoma Raised lesion from back.

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

Animal Number: 1R-3537 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Found Dead

Macroscopic Observations:	
Liver	-Very pale
Lymph Node (abdominal)	-Renal lymph nodes enlarged.
Abdomen (internal)	-Multilobular, fleshy mass, 4 x 3.5 x 3.5 attached to omentum, left inguinal area.
Pituitary	-Hemorrhagic mass, 0.7 cm dia.
Microscopic Observations:	
Eye	-Not examined, missing
Heart	-Malignant lymphoma, histiocytic
Liver	-Hepatocyte vacuolation, diffuse, marked Malignant lymphoma, histiocytic
Lung	-Malignant lymphoma, histiocytic Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Not examined, missing
Parathyroid	-Not examined, missing

Animal Number: 1R-3537 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Found Dead

Microscopic Observations (continued):

Pituitary	-Adenoma
Skin	-Malignant lymphoma, histiocytic Mass from inguinal area was malignant lymphoma. There was extensive necrosis in tumor.
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing

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

Animal Number: 1R-3538 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Small hemorrhagic area, 0.2 cm dia.
Liver	-Multiple pale foci, all lobes.
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Malignant lymphoma, histiocytic
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Malignant lymphoma, histiocytic Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Hemorrhage, minimal
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, marked
Spleen	-Malignant lymphoma, histiocytic
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

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

Animal Number: 1R-3539 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Spleen	-Hemosiderosis, mild
Thyroid	-Ultimobranchial cyst

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

Animal Number: 1R-3540 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Bone Marrow	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Prostate	-Not examined, missing
Spinal Cord	-Not examined, missing
Thyroid	-Ultimobranchial cyst
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spleen, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3541 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Raised lesion on left rear footpad.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Hemorrhage, diffuse, marked Perivascular mononuclear infiltrate, mild
Prostate	-Not examined, missing
Skin	-Pododermatitis, ulcerative, hindleg, marked
Testis/Epididymis	-Not examined, missing
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, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3542 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Testis/Epididymis	-Both testes small.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, minimal
Lymph Node (mesenteric)	-Hemorrhage, minimal
Pancreas	-Hyperplasia, islet cell, moderate
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, marked Polyarteritis, mild
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, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Salivary Gland, Eye, Esophagus.

Animal Number: 1R-3544 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic lesion, 0.7 cm dia.
Kidney	-Both enlarged, pale and pitted.
Testis/Epididymis	-Left testis small.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, moderate
	Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, marked
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Pancreas	-Acinar atrophy, mild
	Polyarteritis, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
	Polyarteritis, marked

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

Animal Number: 1R-3545 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 104) Found Dead

Macroscopic Observations:	
Skin	-Circular lesions, 2.5 cm dia. on both hind footpads.
Liver	-Slightly pale
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
	Cortical vacuolation, multifocal, moderate
Eye	-Not examined, missing
Heart	-Myocardial fibrosis, local areas, mild
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Pancreas	-Acinar atrophy, moderate
Pituitary	-Adenoma

Animal Number: 1R-3545 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 104) Found Dead

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Microscopic Observations (continued):

Skin	-Pododermatitis, ulcerative, hindleg, bilateral, marked
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Liver, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland.

Animal Number: 1R-3547 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Mass, 0.4 cm dia.
Liver	-Pale

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Brain	-Oligodendroglioma, benign Large neoplasm composed of large, fairly uniform polyhedral cells in cerebral cortex.
Kidney	-Chronic progressive nephropathy, minimal Pyelonephritis, acute, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild
Pituitary	-Adenoma
Stomach	-Edema, submucosal, moderate

The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Spleen, Heart, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3548 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild

Animal Number: 1R-3548 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, mild Hepatocyte vacuolation limited to one area of liver.
Lung	-Vascular mineralization, mild Alveolar macrophages, minimal Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Thyroid	-C cell carcinoma

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

Animal Number: 1R-3549 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 86) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1.4 x 0.8 cm.
Liver	-Slightly pale

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, minimal
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Kidney, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3552 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Spleen	-Circular raised lesion, 1.2 cm dia.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, local areas, moderate
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, mild
Spleen	-Hemangiosarcoma

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

Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Macroscopic Observations:	
Adrenal	-Left enlarged by a 1 cm dia. mass.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild Pheochromocytoma, benign, unilateral
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, moderate Hepatocyte vacuolation, multifocal, mild Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing

Animal Number: 1R-3553 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Microscopic Observations (continued):

Pancreas	-Not examined, missing
Pituitary	-Cyst, pars distalis
Salivary Gland	-Not examined, missing
Small Intestine	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3554 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Alveolar macrophages, multifocal, moderate Perivascular mononuclear infiltrate, moderate Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, moderate
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, moderate

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

Animal Number: 1R-3555 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Sacrificed in extremis

Macroscopic Observations:

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

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate

Animal Number: 1R-3555 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Sacrificed in extremis

Microscopic Observations (continued):

Aorta	-Mineralization, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Nephrosis, tubular, moderate Papillary necrosis, moderate Hydronephrosis, mild Tubules dilated with low, basophilic epithelium, scattered mineralized tubules.
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, focal, mild
Parathyroid	-Not examined, not in plane of section
Prostate	-Prostatitis, acute, suppurative, mild Edema, intersititial, moderate
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hemosiderosis, mild
Stomach	-Edema, submucosal, moderate
Urinary Bladder	-Hemorrhage, marked Epithelial hyperplasia, simple, diffuse, mild Cystitis, acute, moderate

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Large Intestine, Testis/Epididymis, Pituitary, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3556 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Adrenal	-Right enlarged by mass, 2 x 1 cm.

Microscopic Observations:

Adrenal	-Carcinoma, cortical, unilateral Large neoplasm, mostly necrotic. Cells foamy, polyhedral arranged in cords and sheets. High mitotic activity. Multiple lung metastases.
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild

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Animal Number: 1R-3556 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Lung	-Pneumonia, interstitial, chronic, multifocal, mild
	Metastatic neoplasm
	Perivascular mononuclear infiltrate, mild
	Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-3557 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
Thyroid	-Hyperplasia, C cell, mild

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

Animal Number: 1R-3558 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.9 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild
	Calculus, pelvic, minimal
Liver	-Cystoid degeneration, focal, minimal

Animal Number: 1R-3558 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3560 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 35) Sacrificed in extremis

Macroscopic Observations:

Brain	-Focal circumscribed dark area, dorsal surface, left cerebral hemisphere (0.2 cm dia.) and lateral surface of right cerebral hemisphere (0.2 cm dia.)
Lung	-Dark red diffuse mottling, all lobes; red frothy exudate at trachea.
Spleen	-Enlarged
Lymph Node (abdominal)	-Hepatic and renal nodes enlarged.
Liver	-Pale, appears enlarged.

Microscopic Observations:

Brain	-Abscess, mild Hemorrhage, multifocal, moderate
Liver	-Malignant lymphoma, histiocytic
Lung	-Malignant lymphoma, histiocytic Hemorrhage, diffuse, marked Necrosis, local areas, marked
Lymph Node (mesenteric)	-Hemorrhage, minimal
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hematopoiesis, extramedullary, increased, marked

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

Animal Number: 1R-3561 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Soft Tissues (leg)	-Right and left hindpaw and right forepaw swollen.
Kidney	-Right kidney polycystic.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, mild
Bone	-Arthritis, synovitis; joints, hindleg, foreleg, marked
Bone Marrow	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Cyst, cortical, unilateral, marked
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Perivascular mononuclear infiltrate, mild Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Hemorrhage, local areas, moderate
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, spermatogenesis, moderate Polyarteritis, marked
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Heart, Stomach, Small Intestine, Urinary Bladder, Aorta, Prostate, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3562 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Raised ulcerated inflamed lesion, right rear footpad.
Spleen	-Several pale foci.
Microscopic Observations:	
Adrenal	-Nodular hyperplasia, cortex, unilateral, moderate

Species: Rat
Project Number: 028ICR0012

Table: 2

Animal Number: 1R-3562 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, mild Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Skin	-Pododermatitis, ulcerative, hindleg, marked

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3563 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Thyroid	-One side enlarged, 1 x 0.8 cm.
Skin	-Mass, 1.7 x 1.4 cm, dorsal area.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Sinusoidal ectasia, cortex, minimal
Brain	-Astrocytoma, benign Poorly defined lesion in basal area of cerebrum. Tumor cells spindelate.
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, moderate

Animal Number: 1R-3563 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Skin	-Keratoacanthoma, back
Thyroid	-C cell carcinoma

The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3564 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Pale area in cortex of one kidney.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, moderate
Bone Marrow	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Cyst, unilateral, moderate Area of multilocular cysts in cortex with lipid change in surrounding parenchyma.
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spinal Cord	-Not examined, missing
Testis/Epididymis	-Mineralization, focal, mild

The following tissues were found to be within normal limits:
Brain, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Table: 2

Animal Number: 1R-3565 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 84) Found Dead

Macroscopic Observations:	
Skin	-Large mass, 7 x 7 cm, scrotal area.
Liver	-Pale
Microscopic Observations:	
Adrenal	-Not examined, missing
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Eye	-No diagnosis, inadequate section
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-No diagnosis, inadequate section
Liver	-Hepatocyte vacuolation, multifocal, mild Necrosis, multifocal, moderate
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Not examined, missing
Parathyroid	-Not examined, missing
Pituitary	-Not examined, missing
Prostate	-Not examined, missing
Salivary Gland	-Not examined, missing
Skin	-Liposarcoma The scrotal mass was composed of large, vacuolated mononuclear cells. The degree of autolysis made diagnosis somewhat uncertain.
Small Intestine	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, mild
Thyroid	-Not examined, missing
Trachea	-Not examined, missing
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Testis/Epididymis.

Animal Number: 1R-3566 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Small dark lesion.
Microscopic Observations:	
Adrenal	-Within normal limits One of pair present
Kidney	-Chronic progressive nephropathy, mild

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Animal Number: 1R-3566 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Pancreas	-Polyarteritis, moderate
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3567 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin	-Raised papilloma type mass on back; raised inflamed lesion, right rear footpad.
Spleen	-Two pale foci.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
	Nodular hyperplasia, cortex, focal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, minimal
	Perivascular mononuclear infiltrate, minimal
Skin	-Papilloma, back
	Pododermatitis, ulcerative, hindleg, marked
Spleen	-Necrosis, local areas, moderate

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

Animal Number: 1R-3569 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Kidney	-Bilaterally enlarged; pale, pitted.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, minimal
	Sinusoidal ectasia, cortex, mild
	Medullary cell hyperplasia, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Pituitary	-Hyperplasia, focal, pars distalis, mild
Testis/Epididymis	-Polyarteritis, moderate

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

Animal Number: 1R-3571 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Pale
Kidney	-Pale, pitted, enlarged.
Mesentery	-Mesenteric vessels thickened
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, minimal
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, minimal
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, minimal
Mesentery	-Polyarteritis, marked
Pancreas	-Polyarteritis, marked
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

Animal Number: 1R-3571 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Small Intestine	-Polyarteritis, mesentery, marked
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Polyarteritis, marked

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

Animal Number: 1R-3572 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Pancreas	-Hyperplasia, islet cell, moderate
Parathyroid	-Not examined, not in plane of section
Stomach	-Not examined, missing

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

Animal Number: 1R-3573 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pancreas	-Small circular pale mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Portal mononuclear cell infiltrate, mild

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Table: 2

Animal Number: 1R-3573 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Pancreas	-Acinar atrophy, moderate
	Islet cell adenoma
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Skin	-Ulcerated right and left hind footpads;
	circular white subcutaneous mass,
	1.5 cm dia., in right inguinal area.
Thorax (internal)	-Filled with fluid.
Heart	-Slightly pale and flaccid.
Liver	-Slightly pale
Kidney	-Pale and pitted; 1.5 cm cyst in right kidney.
Testis/Epididymis	-Testes small

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, mild
Aorta	-Necrosis, local areas, moderate
	Uniform intimal necrosis with reactive
	cellular infiltrate.
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
	Cyst, unilateral, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Pneumonia, interstitial, chronic, diffuse,
	moderate
	Perivascular mononuclear infiltrate, mild
	Edema, local areas, marked
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-3574 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Microscopic Observations (continued):

Pituitary	-Cyst, pars intermedia
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Not examined, missing
Skin	-Fibroma, subcutaneous, inguinal
	Pododermatitis, ulcerative, hindleg, marked
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, moderate

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

Animal Number: 1R-3576 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 55) Sacrificed in extremis

Macroscopic Observations:

Skin	-Moist area around genital papilla.
Abdomen (internal)	-Large amount of gas in gastrointestinal tract; no food in stomach.

Microscopic Observations:

Kidney	-Pelvic mineralization, mild
Lung	-Hemorrhage, diffuse, marked
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Not examined, missing

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

Animal Number: 1R-3577 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

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

Animal Number: 1R-3577 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
Mesentery	-Polyarteritis, marked
Pancreas	-Polyarteritis, marked
Small Intestine	-Polyarteritis, mesentery, moderate
Spleen	-Hemosiderosis, mild
Thyroid	-Cyst, colloid, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-3578 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.7 cm dia.
Skin	-Raised ulcerated inflamed lesion, 1.5 cm dia., left hind footpad.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild Hydronephrosis, unilateral, moderate Calculi present in ureter of hydronephrotic kidney.
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Sialadenitis, chronic, minimal Very minimal lesion, only one duct affected.
Skin	-Pododermatitis, ulcerative, hindleg, marked

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

Animal Number: 1R-3579 Sex: Male Group: (1) CONTROL 0 ppm
Fate: (Week= 86) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 0.8 cm dia.
Liver	-Raised pale 2 cm dia. mass in right lateral lobe.
Skin	-Mass seen clinically on right side appears to be healed lesion.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal bile duct proliferation, mild Hepatocellular carcinoma Portal mononuclear cell infiltrate, mild
Lung	-Perivascular mononuclear infiltrate, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Keratoacanthoma Skin lesion from right side.
Small Intestine	-Within normal limits Fewer than protocol number
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, mild Polyarteritis, mild

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

Animal Number: 1R-4576 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 25) Sacrificed in extremis

Macroscopic Observations:	
Liver	-Enlarged; mottled yellow color.
Lymph Node (bronchial)	-Enlarged
Lung	-Pale
Spleen	-Enlarged
Stomach	-Red patchy areas on mucosa.
Lymph Node (mesenteric)	-Enlarged and reddened.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Bone Marrow	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic Mineralization, cortical, mild

Animal Number: 1R-4576 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 25) Sacrificed in extremis

Microscopic Observations (continued):

Liver	-Malignant lymphoma, lymphocytic
Lung	-Malignant lymphoma, lymphocytic
	Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Malignant lymphoma, lymphocytic
Pancreas	-Malignant lymphoma, lymphocytic
Salivary Gland	-Not examined, missing
Spinal Cord	-Malignant lymphoma, lymphocytic
Spleen	-Malignant lymphoma, lymphocytic
Stomach	-Ulcer
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:
Brain, Heart, Small Intestine, Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Thyroid, Parathyroid, Esophagus, Eye.

Animal Number: 1R-4577 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.8 cm dia.
Mammary Gland	-Multilobular mass, 4.5 x 3.5 x 2 cm, in right axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pelvic mineralization, mild
	Nephrosis, tubular, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Lobular hyperplasia
Pituitary	-Hemorrhage, marked
	Necrosis, moderate
Spleen	-Hemosiderosis, mild
Uterus	-Cystic glands, moderate

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

Animal Number: 1R-4579 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 84) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 0.5 cm dia.
Skin	-Raised thickened lesion with scab on right side.
Liver	-Slightly pale
Stomach	-Somewhat reddened
Kidney	-Fluid filled cyst in left kidney.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Aorta	-Mineralization, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, moderate
Kidney	-Nephrosis, tubular Pelvic mineralization, marked Cyst, cortical, moderate Hyperplasia, pelvic epithelium, diffuse, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Ulcer, marked Skin lesion from side.
Spleen	-Hemosiderosis, mild
Stomach	-Mineralization, mucosal, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Small Intestine, Large Intestine, Urinary Bladder, Uterus, Ovary, Mammary Gland, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4580 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 52) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Enlarged; dark red mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-4580 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 52) Sacrificed in extremis

Microscopic Observations (continued):

Pituitary	-Adenoma
Spleen	-Hemosiderosis, moderate

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Liver, Kidney, Heart, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Uterus, Ovary, Trachea, Thyroid, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4581 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland	-Ulcerated mass, 6 x 6 x 3 cm behind right shoulder.
Liver	-Possibly slightly pale and swollen.
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, basophilic, mild Hematopoiesis, extramedullary, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Adenocarcinoma
Parathyroid	-Not examined, not in plane of section
Spleen	-Hematopoiesis, extramedullary, increased, marked

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

Animal Number: 1R-4583 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Extensive post bleeding inflammation of right eye.
Mammary Gland	-Firm nodular mass, 6 x 5 x 3 cm, left inguinal.

Animal Number: 1R-4583 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, marked
Eye	-Panophthalmitis, unilateral, marked
Kidney	-Pelvic mineralization, mild
	Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild
	Necrosis, focal, mild
Lung	-Alveolar macrophages, mild
	Perivascular mononuclear infiltrate, mild
Mammary Gland	-Fibroadenoma
Ovary	-Tubular adenoma, unilateral
Parathyroid	-Not examined, not in plane of section
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Uterus	-Cystic glands, marked

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

Animal Number: 1R-4584 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Slight atrophy with corneal opacity, right eye.
Pituitary	-Enlarged
Adrenal	-Left adrenal enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex
Eye	-Phthsis bulbi, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild
	Perivascular mononuclear infiltrate, mild
	Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-4584 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4586 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised dark mass, 0.3 cm dia.
Uterus	-Dark area, 0.5 x 0.5 cm, in left horn near cervix.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Perivascular mononuclear infiltrate, minimal
Ovary	-Not examined, missing
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, marked

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

Animal Number: 1R-4587 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Small nodular mass, 3 x 2 cm, axillary; large mass, 8 x 8 x 3 cm, throat area.

Animal Number: 1R-4587 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, marked
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, minimal
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Skin	-Fibroma, subcutaneous
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

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

Animal Number: 1R-4591 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Pancreas	-Acinar atrophy, focal, minimal
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Table: 2

Animal Number: 1R-4592 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 88) Found Dead

Macroscopic Observations:	
Pituitary	-Enlarged, 0.9 x 1 cm.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Lobular hyperplasia, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4593 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Liver	-Hepatocyte alteration, vacuolated, mild
	Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-4594 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 79) Found Dead

Macroscopic Observations:	
Kidney	-Right kidney appears slightly enlarged; filled with yellow milky fluid.
Urinary Bladder	-Enlarged, 4.5 x 2 cm; filled with large, hard calculi.
Pituitary	-Hemorrhagic mass, 0.9 x 0.6 cm
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate One of pair present
Aorta	-Not examined, missing
Kidney	-Pyelonephritis, acute, bilateral, moderate Hydronephrosis, bilateral, moderate Nephrosis, tubular, bilateral, moderate
Liver	-Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Ovary	-Within normal limits One of pair present
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Small Intestine	-Not examined, missing
Spleen	-Hemosiderosis, moderate
Urinary Bladder	-Epithelial hyperplasia, papillary, diffuse, marked Calculus

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Large Intestine, Uterus, Mammary Gland, Trachea, Thyroid, Esophagus, Salivary Gland, Eye.

Animal Number: 1R-4595 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.8 cm dia.
Mammary Gland	-Small lobular mass, 2.7 x 1.5 x 1.8 cm, left axilla.
Pancreas	-Small lobular mass, 1 x 0.7 cm, in area of pancreas.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate

Animal Number: 1R-4595 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

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Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild
Lung	-Alveolar macrophages, mild
Mammary Gland	-Lobular hyperplasia
Pancreas	-Islet cell carcinoma Partially encapsulated with invasion of capsule. Well differentiated.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Adenoma Small circumscribed papillary lesion.

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

Animal Number: 1R-4596 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 78) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Mass, 0.8 x 0.6 cm.
Mammary Gland	-Mass, 2.5 x 2 x 1.5 cm, in left axilla.
Liver	-Very pale
Kidney	-Bilaterally pale and pitted; slightly enlarged; 0.4 cm dia. cyst in right.
Adrenal	-Pale, bilaterally

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, moderate Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild Cortical degeneration, local areas, moderate
Aorta	-Mineralization, mild Mineralization also in media of an elastic artery in section of mesentery submitted for mesenteric lymph node.
Kidney	-Chronic progressive nephropathy, marked Cyst, cortical, moderate
Liver	-Hepatocyte vacuolation, diffuse, marked

Animal Number: 1R-4596 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 78) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Alveolar macrophages, minimal
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, moderate
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Uterus, Ovary, Trachea, Thyroid, Esophagus, Pancreas, Eye.

Animal Number: 1R-4597 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Adrenal	-Right adrenal enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
	Medullary cell hyperplasia, focal, mild
Kidney	-Chronic progressive nephropathy, minimal
	Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Alveolar macrophages, mild
	Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-No diagnosis, inadequate section
Ovary	-Tubular adenoma, unilateral
Pancreas	-Cyst
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits
	Fewer than protocol number

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

Animal Number: 1R-4598 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 0.7 cm dia.
Adrenal	-Left adrenal greatly enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Brain	-Oligodendroglioma, benign
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Ovary	-Tubular adenoma
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4599 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Found Dead

Macroscopic Observations:	
Mammary Gland	-Subcutaneous mass, 2.5 x 2 x 1 cm, in perineal area.
Liver	-Appears mottled
Stomach	-Areas of enlongated ulceration.
Urinary Bladder	-Thickened walls; mass 1.5 x 1 cm, with adhesions to abdominal wall.
Eye	-No tissue taken due to postmortem changes
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Malignant lymphoma, histiocytic
Esophagus	-Malignant lymphoma, histiocytic
Eye	-Not examined, missing

Animal Number: 1R-4599 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 102) Found Dead

Microscopic Observations (continued):

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Malignant lymphoma, histiocytic Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild Nephrosis, tubular, mild
Large Intestine	-Malignant lymphoma, histiocytic
Liver	-Malignant lymphoma, histiocytic Necrosis, local areas, marked
Lung	-Malignant lymphoma, histiocytic Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Malignant lymphoma, histiocytic
Mammary Gland	-Malignant lymphoma, histiocytic
Ovary	-Malignant lymphoma, histiocytic
Pancreas	-Malignant lymphoma, histiocytic
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Stomach	-Necrosis, mucosal, moderate
Thyroid	-Malignant lymphoma, histiocytic
Urinary Bladder	-Malignant lymphoma, histiocytic Epithelial hyperplasia, simple, diffuse, mild
Uterus	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Small Intestine, Trachea, Salivary Gland.

Animal Number: 1R-4600 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Mammary Gland	-Subcutaneous cystic mass, 4 x 3.5 x 2 cm, in region of throat; subcutaneous multilobular mass, 5 x 4 x 2 cm, in right axilla.
Liver	-Appears mottled

Microscopic Observations:

Adrenal	-Necrosis, unilateral, marked
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild

Animal Number: 1R-4600 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Found Dead

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
	Pelvic mineralization, mild
	Nephrosis, tubular, moderate
Liver	-Portal mononuclear cell infiltrate, moderate
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
	Hepatocyte alteration, eosinophilic, moderate
	Telangiectasis, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Adenoma, papillary
	Lobular hyperplasia
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4602 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Eye	-Cornea appears cloudy.
Pituitary	-Raised mass, 1 cm dia.
Adrenal	-Right adrenal enlarged.
Kidney	-Pale and pitted.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
	Cortical degeneration, diffuse, marked
Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
	Pelvic mineralization, mild
	Cyst, cortical
Liver	-Hepatocyte alteration, basophilic, mild
Lung	-Hemorrhage, local areas, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Animal Number: 1R-4602 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits
	Fewer than protocol number

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

Animal Number: 1R-4603 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Liver	-Circular raised lesion, 0.6 cm dia., left lateral lobe.
Skin	-Hair loss on forelimbs.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
	Cortical degeneration, diffuse, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte alteration, vacuolated, mild
Lung	-Perivascular mononuclear infiltrate, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Acanthosis, mild
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4604 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Adrenal	-Left adrenal enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Large Intestine	-Not examined, missing
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hyperplastic nodule
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Uterus	-Within normal limits Fewer than protocol number

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

Animal Number: 1R-4605 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 77) Sacrificed in extremis

Macroscopic Observations:	
Kidney	-Slightly pitted
Lung	-Right apical lobe consolidated and somewhat enlarged; possibly tumor, mass, chronic pneumonia.
Microscopic Observations:	
Adrenal	-Necrosis, local areas, moderate Hematopoiesis, extramedullary, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, moderate Malignant lymphoma, lymphocytic
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, midzonal, moderate Malignant lymphoma, lymphocytic
Lung	-Vascular mineralization, mild Malignant lymphoma, lymphocytic Large circumscribed mass with extensive necrosis.

Animal Number: 1R-4605 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 77) Sacrificed in extremis

Microscopic Observations (continued):

Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-Malacia, local areas, moderate
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, moderate

The following tissues were found to be within normal limits:
Brain, Bone Marrow, Stomach, Small Intestine, Large Intestine, Aorta, Uterus, Mammary Gland, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4606 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Small mass, 1.4 cm dia., left lateral area.
Pituitary	-Enlarged; circular dark lesion, 0.4 cm dia.
Uterus	-Dark fluid filled lesion, 0.5 x 0.6 cm, right horn.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Cortical degeneration, bilateral, moderate Pheochromocytoma, benign, unilateral
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Pigment, moderate Scattered small foci of dark brown pigment-laden macrophages within alveoli.
Lymph Node (mesenteric)	-Hemorrhage, mild
Mammary Gland	-Adenocarcinoma
Ovary	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Hydrometra, marked

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine,

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Animal Number: 1R-4606 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Urinary Bladder, Aorta, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4607 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 40) Sacrificed in extremis

Macroscopic Observations:

Soft Tissues (neck)	-Reddened gland like structures, possibly enlarged lymph nodes or salivary glands.
Lymph Node	-Enlarged axillary, hepatic, mesenteric and internal iliac lymph nodes.
Liver	-Possibly slightly pale.
Spleen	-Considerably enlarged.

Microscopic Observations:

Adrenal	-Malignant lymphoma, lymphocytic
Aorta	-Malignant lymphoma, lymphocytic
Bone Marrow	-Malignant lymphoma, lymphocytic
Esophagus	-No diagnosis, inadequate section
Eye	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic
Liver	-Malignant lymphoma, lymphocytic
Lung	-Malignant lymphoma, lymphocytic Hemorrhage, local areas, mild Abscess
Lymph Node (mesenteric)	-Hemorrhage, moderate Malignant lymphoma, lymphocytic Massive enlargment of node by mature appearing lymphocytes. All other nodes examined were similarily involved.
Mammary Gland	-Malignant lymphoma, lymphocytic
Ovary	-Malignant lymphoma, lymphocytic
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Spleen	-Malignant lymphoma, lymphocytic
Stomach	-Hemorrhage, submucosal, moderate Malignant lymphoma, lymphocytic
Thyroid	-Malignant lymphoma, lymphocytic
Uterus	-Malignant lymphoma, lymphocytic

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Heart, Small Intestine, Large Intestine, Urinary Bladder, Pituitary,

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Animal Number: 1R-4607 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 40) Sacrificed in extremis

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Trachea, Pancreas.

Animal Number: 1R-4609 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 1 cm dia.
Mammary Gland	-Mass, 5 x 4 cm, throat area; 3 cm dia., left axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, moderate
Large Intestine	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Carcinoma Highly cellular very undifferentiated tumor.
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-C cell adenoma
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4611 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

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

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, local areas, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, eosinophilic, mild
Lung	-Hemorrhage, multifocal, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 0.7 cm dia.
Mammary Gland	-Mass, 3 cm dia., left axilla; 4 cm dia., right axilla; 7 x 6 x 2 cm, right side.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Eye	-No diagnosis, inadequate section
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Hemorrhage, diffuse, marked Alveolar macrophages, mild
Mammary Gland	-Galactocele Fibroadenoma Fibroadenoma Two tumors present.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Kidney, Heart, Stomach, Small Intestine,

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Animal Number: 1R-4612 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4613 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 89) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Somewhat enlarged
Mammary Gland	-Mass, 10 x 8 x 5 cm, inguinal area; surface ulcerated.
Liver	-Appears pale

Microscopic Observations:

Adrenal	-Hematopoiesis, extramedullary, mild Sinusoidal ectasia, cortex, mild Cortical vacuolation, focal, mild
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, mild Hyperplasia, pelvic epithelium, local areas, mild
Large Intestine	-Not examined, missing
Liver	-Hepatocyte vacuolation, periportal, mild Necrosis, multifocal, mild Hematopoiesis, extramedullary, mild
Lung	-Hemorrhage, multifocal, mild Pneumonia, interstitial, chronic, multifocal, mild
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild
Uterus	-Within normal limits Fewer than protocol number

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Aorta, Ovary, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4614 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass in perineal area; possible milk cyst.
Uterus	-Large gelatinous cervical mass, 2 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pelvic mineralization, minimal Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Mammary Gland	-Adenocarcinoma
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-No diagnosis, inadequate section
Spleen	-Hemosiderosis, mild
Thyroid	-Ultimobranchial cyst
Uterus	-Polyp This was the mass at cervix noted at necropsy.

The following tissues were found to be within normal limits:
Brain, Bone Marrow, Heart, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4615 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, mild
Lung	-Pneumonia, interstitial, chronic, mild Alveolar macrophages, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits Fewer than protocol number

Animal Number: 1R-4615 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

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

Animal Number: 1R-4616 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations: -No visible lesions.

Microscopic Observations:

Adrenal	-Cortical degeneration, unilateral, marked
Heart	-Myocardial fibrosis, focal, mild Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Perivascular mononuclear infiltrate, moderate Vascular mineralization, mild Alveolar macrophages, mild
Mammary Gland	-Not examined, missing
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild

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

Table: 2

Animal Number: 1R-4617 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 73) Sacrificed in extremis

Macroscopic Observations:	
Ovary	-Hemorrhagic mass, 5 cm dia., left ovary.
Liver	-Pale; left lateral lobe dark red.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild One of pair present
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, diffuse, marked Massive necrosis of one lobe with compensatory increase in mitoses in another lobe.
Lung	-Vascular mineralization, mild
Mammary Gland	-Not examined, missing
Ovary	-Leiomyoma Large well differentiated neoplasm, mostly necrotic, probably arises from an oviduct.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing

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

Animal Number: 1R-4618 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 93) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 1.1 cm dia.
Mammary Gland	-Large ulcerated mass, 10 x 7 x 9 cm, right axillary area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Animal Number: 1R-4618 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 93) Sacrificed in extremis

Microscopic Observations (continued):

Skin	-Fibroma, subcutaneous Large neoplasm with extensive collagen formation, large portion necrotic. Described as mammary lesion but no mammary tissue present in section.
Thyroid	-Ultimobranchial cyst
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

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

Animal Number: 1R-4619 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Macroscopic Observations:

Spleen	-Slightly enlarged
Liver	-Pale with an irregular surface on all lobes.
Pituitary	-Enlarged with hemorrhagic foci.

Microscopic Observations:

Adrenal	-Necrosis, diffuse, marked Malignant lymphoma, histiocytic
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Kidney	-Nephrosis, tubular, marked
Liver	-Portal bile duct proliferation, marked Necrosis, local areas, moderate Malignant lymphoma, histiocytic
Lung	-Vascular mineralization, mild Malignant lymphoma, histiocytic
Lymph Node (mesenteric)	-Hemorrhage, mild
Mammary Gland	-Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Malignant lymphoma, histiocytic Hematopoiesis, extramedullary, increased, moderate
Stomach	-Necrosis, mucosal, mild
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Small Intestine, Large Intestine, Aorta, Uterus, Ovary,

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Animal Number: 1R-4619 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 64) Found Dead

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Trachea, Thyroid, Pancreas.

Animal Number: 1R-4621 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Slightly enlarged
Mammary Gland	-Subcutaneous ulcerated mass, 5 x 4 x 1.5 cm, in right axilla.
Liver	-Appears mottled.
Adrenal	-Slightly enlarged.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Nephrosis, tubular, moderate
Liver	-Portal mononuclear cell infiltrate, minimal Hepatocyte vacuolation, periportal, mild
Lung	-Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, mild
Mammary Gland	-Fibroadenoma Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild

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

Animal Number: 1R-4622 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 62) Found Dead

Macroscopic Observations:	
Skin	-Small circular lesion on back; slight hair loss on left lateral side.
Mammary Gland	-Mass, 2 cm dia., right axillary area; 1.5 cm dia., left inguinal area.
Kidney	-Raised area, 0.3 cm dia., on surface of right kidney; appears fluid filled.
Pituitary	-Dark red gelatinous mass.
Lung	-Slightly mottled
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, moderate Hyperplasia, pelvic epithelium, local areas, mild
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Alveolar macrophages, mild
Mammary Gland	-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 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:	
Eye	-Opacity, right eye.
Mammary Gland	-Multilobular mass, 11 x 12 x 3 cm, right axilla.
Adrenal	-Appear enlarged
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Eye	-Cataract, unilateral
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, mild

Animal Number: 1R-4623 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 96) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Pneumonia, interstitial, chronic, multifocal, mild
	Alveolar macrophages, mild
	Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Sinusoidal ectasia, moderate
Mammary Gland	-Fibroadenoma
Pituitary	-Adenoma
Thyroid	-Follicular hyperplasia, cystic, unilateral, mild
Uterus	-Within normal limits
	Fewer than protocol number

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Ovary, Trachea, Parathyroid, Pancreas, Salivary Gland.

Animal Number: 1R-4624 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.6 cm dia.
Mammary Gland	-Ulcerated, cystic mass, 4 x 4 x 3.5 cm, in left axilla-throat area; multilobular mass, 8.5 x 5.5 x 3 cm, in right inguinal area.
Lung	-Raised circular nodule, 0.6 cm dia., in left lobe.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal
	Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, mild
	Metastatic neoplasm
	Large metastasis of mammary adenocarcinoma.
Mammary Gland	-Fibroadenoma
	Adenocarcinoma
Ovary	-Cyst, unilateral

Animal Number: 1R-4624 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Microscopic Observations (continued):

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

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

Animal Number: 1R-4625 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 100) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged due to raised mass, 1.2 cm dia.
Mammary Gland	-Cystic mass, 2 cm dia., left axilla.
Adrenal	-Both appear enlarged.
Kidney	-Somewhat pitted

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, local areas, mild
Esophagus	-Not examined, missing
Eye	-No diagnosis, inadequate section
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, minimal
Lung	-Hemorrhage, local areas, moderate
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4626 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.9 cm dia.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4627 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 1 x 0.6 cm.
Mammary Gland	-Firm mass, 5.5 x 4 x 3.5 cm, right lateral area; lobular mass, 7 x 6 x 5 cm, left axilla.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Medullary cell hyperplasia, multifocal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, moderate Hepatocyte alteration, basophilic, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Adenocarcinoma Neoplasm arises in several places in a fibroadenoma.
Ovary	-Tubular adenoma, unilateral Cyst, bilateral

Animal Number: 1R-4627 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Pancreas	-Islet cell adenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Fibroma, subcutaneous
Uterus	-Cystic glands, mild

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

Animal Number: 1R-4628 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 1.2 cm dia.
Mammary Gland	-Small nodule, 1.5 cm dia., right axilla; possible milk cyst.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Galactocele Adenoma, papillary Small highly cellular neoplasm lying adjacent to several large galactocoels.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Animal Number: 1R-4633 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 63) Sacrificed in extremis

Macroscopic Observations:	
Liver	-Very pale
Spleen	-Slightly enlarged
Mammary Gland	-Large subcutaneous mass, 6 x 10 x 2.5 cm, with necrotic areas, containing dark brown fluid, ventral abdomen.
Microscopic Observations:	
Adrenal	-Hematopoiesis, extramedullary, cortical, mild Sinusoidal ectasia, cortex, mild
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal Vacuolation, conv. tub. epithelium, moderate
Liver	-Hepatocyte vacuolation, centrilobular, marked
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Mammary Gland	-Adenocarcinoma Well differentiated, ductular pattern, areas of moderate mitotic activity, large areas of necrosis.
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, moderate

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

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 0.7 cm dia.
Mammary Gland	-Lobular mass, 8 x 6 x 4 cm, right axilla; lobular mass, 9 x 7 x 3.5 cm, left inguinal.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild

Animal Number: 1R-4634 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, mild Hepatocyte alteration, basophilic, moderate Hepatocyte alteration, eosinophilic, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma Fibroadenoma Both masses were fibroadenomas. Areas of necrosis and cystic areas in tumors.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild Hemosiderosis, mild

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

Animal Number: 1R-4635 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 94) Found Dead

Macroscopic Observations:

Small Intestine	-Jejunum appears inflamed with reddish fluid; ileum appears inflamed near cecum.
Mammary Gland	-Mass, 7 x 7.5 x 2 cm, multilobular and ulcerated, right inguinal; mass, light beige in color, spherical, 2 cm dia., in left axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Hematopoiesis, extramedullary, cortical, moderate
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal

Animal Number: 1R-4635 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 94) Found Dead

Microscopic Observations (continued):

Liver	-Hepatocyte vacuolation, diffuse, mild
	Hematopoiesis, extramedullary, mild
	Mitotic activity, increased, moderate
Lung	-Vascular mineralization, mild
	Metastatic neoplasm
Mammary Gland	-Adenoma
	Adenocarcinoma
	Extensive necrosis.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, marked
Thyroid	-Ultimobranchial cyst

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Ovary, Trachea, Lymph Node (mesenteric), Pancreas.

Animal Number: 1R-4636 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Mass in right axilla appears to be milk cyst.
Liver	-Slightly raised dark mass, 0.6 cm dia., left lateral lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
	Sinusoidal ectasia, cortex, mild
Heart	-Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Hepatocyte vacuolation, multifocal, mild
	Hepatocyte alteration, vacuolated, mild
	Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Mammary Gland	-Lobular hyperplasia
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Animal Number: 1R-4636 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4637 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 82) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Reddened mass, 1 cm dia.
Lung	-Focal areas of consolidation in anterior part of right and left lung.
Liver	-Possibly pale

Microscopic Observations:

Eye	-Keratitis, acute, marked
Kidney	-Pelvic mineralization, mild Mineralization, cortical, mild Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Pneumonia, acute exudative, local areas, moderate Hemorrhage, multifocal, mild
Mammary Gland	-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, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing

Animal Number: 1R-4638 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, moderate
Lung	-Vascular mineralization, mild
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-No diagnosis, inadequate section
Spleen	-Hemosiderosis, mild
Uterus	-Cystic glands, marked

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

Animal Number: 1R-4639 Sex: Female Group: (1) CONTROL 0 ppm
Fate: (Week= 56) Sacrificed in extremis

Macroscopic Observations:

Skin	-Midsternal subcutaneous mass, 8 x 8 x 3 cm.
Liver	-Slightly pale

Microscopic Observations:

Kidney	-Pelvic mineralization, mild
	Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, mild
Uterus	-Within normal limits
	Fewer than protocol number

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

Animal Number: 1R-3581 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
	Hepatocyte alteration, vacuolated, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Hemorrhage, multifocal, moderate
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-C cell adenoma

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-3582 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Ulcerated mass, 2.8 cm dia., dorsal.
Pituitary	-Hemorrhagic lesion, 0.2 cm dia.
Kidney	-Pale
Adrenal	-Left adrenal enlarged, 0.7 cm dia. mass.
Testis/Epididymis	-Testes small, bilateral.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Eye	-Retinal atrophy, diffuse, marked
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, focal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Skin	-Keratoacanthoma, back

Animal Number: 1R-3582 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, spermatogenesis, bilateral, mild
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas.

Animal Number: 1R-3583 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Pale raised masses, 1.3 cm dia., right lateral lobe; 0.6 cm dia., left lateral lobe.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocellular carcinoma Megalocytosis, mild Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral Vascular mineralization, mild

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

Animal Number: 1R-3585 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Lung	-Raised pale lesion, 0.5 cm dia., left lobe.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild

Animal Number: 1R-3585 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, multifocal, mild
	Malignant lymphoma, lymphocytic
	Hepatocyte alteration, basophilic, moderate
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Fibrosis, pleural, moderate
Pancreas	-Acinar atrophy, mild
	Hyperplasia, acinar cell, mild

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

Animal Number: 1R-3586 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Possible pale foci on one lobe.
Testis/Epididymis	-Pale mass, 1 cm dia.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
	Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, multifocal, moderate
	Megalocytosis, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, moderate
Salivary Gland	-Sialadenitis, chronic, moderate
Testis/Epididymis	-Tubule atrophy, spermatogenesis, moderate
	Mineralization, tubular, mild
	Leydig cell adenoma, bilateral

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

Animal Number: 1R-3587 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Eye	-Hypopyon, right eye.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, minimal
Eye	-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, basophilic, minimal Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, minimal
Pancreas	-Hyperplasia, islet cell, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Salivary Gland	-Sialadenitis, chronic, moderate Moderate reactive hyperplasia of included lymph node.
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Trachea, Esophagus, Lymph Node (mesenteric).

Animal Number: 1R-3590 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 19) Sacrificed in extremis

Macroscopic Observations:	
Thymus	-Enlarged, 1.5 x 1.5 x 0.3 cm, dark red.
Liver	-Enlarged, brown/yellow mottling.
Spleen	-Markedly enlarged, 8 x 2 x 1 cm.
Lymph Node (mesenteric)	-Enlarged
Lymph Node (abdominal)	-Hepatic lymph nodes enlarged.
Small Intestine	-Peyer's patches enlarged and reddened.
Large Intestine	-Peyer's patches enlarged and reddened.
Kidney	-Slight dilatation of renal pelvis, bilateral.
Urinary Bladder	-Distended with urine.
Penis	-Swollen

Animal Number: 1R-3590 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 19) Sacrificed in extremis

Microscopic Observations (continued):

Adrenal	-Malignant lymphoma, lymphocytic
Bone Marrow	-Malignant lymphoma, lymphocytic
Brain	-Malignant lymphoma, lymphocytic
Eye	-Malignant lymphoma, lymphocytic
Kidney	-Malignant lymphoma, lymphocytic
Liver	-Malignant lymphoma, lymphocytic Parenchyma almost completely replaced by diffuse neoplastic cell infiltrate.
Lung	-Malignant lymphoma, lymphocytic Hemorrhage, local areas, moderate
Lymph Node (abdominal)	-Malignant lymphoma, histiocytic Extensive neoplastic involvement of hepatic node.
Lymph Node (mesenteric)	-Malignant lymphoma, lymphocytic
Parathyroid	-Not examined, missing
Pituitary	-No diagnosis, inadequate section
Small Intestine	-Malignant lymphoma, lymphocytic
Spleen	-Malignant lymphoma, lymphocytic
Thymus	-Malignant lymphoma, histiocytic
Thyroid	-Not examined, missing
Urinary Bladder	-Malignant lymphoma, lymphocytic Epithelial hyperplasia, simple, diffuse, mild

The following tissues were found to be within normal limits:
Heart, Stomach, Large Intestine, Aorta, Testis/Epididymis, Prostate, Trachea, Esophagus, Pancreas, Salivary Gland, Spinal Cord.

Animal Number: 1R-3591 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-No diagnosis, inadequate section
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, moderate Hepatocyte alteration, basophilic, moderate Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate

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:	
Kidney	-Chronic progressive nephropathy, mild
Liver	-Megalocytosis, minimal Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Hepatocellular carcinoma Well differentiated, trabecular pattern, moderate mitotic activity, vascular invasion.
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Parathyroid	-Not examined, not in plane of section
Thyroid	-C cell adenoma

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

Animal Number: 1R-3594 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Pale foci throughout.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, mild

Animal Number: 1R-3594 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Hepatocyte vacuolation, diffuse, moderate Cystoid degeneration, mild Hepatocyte alteration, vacuolated, moderate Megalocytosis, moderate Centrilobular cells enlarged with finely granular, eosinophilic, "ground glass" appearing cytoplasm.
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Testis/Epididymis	-Vascular mineralization, moderate
Thyroid	-Hyperplasia, C cell, mild

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

Animal Number: 1R-3595 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Firm mass, 3 x 2 x 1.5 cm, right axilla.
Pituitary	-Hemorrhagic mass, 0.5 x 0.7 cm.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Bone Marrow	-Not examined, missing
Kidney	-Pelvic mineralization, mild Pyelonephritis, acute, mild Hyperplasia, pelvic epithelium, diffuse, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, acute, moderate Mass described at necropsy as mammary gland was apparently the enlarged, inflamed salivary gland. No mammary tissue was present on any slide.

Animal Number: 1R-3595 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Brain, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3596 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Pale, enlarged and pitted, bilateral.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, minimal Medullary cell hyperplasia, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked Cyst, cortical, moderate
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, marked
Pituitary	-Adenoma
Testis/Epididymis	-Polyarteritis, moderate

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

Animal Number: 1R-3597 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild

Animal Number: 1R-3597 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte alteration, vacuolated, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, mild
Prostate	-Prostatitis, acute, suppurative, minimal

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

Animal Number: 1R-3599 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Hydronephrosis, right kidney.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
	Pelvic mineralization, mild
	Hyperplasia, pelvic epithelium, multifocal, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Cystoid degeneration, multifocal, mild
	Megalocytosis, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Alveolar macrophages, mild
	Hemorrhage, local areas, moderate
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3600 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Mottled
Microscopic Observations:	
Adrenal	-Cortical vacuolation, mild
Bone Marrow	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild Megalocytosis, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Hemorrhage, minimal
Pituitary	-Not examined, missing
Spinal Cord	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Vascular mineralization, mild

The following tissues were found to be within normal limits:
Brain, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

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

Macroscopic Observations:	
Liver	-Mottled; yellow raised lesions, 0.7 and 0.9 cm dia., posterior caudate lobes.
Lymph Node (mesenteric)	-Enlarged
Stomach	-Enlarged gastric rugae
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, moderate Hepatocyte alteration, vacuolated, mild Megalocytosis, moderate Hepatocyte alteration, basophilic, moderate

Table: 2

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

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Hemorrhage, local areas, marked
Lymph Node (mesenteric)	-Hemorrhage, mild
	Hemangiosarcoma
Pancreas	-Acinar atrophy, moderate
Pituitary	-Cyst, pars distalis
Stomach	-Adenocarcinoma
	Extensive infiltration into submucosa and muscularis. Well differentiated, high mitotic index. Probably parietal cell origin. Tumor cells in lymphatics.

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

Animal Number: 1R-3602 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, focal, mild
	Medullary cell hyperplasia, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Pancreas	-Islet cell adenoma
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Vascular mineralization, mild
Thyroid	-C cell adenoma

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

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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	-Sinusoidal ectasia, cortex, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, focal, mild
	Megalocytosis, minimal
	Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-3605 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Pale, mottled
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, multifocal, mild
	Cystoid degeneration, multifocal, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Alveolar macrophages, moderate
	Perivascular mononuclear infiltrate, moderate
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hematopoiesis, extramedullary, increased, mild
	Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
	Vascular mineralization, mild

Animal Number: 1R-3605 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

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

Animal Number: 1R-3606 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations: -No visible lesions.

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, focal, mild
Kidney	-Chronic progressive nephropathy, minimal
	Pyelonephritis, acute, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild

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

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

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1 x 0.7 cm.

Microscopic Observations:

Adrenal	-Cortical vacuolation, multifocal, moderate
	Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild
	Pyelonephritis, acute, moderate
	Hyperplasia, pelvic epithelium, diffuse, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Pancreas	-Acinar atrophy, mild
	Hyperplasia, islet cell, moderate

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

Microscopic Observations (continued):

Parathyroid	-Adenoma
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, marked
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild
Thyroid	-Ultimobranchial cyst
Urinary Bladder	-Epithelial hyperplasia, simple, local areas, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3608 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin	-Raised inflamed lesion, left hind footpad.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Nodular hyperplasia, cortex, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild
Skin	-Pododermatitis, ulcerative, hindleg, marked
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, moderate
Thyroid	-Ultimobranchial cyst

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

Table: 2

Animal Number: 1R-3609 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Nodular hyperplasia, cortex, focal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Megalocytosis, mild
Lung	-Vascular mineralization, mild
	Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Sinusoidal ectasia, mild
Pancreas	-Acinar atrophy, moderate
	Polyarteritis, moderate
Parathyroid	-Not examined, not in plane of section
Testis/Epididymis	-Leydig cell hyperplasia, focal, mild

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

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

Macroscopic Observations:	
Liver	-Few pale foci.
Testis/Epididymis	-Testes appear somewhat small.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
	Cystoid degeneration, multifocal, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Perivascular mononuclear infiltrate, minimal
	Hemorrhage, local areas, moderate
Pancreas	-Acinar atrophy, mild
Testis/Epididymis	-Mineralization, tubular, mild
	Tubule atrophy, aspermatogenesis, bilateral, marked

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, moderate

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

Animal Number: 1R-3611 Sex: Male Group: (5) FC-143 300 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	-Sinusoidal ectasia, cortex, mild Cortical vacuolation, focal, minimal
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Cystoid degeneration, multifocal, mild Hepatocyte alteration, vacuolated, mild Megalocytosis, minimal Hyperplastic nodule Cells in cords of single cell thickness. Many cells vacuolated. Large central blood filled space.
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, missing
Salivary Gland	-Sialadenitis, chronic, marked Extensive squamous metaplasia of duct epithelium with some ducts occluded by hyperplastic, metaplastic epithelium.
Thyroid	-Not examined, missing

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

Microscopic Observations (continued):

Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3612 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 99) Found Dead

Macroscopic Observations:

Liver	-Multilobular mass, 4.5 x 4 x 3 cm in area of right lateral lobe, attached to caudate lobe.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, minimal
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocellular carcinoma Well differentiated, trabecular pattern, large areas of necrosis within tumor.
Lung	-Vascular mineralization, mild Alveolar macrophages, marked Medial hypertrophy, arteries, moderate
Pancreas	-Hyperplasia, islet cell, moderate
Thyroid	-Cyst, colloid, mild

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

Animal Number: 1R-3614 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis	-Pale masses of various sizes in both testes.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, minimal

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Table: 2

Animal Number: 1R-3614 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Prostate	-Not examined, missing
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, moderate
	Leydig cell adenoma, unilateral

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

Animal Number: 1R-3615 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.8 cm dia.
Testis/Epididymis	-Right testis small.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, multifocal, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
	Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, marked
	Extensive hyperplasia and metaplasia of duct epithelium.
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

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

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Animal Number: 1R-3616 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 72) Found Dead

Macroscopic Observations:	
Fituitary	-Enlarged, 0.9 cm dia.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, minimal
	Cystoid degeneration, multifocal, mild
	Necrosis, multifocal, moderate
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
	Hemorrhage, diffuse, marked
Pancreas	-Hyperplasia, acinar cell, moderate
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine,
Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea,
Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-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., caudate lobe.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild
	Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, minimal
	Necrosis, focal, minimal
	Megalocytosis, minimal
	Hepatocellular carcinoma
	Trabecular pattern, many tumor cells vacuolated, moderate mitotic activity.
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,

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

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

Animal Number: 1R-3619 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Raised lesions, 2 x 1.5 cm, median lobes.
Kidney	-Hydronephrosis, left kidney.
Urinary Bladder	-Distended into abdomen, filled with dark colored fluid.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Nodular hyperplasia, cortex, focal, moderate
Kidney	-Chronic progressive nephropathy, minimal Hydronephrosis, bilateral, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, mild Hepatocellular carcinoma Poorly differentiated, adenoid and trabecular patterns, moderate mitotic activity.
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Salivary Gland	-Not examined, missing
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Hemorrhage, focal, minimal

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

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

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal

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

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, multifocal, mild
	Megalocytosis, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3623 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
	Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, mild
	Necrosis, multifocal, mild
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Alveolar macrophages, mild
Lymph Node (mesenteric)	-Hemorrhage, mild
Pituitary	-Not examined, missing
Prostate	-Prostatitis, acute, suppurative, moderate
Salivary Gland	-Sialadenitis, chronic, marked
Testis/Epididymis	-Vascular mineralization, mild

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

Animal Number: 1R-3624 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 90) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 1 x 0.5 cm.
Liver	-Possibly pale
Kidney	-Slightly enlarged and pitted.
Testis/Epididymis	-Both testes appear somewhat small.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild Medullary cell hyperplasia, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, multifocal, mild
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, suppurative, marked
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, marked

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

Animal Number: 1R-3625 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 27) Sacrificed in extremis

Macroscopic Observations:	
Soft Tissues (neck)	-Large multinodular mass, 9 x 8 x 6 cm, in left neck and throat region. Possibly of mammary gland or salivary gland origin. Mass contained several cystic areas that were filled with dark fluid.
Spleen	-Possibly slightly enlarged.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, focal, mild Megalocytosis, minimal
Lung	-Metastatic neoplasm Thrombus Large thrombus containing tumor cells from salivary gland tumor. Multiple small metastases of salivary tumor throughout lung.

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Animal Number: 1R-3625 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 27) Sacrificed in extremis

Microscopic Observations (continued):

Salivary Gland	-Carcinoma Highly cellular, anaplastic tumor. Appears to have arisen in parotid gland duct. Small rim of salivary gland tissue around mass.
Spleen	-Hematopoiesis, extramedullary, increased, moderate

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

Animal Number: 1R-3628 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, moderate
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, moderate Alveolar macrophages, mild Hemorrhage, local areas, moderate
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3629 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, local areas, moderate
Salivary Gland	-Sialadenitis, chronic, marked
Thyroid	-Ultimobranchial cyst

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Adrenal, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3630 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Myocardial fibrosis, local areas, mild Myocarditis, chronic nonsuppurative, local areas, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Pituitary	-Not examined, missing
Testis/Epididymis	-Vascular mineralization, mild

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

Table: 2

Animal Number: 1R-3631 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Nodular hyperplasia, cortex, focal, mild Medullary cell hyperplasia, focal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, local areas, mild Megalocytosis, minimal
Lung	-Vascular mineralization, moderate Alveolar macrophages, mild Hemorrhage, local areas, moderate
Salivary Gland	-Sialadenitis, chronic, marked There were two sections of gland on the slide, only one was involved.
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3632 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Few pale foci.
Testis/Epididymis	-Pale mass, 1.5 cm dia.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Megalocytosis, mild Hepatocyte alteration, basophilic, mild Single subcapsular area of basophilic alteration. About one half of the cells have multiple cytoplasmic vacuoles.
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Hemorrhage, focal, mild
Pancreas	-Hyperplasia, islet cell, moderate

Table: 2

Animal Number: 1R-3632 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
	Leydig cell adenoma, unilateral

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

Animal Number: 1R-3633 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Eye	-Opacity, right eye.
Kidney	-Bilaterally pale and pitted.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
	Ganglioneuroma
	Large, well differentiated tumor arising in medulla of one gland. Composed of nerve fibers and large ganglion cells.
Eye	-Keratitis, chronic, moderate
Heart	-Myocarditis, chronic nonsuppurative, local areas, mild
Kidney	-Chronic progressive nephropathy, marked
	One of pair present
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Cystoid degeneration, multifocal, mild
	Hepatocyte alteration, vacuolated, mild
	Megalocytosis, moderate
Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
	Perivascular mononuclear infiltrate, minimal
	Hemorrhage, local areas, mild
Thyroid	-Cyst, colloid

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

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Table: 2

Animal Number: 1R-3634 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Testis/Epididymis	-Pale masses, 1 cm dia., in each testis.
Mesentery	-Mass, 3 x 1.5 cm in area of pancreas.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Hepatocyte alteration, vacuolated, moderate Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Pancreas	-Adenocarcinoma Large, highly cellular, well differentiated neoplasm with high mitotic index. Lymphatic invasion.
Parathyroid	-Not examined, not in plane of section
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, marked Leydig cell adenoma, bilateral

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

Animal Number: 1R-3635 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic area, 0.5 x 0.2 cm.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, focal, minimal
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, minimal
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, marked

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine,

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Species: Rat
Project Number: 0281CR0012

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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, Aorta, Testis/Epididymis, Prostate, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-3636 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Bone	-Swollen metatarsal joints, bilateral hind limbs.
Testis/Epididymis	-Both testes appear small.

Microscopic Observations:

Bone	-Arthritis, synovitis; joints, hindleg, moderate
Heart	-Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, focal, minimal Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Lymph Node (mesenteric)	-Granuloma, multifocal, moderate
Pancreas	-Polyarteritis, moderate
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, marked Polyarteritis, moderate Vascular mineralization, mild

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

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

Macroscopic Observations:	
Thyroid	-Possibly slightly enlarged.
Pituitary	-Mass, 0.5 cm dia.
Thymus	-Slightly enlarged and hemorrhagic.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, multifocal, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Necrosis, multifocal, moderate
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Pancreas	-Acinar atrophy, minimal
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Thymus	-Hemorrhage, marked

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Eye.

Animal Number: 1R-3639 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised dark mass, 0.7 cm dia.
Adrenal	-Enlarged, right adrenal
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, marked Medullary cell hyperplasia, focal, mild
Kidney	-Mineralization, cortical, mild
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, moderate Granuloma Fragment of unidentified foreign material in granuloma.

Animal Number: 1R-3639 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-3640 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 72) Sacrificed in extremis

Macroscopic Observations:

Spleen	-Possibly smaller than normal.
Abdomen (internal)	-Gastrointestinal tract from stomach to cecum distended with gas.
Eye	-Right eye slightly atrophied

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, focal, minimal
Eye	-Keratitis, acute, marked Lesion in right eye. Extensive corneal ulceration.
Kidney	-Calculus, pelvic, mild
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, mild
Spleen	-Hemosiderosis, mild Atrophy, moderate
Stomach	-Gastritis, acute, diffuse, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Testis/Epididymis, Prostate, Pituitary, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland.

Animal Number: 1R-3641 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Yellowish foci, 0.3 cm dia., median lobe.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, local areas, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, multifocal, mild Megalocytosis, minimal Hyperplastic nodule Circumscribed, expansive lesion with preservation of normal architecture. Portal areas present. Cells in nodule more basophilic, vacuolated.
Lung	-Vascular mineralization, mild Hemorrhage, focal, mild
Pancreas	-Acinar atrophy, moderate
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral

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

Animal Number: 1R-3644 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Appears mottled; small pale area in median lobe.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild Nodular hyperplasia, cortex, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Megalocytosis, minimal Hyperplastic nodule Cells of nodule have slightly more basophilic cytoplasm; many are vacuolated.

Animal Number: 1R-3644 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Alveolar macrophages, mild
Salivary Gland	-Sialadenitis, chronic, marked
Testis/Epididymis	-Vascular mineralization, moderate

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

Animal Number: 1R-3645 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis	-Pale mass, 1.3 cm dia., in left testis.

Microscopic Observations:

Adrenal	-Nodular hyperplasia, cortex, multifocal, mild
Aorta	-Metastatic neoplasm
Esophagus	-Metastatic neoplasm
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, minimal
	Portal bile duct proliferation, minimal
	Megalocytosis, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
	Alveolar macrophages, mild
	Hemorrhage, focal, mild
Pancreas	-Acinar atrophy, mild
Parathyroid	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Soft Tissues (thorax)	-Histiocytoma, malignant
	Diffuse infiltrate of histiocytic cells in mediastinal tissues. Moderate number of multinucleate giant cells. Infiltrate extends into muscle around bone.
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Leydig cell adenoma, unilateral
Trachea	-Metastatic neoplasm
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, minimal

Animal Number: 1R-3645 Sex: Male Group: (5) FC-143 300 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Heart, Stomach, Small Intestine, Large Intestine, Prostate, Pituitary, Thyroid, Lymph Node (mesenteric), Eye.

Animal Number: 1R-4641 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 73) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland	-Large multilobular subcutaneous mass, left inguinal and perineal area, 10 x 7 x 3.5 cm. Mass ulcerated on the dorsal surface; inside cystic with milky fluid present.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, focal, minimal
Lung	-Hemorrhage, local areas, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Ovary	-Not examined, missing
Salivary Gland	-Not examined, missing

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

Animal Number: 1R-4643 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 78) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.8 cm dia.

Microscopic Observations:

Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, diffuse, mild

Pathology and Toxicology
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3M

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

(RIKER EXPERIMENT NO. 0281CR0012)

VOLUME 2 OF 4

CONDUCTED DURING
APRIL, 1981 - MAY, 1983

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

000679

Animal Number: 1R-4643 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 78) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Hemorrhage, diffuse, marked
Lymph Node (mesenteric)	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, moderate
Uterus	-Cystic glands, 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, Ovary, Mammary Gland, Trachea, Adrenal, Thyroid, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4644 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Lobular mass, 3 cm dia., right axilla.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild
	Hepatocyte alteration, vacuolated, focal, mild
	Hepatocyte alteration, basophilic, focal, minimal
	Hyperplastic nodule
Lung	-Vascular mineralization, mild
	Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Pancreas	-Not examined, missing
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, Uterus, Ovary, Pituitary, Trachea, Thyroid, Parathyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4645 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Large mass, 10 x 4 cm, right axilla; lobular mass, 5.5 x 5 x 4 cm, left inguinal.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Aorta	-Not examined, missing
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Alveolar macrophages, multifocal, mild Hemorrhage, local areas, mild
Lymph Node (mesenteric)	-Hemorrhage, marked
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Animal Number: 1R-4646 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Small nodular mass, 1 cm dia., left axilla; nodular mass, 4 x 2.5 cm, right axilla.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Heart	-Myocardial fibrosis, focal, minimal Myocarditis, chronic nonsuppurative, focal, minimal
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, marked
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Hemorrhage, local areas, moderate
Mammary Gland	-Adenocarcinoma Fibroadenoma
Ovary	-Tubular hyperplasia, moderate
Pancreas	-Acinar atrophy, minimal
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-4646 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Uterus	-Cystic glands, mild

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

Animal Number: 1R-4647 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, moderate
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
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, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Uterus, Mammary Gland, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4648 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 88) Found Dead

Macroscopic Observations:

Mammary Gland	-Large firm subcutaneous mass, 12 x 9 x 5 cm, on left side.

Microscopic Observations:

Eye	-Not examined, missing
Kidney	-Pelvic mineralization, mild
Large Intestine	-Not examined, missing

Animal Number: 1R-4648 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 88) Found Dead

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Alveolar macrophages, multifocal, mild
	Perivascular mononuclear infiltrate, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Skin	-Fibroma
Small Intestine	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Heart, Stomach, Urinary Bladder, Aorta, Uterus, Ovary, Pituitary, Trachea, Adrenal, Thyroid, Esophagus, Pancreas, Salivary Gland.

Animal Number: 1R-4649 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 0.8 cm dia.
Mammary Gland	-Small mass, 1 cm dia., possibly inflamed milk cyst, perineal area.

Microscopic Observations:

Adrenal	-Cortical atrophy, bilateral, moderate
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Perivascular mononuclear infiltrate, minimal
Mammary Gland	-Galactocele
	Fibroadenoma
Ovary	-Tubular hyperplasia, bilateral, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing

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

Table: 2

Animal Number: 1R-4650 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 104) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.1 cm dia.
Skin	-Raised circular inflamed lesion on left rear footpad.
Mammary Gland	-Round mass, 1 cm dia., in inguinal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild Medullary cell hyperplasia, unilateral, moderate Pheochromocytoma, malignant, unilateral Infiltration of neoplastic tissue into surrounding connective tissue.
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, minimal
Mammary Gland	-Galactocele
Ovary	-Tubular hyperplasia, bilateral, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Skin	-Pododermatitis, ulcerative, hindleg, 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, Uterus, Trachea, Thyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4651 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 1.1 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Large Intestine	-Not examined, missing
Liver	-Hepatocyte alteration, vacuolated, focal, mild

Table: 2

Animal Number: 1R-4651 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 96) Sacrificed in extremis

Microscopic Observations (continued):

Ovary	-No diagnosis, inadequate section
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Thyroid	-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, Lung, Stomach, Small Intestine, Aorta, Uterus, Mammary Gland, Lymph Node (mesenteric), Pancreas, Trachea.

Animal Number: 1R-4653 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 87) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1 cm dia.
Mammary Gland	-Milk cyst in right inguinal area.
Liver	-Pale

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, diffuse, marked Mononuclear cell infiltration, multifocal, parenchymal, mild
Lung	-Pneumonia, interstitial, chronic, multifocal, minimal
Mammary Gland	-Within normal limits Milk cyst not included with section examined.
Pancreas	-Acinar atrophy, mild
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Table: 2

Animal Number: 1R-4654 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 57) Found Dead

Macroscopic Observations:	
Mammary Gland	-Subcutaneous mass, 6 x 5 x 2 cm, in left axilla. Mass was multilobular and reddish pink.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, focal, minimal
Liver	-Portal bile duct proliferation, mild
Lung	-Pneumonia, interstitial, chronic, focal, mild
Mammary Gland	-Fibroadenoma
Pancreas	-Pancreatitis, chronic, diffuse, moderate

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, Uterus, Ovary, Pituitary, Trachea, Thyroid, Parathyroid, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4657 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Lobular mass, 2 x 1.5 x 1 cm, in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Eye	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild
Mammary Gland	-Fibroadenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Not examined, missing

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

Animal Number: 1R-4658 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Milk cyst in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, mild Megalocytosis, minimal
Lymph Node (mesenteric)	-Hemorrhage, moderate Pigment, brown, moderate
Mammary Gland	-Fibrosis, mild
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, missing
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Lung, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Pituitary, Pancreas, Eye.

Animal Number: 1R-4659 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Lobular 3 x 3 cm mass in throat area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, minimal Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Fibroadenoma
Pancreas	-Acinar atrophy, mild Islet cell adenoma

Animal Number: 1R-4659 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Uterus	-Polyp

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

Animal Number: 1R-4660 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.6 cm dia.
Mammary Gland	-Mass, 2.5 x 2 x 3 cm, left axilla; mass, 4.4 x 4 x 2 cm, left inguinal.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Large Intestine	-Nematodiasis, colon
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, minimal Cystoid degeneration, focal, minimal
Lung	-Alveolar macrophages, focal, mild
Lymph Node (mesenteric)	-Pigment, brown, mild
Mammary Gland	-Fibroadenoma Fibroadenoma
Pancreas	-Islet cell carcinoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, minimal

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

Animal Number: 1R-4661 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, multifocal, mild
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-4662 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Ulcerated necrotic mass, 4 x 3 cm, in right inguinal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
	Hemorrhage, multifocal, mild
Lymph Node (mesenteric)	-Pigment, brown, moderate
Mammary Gland	-Fibroadenoma
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, 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, Uterus, Ovary, Trachea, Thyroid, Parathyroid, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4663 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass, 3 x 2.5 cm, in the throat area.
Adrenal	-Right adrenal appears small.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, unilateral, moderate
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, focal, mild
Lung	-Alveolar macrophages, local areas, mild Hemorrhage, mild
Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section

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

Animal Number: 1R-4665 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised red mass, 1.2 cm dia.
Mammary Gland	-Small milk cyst present.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Lobular hyperplasia, moderate
Ovary	-Tubular hyperplasia, moderate
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

Animal Number: 1R-4665 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 94) Sacrificed in extremis

Microscopic Observations (continued):

Uterus	-Hydrometra, marked

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

Animal Number: 1R-4667 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 1.2 cm dia.
Urinary Bladder	-Wall appears thickened.

Microscopic Observations:

Adrenal	-Cortical atrophy, bilateral, moderate
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Megalocytosis, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, local areas, moderate Hemorrhage, local areas, moderate Granuloma, multiple
Mammary Gland	-Not examined, missing
Ovary	-Tubular hyperplasia, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Hypertrophy, muscularis, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Small Intestine, Large Intestine, Aorta, Uterus, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Eye.

Table: 2

Animal Number: 1R-4668 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 81) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Enlarged due to red mass, 1 x 0.8 cm.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild
	Hemorrhage, local areas, mild
Mammary Gland	-Not examined, missing
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Thyroid	-Not examined, missing
Urinary Bladder	-Not examined, missing

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

Animal Number: 1R-4670 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 92) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised hemorrhagic mass, 1 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, unilateral, mild
	Medullary cell hyperplasia, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
	Pelvic mineralization, moderate
Liver	-Pigment, Kupfer cell, brown, mild
Lung	-Alveolar macrophages, focal, mild
	Perivascular mononuclear infiltrate, minimal
Mammary Gland	-Not examined, missing
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Table: 2

Animal Number: 1R-4672 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.9 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, minimal
Esophagus	-Not examined, missing
Lung	-Hemorrhage, local areas, moderate
Lymph Node (mesenteric)	-Pigment, brown, minimal
Ovary	-Tubular hyperplasia, unilateral, moderate
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Stomach, Small Intestine, Large Intestine, Urinary Bladder, Aorta, Uterus, Mammary Gland, Pancreas, Eye.

Animal Number: 1R-4673 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 79) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Large hemorrhagic mass, 1.5 x 1 cm dia.
Skin	-Subcutaneous masses, 1.5 x 1.5 x 1 cm, right axilla; 3.5 x 3 x 2 cm left axilla.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Adenocarcinoma Galactocele Lobular hyperplasia, moderate One of the grossly described masses was an area of galactocoels and lobular hyperplasia.
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
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, Aorta, Uterus, Ovary, Trachea, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4675 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Lung	-Apparent areas of consolidation.
Kidney	-Somewhat pale and pitted.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Cortical vacuolation, mild
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, local areas, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Granuloma, diffuse, marked Large area of granuloma with many giant cells. Few fragments of foreign material present.
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Animal Number: 1R-4677 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass, 2 x 1.5 cm, in left axilla; multilobular mass, 6.5 x 5.5 x 2 cm, in perineal area.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, mild Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Pigment, conv. tub. epithelium, brown, minimal
Liver	-Portal mononuclear cell infiltrate, moderate Portal bile duct proliferation, moderate Megalocytosis, minimal
Lung	-Vascular mineralization, mild

Animal Number: 1R-4677 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Lymph Node (mesenteric)	-Sinusoidal ectasia, moderate
Mammary Gland	-Fibroadenoma
	Fibroadenoma
Ovary	-Tubular adenoma, unilateral
Pituitary	-Adenoma

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

Animal Number: 1R-4678 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 49) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged due to mass, 1 x 0.7 cm.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, local areas, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
	Hemorrhage, local areas, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Urinary Bladder	-Not examined, missing

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

Animal Number: 1R-4679 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised hemorrhagic mass, 0.5 cm dia.
Mammary Gland	-Nodular mass, 1 cm dia., in left axilla; large mass, 5 x 5 cm, in right inguinal area.

Animal Number: 1R-4679 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Cortical vacuolation, moderate Sinusoidal ectasia, cortex, moderate Nodular hyperplasia, cortex, focal, moderate
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal bile duct proliferation, mild
Lung	-Pneumonia, interstitial, chronic, focal, minimal Alveolar macrophages, focal, mild Perivascular mononuclear infiltrate, mild Hemorrhage, local areas, moderate
Mammary Gland	-Fibroadenoma
Ovary	-Tubular hyperplasia, bilateral, mild
Pituitary	-Adenoma
Thyroid	-Ultimobranchial cyst
Uterus	-Cystic glands, minimal

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

Animal Number: 1R-4680 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 104) Found Dead

Macroscopic Observations:

Mammary Gland	-Large mass, 9 x 9 x 3.5 cm, in left inguinal area. Mass had necrotic, hemorrhagic surface.
Pituitary	-Dark lesion, 0.4 cm dia.
Liver	-Pale

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, local areas, mild
Kidney	-Pelvic mineralization, minimal
Large Intestine	-Not examined, missing
Liver	-Necrosis, centrilobular, marked
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing

Animal Number: 1R-4680 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 104) Found Dead

Microscopic Observations (continued):

Mammary Gland	-Lymphangiosarcoma Large well differentiated tumor with numerous moderate to large size spaces containing few lymphocytes.
Ovary	-Tubular hyperplasia, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Small Intestine	-Not examined, missing
Uterus	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Stomach, Urinary Bladder, Aorta, Trachea, Thyroid, Esophagus, Pancreas, Salivary Gland.

Animal Number: 1R-4681 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 97) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 1.2 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, minimal Pyelitis, acute, unilateral, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, focal, minimal Perivascular mononuclear infiltrate, minimal Hemorrhage, focal, mild
Ovary	-Tubular hyperplasia, moderate
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Table: 2

Animal Number: 1R-4682 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 94) Found Dead

Macroscopic Observations:	
Mammary Gland	-Large multilobular mass, 11 x 9 x 6 cm, in left axilla.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Large Intestine	-Not examined, missing
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Fibroadenoma
Ovary	-Not examined, missing
Pancreas	-Not examined, missing
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Small Intestine	-Not examined, missing
Stomach	-Not examined, missing
Thyroid	-Not examined, missing
Urinary Bladder	-Not examined, missing
Uterus	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Kidney, Heart, Aorta, Trachea.

Animal Number: 1R-4683 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Adenoma, cortical, unilateral
Esophagus	-Not examined, missing
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Granuloma, multifocal, mild Foreign material in some granulomas. Hemorrhage, local areas, mild
Ovary	-Tubular hyperplasia, bilateral, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

Animal Number: 1R-4683 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

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, Mammary Gland, Trachea, Thyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4684 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 103) Found Dead

Macroscopic Observations:	
Pituitary	-Raised, hemorrhagic, 0.1 cm dia.
Microscopic Observations:	
Adrenal	-Not examined, missing
Aorta	-Not examined, missing
Esophagus	-Not examined, missing
Lung	-Vascular mineralization, mild
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Not examined, missing
Ovary	-Tubular hyperplasia, moderate
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Thyroid	-Not examined, missing
Trachea	-Not examined, missing
Unidentified Tissue	-Lipoma Large necrotic tumor of adipose tissue. Site unspecified.

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, Uterus, Pancreas, Eye.

Animal Number: 1R-4685 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 75) Sacrificed in extremis

Macroscopic Observations:	
Mammary Gland	-Large mass, 15 x 9 x 4 cm, somewhat firm and multilobular.
Adrenal	-Both appeared enlarged with dark foci.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate

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Animal Number: 1R-4685 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 75) Sacrificed in extremis

Microscopic Observations (continued):

Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, marked
Liver	-Necrosis, multifocal, mild Hematopoiesis, extramedullary, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, focal, minimal Hemorrhage, local areas, moderate
Mammary Gland	-Fibroadenoma
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, 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, Pituitary, Trachea, Thyroid, Parathyroid, Lymph Node (mesenteric), Pancreas, Eye.

Animal Number: 1R-4686 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Small hemorrhagic mass, 0.3 cm dia.
Mammary Gland	-Large multilobular mass, 10 x 7 x 4 cm, in right axilla.
Liver	-Mass, 5 x 3 cm, in right lateral lobe.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Liver	-Portal bile duct proliferation, mild Hepatocellular carcinoma
Lung	-Alveolar macrophages, focal, mild Perivascular mononuclear infiltrate, minimal Hemorrhage, local areas, mild
Mammary Gland	-Fibroadenoma
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, Parathyroid, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Table: 2

Animal Number: 1R-4688 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Mass, 0.9 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Large Intestine	-Nematodiasis, colon
Mammary Gland	-Not examined, missing
Ovary	-Tubular hyperplasia, moderate
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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

Animal Number: 1R-4690 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, unilateral, marked
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, local areas, mild
Lymph Node (mesenteric)	-Pigment, brown, mild
Parathyroid	-Not examined, not in plane of section
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, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Esophagus, Salivary Gland, Eye, Pancreas.

Table: 2

Animal Number: 1R-4691 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 100) Sacrificed in extremis

Macroscopic Observations:	
Liver	-Appear enlarged with multiple pale foci in all lobes.
Adrenal	-Left adrenal appears enlarged.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, mild Sinusoidal ectasia, cortex, unilateral, marked
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal Protein resorption droplets, tubular, marked
Liver	-Malignant lymphoma, histiocytic
Lung	-Vascular mineralization, mild Malignant lymphoma, histiocytic Hemorrhage, local areas, mild
Pancreas	-Edema, intersititial, moderate
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Stomach	-Edema, submucosal, moderate
Thyroid	-Hyperplasia, C cell, focal, mild
Urinary Bladder	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Small Intestine, Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Parathyroid, Esophagus, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4693 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Dark raised lesion, 0.3 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, local areas, mild Alveolar macrophages, local areas, mild Perivascular mononuclear infiltrate, mild
Pituitary	-Adenoma

Species: Rat
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000702

Animal Number: 1R-4693 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

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

Animal Number: 1R-4694 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 1.2 cm dia.
Mammary Gland	-Small nodular lesion, 0.8 cm dia., in right axilla; possible milk cyst.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Lung	-Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, moderate

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

Animal Number: 1R-4695 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.8 cm dia.
Mammary Gland	-Lobular cystic mass, 4.5 x 3 x 2 cm, in left axilla.
Liver	-Mass, 3.5 x 3 x 2 cm, in median lobe.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, unilateral, marked
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild

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Table: 2

Animal Number: 1R-4695 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Liver	-Portal mononuclear cell infiltrate, mild
	Hepatocyte vacuolation, multifocal, mild
	Hyperplastic nodule
	Large lesion with extensive cystoid degeneration within nodule.
Lung	-Perivascular mononuclear infiltrate, minimal
Mammary Gland	-Fibroadenoma
	Adenocarcinoma
	Adenocarcinoma arises in fibroadenoma.
Pituitary	-Adenoma
Uterus	-Cystic glands, 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, Ovary, Trachea, Thyroid, Parathyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4696 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Lobular mass, 5.5 x 4.5 x 2.5 cm, left axilla; multilobular mass, 5.5 x 4 x 2 cm, in perineal and left inguinal area.
Lymph Node (mesenteric)	-Large and cystic.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte alteration, vacuolated, local areas, mild
	Megalocytosis, minimal
	Hepatocyte alteration, basophilic, focal, mild
Lung	-Perivascular mononuclear infiltrate, minimal
	Hemorrhage, local areas, mild
	Granuloma, local areas, mild
Lymph Node (mesenteric)	-Sinusoidal ectasia, marked
	Granuloma, mesentery
Mammary Gland	-Fibroadenoma
	Adenocarcinoma

Animal Number: 1R-4696 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Ovary	-Cyst, unilateral
Pituitary	-Adenoma
Small Intestine	-Granuloma, mesentery
Thyroid	-Hyperplasia, C cell, focal, mild

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Heart, Stomach, Large Intestine, Urinary Bladder, Aorta, Uterus, Trachea, Parathyroid, Esophagus, Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4697 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Hydronephrosis, unilateral
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pituitary	-Adenoma
Thyroid	-Hyperplasia, C cell, focal, mild
Uterus	-Cystic glands, moderate

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, Ovary, Mammary Gland, Trachea, Parathyroid, Esophagus, Lymph Node (mesenteric), Pancreas, Salivary Gland, Eye.

Animal Number: 1R-4698 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Mass, 0.5 cm dia.
Mammary Gland	-Mass, 4 x 3.5 x 3 cm, left inguinal.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, minimal Hepatocyte vacuolation, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild

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Species: Rat
Project Number: 0281CR0012

Table: 2

Animal Number: 1R-4698 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Mammary Gland	-Fibroadenoma
Ovary	-Cyst, unilateral Tubular hyperplasia, moderate
Pituitary	-Adenoma

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

Animal Number: 1R-4700 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland	-Mass, 3 x 2 cm, in left axilla.
Heart	-Appears possibly enlarged.
Adrenal	-Right adrenal appears enlarged.
Kidney	-Pale and pitted.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, unilateral, marked Cortical degeneration, unilateral, marked Cortical atrophy, unilateral, moderate
Aorta	-Not examined, missing
Heart	-Myocardial fibrosis, local areas, mild
Kidney	-Chronic progressive nephropathy, marked
Lung	-Pneumonia, interstitial, chronic, diffuse, marked
Lymph Node (mesenteric)	-Not examined, missing
Mammary Gland	-Fibroadenoma
Ovary	-Tubular hyperplasia, marked
Parathyroid	-Not examined, missing
Small Intestine	-Edema, lamina propria , jejunum, mild
Stomach	-Edema, submucosal, moderate
Thyroid	-Not examined, missing

The following tissues were found to be within normal limits:
Brain, Spinal Cord, Bone Marrow, Spleen, Liver, Large Intestine, Urinary Bladder, Uterus, Pituitary, Trachea, Esophagus, Pancreas, Salivary Gland, Eye.

Table: 2

Animal Number: 1R-4701 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Liver	-Hepatocyte vacuolation, multifocal, minimal Megalocytosis, minimal
Lung	-Pneumonia, interstitial, chronic, focal, mild Alveolar macrophages, focal, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

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

Animal Number: 1R-4702 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 87) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Reddish mass, 1.2 x 0.8 cm.
Mammary Gland	-Lobulated mass, 3 x 2 x 1 cm, in left axillary region.
Liver	-Mottled and slightly pale.
Microscopic Observations:	
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal Pyelitis, acute, unilateral, mild
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Mammary Gland	-Adenocarcinoma
Ovary	-Tubular hyperplasia, moderate
Pancreas	-Not examined, missing
Pituitary	-Adenoma

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, Trachea, Adrenal, Thyroid, Parathyroid, Lymph Node (mesenteric), Salivary Gland, Eye.

Table: 2

Animal Number: 1R-4703 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Lobular mass, 3 x 2 cm, in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, multifocal, minimal Hepatocyte alteration, vacuolated, multifocal, mild
Lung	-Pneumonia, interstitial, chronic, local areas, mild Alveolar macrophages, local areas, mild
Mammary Gland	-Lobular hyperplasia
Pancreas	-Hyperplasia, islet cell, mild
Pituitary	-Adenoma

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, Trachea, Thyroid, Parathyroid, Lymph Node (mesenteric), Salivary Gland, Eye.

Animal Number: 1R-4705 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 62) Found Dead

Macroscopic Observations:	
Pituitary	-Two small hemorrhagic lesions approximately 0.1 cm dia.
Microscopic Observations:	
Esophagus	-Not examined, missing
Eye	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Salivary Gland	-Not examined, missing
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Spinal Cord, Bone Marrow, Stomach, Small Intestine, Large Intestine, Aorta, Uterus, Ovary, Mammary Gland, Pituitary, Trachea, Adrenal, Thyroid, Parathyroid, Lymph Node (mesenteric),

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Table: 2

Animal Number: 1R-4705 Sex: Female Group: (5) FC-143 300 ppm
Fate: (Week= 62) Found Dead

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Pancreas, Brain, Spleen, Kidney.

Table: 2

Animal Number: 1R-3646 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Liver	-Possibly pale, mottled.
Microscopic Observations:	
Heart	-Myocardial fibrosis, mild Myocarditis, chronic nonsuppurative, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, minimal Hepatocyte alteration, vacuolated, focal, mild
Lung	-Vascular mineralization, mild
Pancreas	-Not examined, missing
Salivary Gland	-Sialadenitis, chronic, marked
Thyroid	-Hyperplasia, C cell, focal, mild

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Parathyroid, Trachea, Esophagus, Pituitary.

Animal Number: 1R-3647 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 101) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised hemorrhagic mass, 0.8 cm dia.
Skin	-Raised ulcerated lesions on both hind footpads.
Stomach	-Possible area of ulceration in cardia.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, multifocal, mild
Pituitary	-Adenoma
Skin	-Pododermatitis, ulcerative, bilateral, marked
Stomach	-Ulcer, marked
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, mild Vascular mineralization, mild

Species: Rat
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Table: 2

Animal Number: 1R-3647 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 101) Sacrificed in extremis

Microscopic Observations (continued):

Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Epithelial hyperplasia, papillary, local areas, mild Calculus

The following tissues were found to be within normal limits:
Spleen, Prostate, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3648 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 66) Sacrificed in extremis

Macroscopic Observations:

Thymus	-Lobulated, light-green mass, 2.5 x 1 cm, in thymus area.
Liver	-Possibly slightly pale.
Spleen	-Enlarged
Lymph Node (abdominal)	-Renal, internal iliac lymph nodes slightly enlarged and light greenish in color.

Microscopic Observations:

Kidney	-Leukemia, myeloid Protein resorption droplets, mild Extensive infiltration of proliferating cells of early myeloid series in hilus.
Liver	-Leukemia, myeloid
Lung	-Leukemia, myeloid Hemorrhage, multifocal, mild
Lymph Node (abdominal)	-Leukemia, myeloid
Pancreas	-Not examined, missing
Pituitary	-Not examined, missing
Spleen	-Leukemia, myeloid
Thymus	-Leukemia, myeloid

The following tissues were found to be within normal limits:
Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Table: 2

Animal Number: 1R-3649 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, mild
Pituitary	-Hyperplasia, multifocal, pars distalis, mild
Salivary Gland	-Sialadenitis, chronic, moderate
Thyroid	-Hyperplasia, C cell, multifocal, moderate Ultimobranchial cyst

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3650 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Cortical degeneration, focal, moderate Pheochromocytoma, malignant, unilateral Neoplastic cells highly pleomorphic.
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, focal, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild
Pancreas	-Acinar atrophy, moderate
Salivary Gland	-Sialadenitis, chronic, marked

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary.

Table: 2

Animal Number: 1R-3651 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Kidney	-Multiple cysts in one area of right kidney.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, mild Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, minimal
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, minimal Cyst, cortical, multiple
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, focal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild
Pancreas	-Not examined, missing
Pituitary	-Hyperplasia, focal, pars distalis

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Salivary Gland.

Animal Number: 1R-3652 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Enlarged due to mass, 1.2 cm dia.
Stomach	-Lining appears thickened (edematous); possible ulcer in cardia.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, multifocal, mild
Kidney	-Vacuolation, conv. tub. epithelium, minimal
Liver	-Portal bile duct proliferation, mild Hepatocyte vacuolation, diffuse, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, marked
Spleen	-Hemosiderosis, mild
Stomach	-Ulcer, marked
Thyroid	-Hyperplasia, C cell, multifocal, mild
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild

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Animal Number: 1R-3652 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Microscopic Observations (continued):

The following tissues were found to be within normal limits:
Heart, Testis/Epididymis, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3653 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Testis/Epididymis	-Right testis small.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, moderate
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3654 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Brain	-Dark area, possibly old hemorrhage, in anterior part of right cerebral hemisphere.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Pheochromocytoma, benign, bilateral
Brain	-Astrocytoma, benign Large neoplasm occupying much of cerebrum.
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, moderate
Liver	-Hepatocyte alteration, vacuolated, focal, mild Megalocytosis, minimal
Lung	-Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, multifocal, mild

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Animal Number: 1R-3654 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Pancreas	-Acinar atrophy, moderate
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary.

Animal Number: 1R-3655 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Soft Tissues (neck)	-Mass, 4 x 2.5 x 2 cm, salivary gland area.
Testis/Epididymis	-Right testis enlarged, pale yellowish 1.5 cm dia. mass.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, local areas, moderate
Salivary Gland	-Sialadenitis, acute, marked
Testis/Epididymis	-Tubule atrophy, spermatogenesis, unilateral, moderate Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary, Pancreas.

Animal Number: 1R-3656 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 85) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Large mass, 1 x 0.7 cm dia.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Hepatocyte vacuolation, diffuse, moderate
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild

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Animal Number: 1R-3656 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 85) Sacrificed in extremis

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Pancreas.

Animal Number: 1R-3657 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 65) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged, 0.8 cm dia.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, focal, moderate
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, local areas, mild
Pancreas	-Acinar atrophy, minimal
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Kidney, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3658 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Eye	-Right eye appears cloudy.

Microscopic Observations:

Eye	-Keratitis, chronic, unilateral, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte alteration, vacuolated, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild

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Animal Number: 1R-3658 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary	-Cyst, pars distalis
Thyroid	-Hyperplasia, C cell, focal, moderate

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3659 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Large hemorrhagic mass, 1.4 x 0.8 cm.
Liver	-Pale and mottled.

Microscopic Observations:

Adrenal	-Cortical vacuolation, diffuse, mild
	Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild
	Pelvic mineralization, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, periportal, moderate
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Testis/Epididymis	-Vascular mineralization, mild

The following tissues were found to be within normal limits:
Heart, Prostate, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3660 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild

Table: 2

Animal Number: 1R-3660 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, focal, mild
	Alveolar macrophages, multifocal, mild
Parathyroid	-Not examined, not in plane of section
Thyroid	-C cell adenoma, unilateral
	Ultimobranchial cyst

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3661 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild
Salivary Gland	-Sialadenitis, chronic, mild

The following tissues were found to be within normal limits:
Spleen, Liver, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary, Pancreas.

Animal Number: 1R-3662 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:

Eye	-Bilateral opacities
Lung	-Multiple white lesions, 0.2 cm dia., in left lobe.
Spleen	-Slightly enlarged
Liver	-Mass, 4.5 x 4 x 2 cm, left lateral lobe.
Kidney	-Both kidneys pale and enlarged.
Testis/Epididymis	-Both testes very small.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild

Animal Number: 1R-3662 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Microscopic Observations (continued):

Eye	-Cataract, bilateral
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, marked Pyelitis, acute, mild Cyst, cortical, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte alteration, vacuolated, focal, mild Hepatocellular carcinoma Large, poorly differentiated neoplasm. Trabecular and adenoid patterns.
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, local areas, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Cyst, pars distalis
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, mild
Thyroid	-Not examined, not in plane of section
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild Cystitis, chronic, diffuse, minimal

The following tissues were found to be within normal limits:
Spleen, Prostate, Stomach, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3663 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Kidney	-Cyst, 4 cm dia.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3664 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Liver	-Hyperplasia, Kupffer cell, diffuse, moderate
Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild

The following tissues were found to be within normal limits:
Spleen, Kidney, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3665 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 40) Sacrificed in extremis

Macroscopic Observations:	
Liver	-Slightly pale
Spleen	-Slightly enlarged
Mammary Gland	-Mass with ulcerated hemorrhagic surface, 6.5 x 6 x 4.5 cm, in right axilla.
Microscopic Observations:	
Liver	-Necrosis, centrilobular, mild Hematopoiesis, extramedullary, mild
Parathyroid	-Not examined, not in plane of section
Skin	-Fibrosarcoma Highly cellular neoplasm with lymphatic invasion. Surface ulcerated.
Spleen	-Hematopoiesis, extramedullary, increased, marked

The following tissues were found to be within normal limits:
Kidney, Heart, Lung, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3666 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Eye	-Opacity, right eye.
Skin	-Hair loss on limbs with scab formation; possible dermatitis.
Pituitary	-Raised dark mass, 0.8 cm dia.

Animal Number: 1R-3666 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations (continued):

Kidney (continued)	-Pale; possibly somewhat enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Eye	-Retinal atrophy, unilateral Cataract, unilateral
Heart	-Myocardial fibrosis, focal, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Portal mononuclear cell infiltrate, mild Mononuclear cell infiltration, multifocal, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild
Pancreas	-Polyarteritis, minimal
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Skin	-Ulcer, marked
Testis/Epididymis	-Polyarteritis, mild

The following tissues were found to be within normal limits:
Spleen, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1P-3667 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pyelitis, acute, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, mild
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, marked
Thyroid	-Hyperplasia, C cell, focal, mild
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Adrenal, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3668 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, focal, mild
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3669 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 70) Sacrificed in extremis

Macroscopic Observations:	
Skin	-Left side of scrotum ulcerated with rectal-scrotal abscess.
Large Intestine	-Marked impaction at terminal colon and dilatation of remaining colon and ileum containing fecal material.
Liver	-Pale
Microscopic Observations:	
Adrenal	-Within normal limits One of pair present
Esophagus	-Not examined, missing
Lung	-Alveolar macrophages, multifocal, mild Hemorrhage, multifocal, mild
Parathyroid	-Not examined, missing
Salivary Gland	-Not examined, missing
Skin	-Abscess, subcutaneous
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Liver, Kidney, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Pituitary, Small Intestine, Large Intestine, Pancreas.

Animal Number: 1R-3670 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Mesentery	-Mass, 1.3 x 1.07 cm in area of pancreas.
Kidney	-Enlarged, pale and pitted.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
Pancreas	-Adenocarcinoma
	Well differentiated, ductular pattern. Large amount of fibrous stroma.
	Acinar atrophy, mild
	Polyarteritis, moderate
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, moderate
Testis/Epididymis	-Polyarteritis, moderate

The following tissues were found to be within normal limits:
Spleen, Heart, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Lymph Node (mesenteric).

Animal Number: 1R-3671 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, marked
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Pancreas	-Acinar atrophy, mild
Parathyroid	-Not examined, missing
Salivary Gland	-Not examined, missing
Testis/Epididymis	-Polyarteritis, moderate
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Prostate, Stomach, Urinary Bladder, Pituitary.

Animal Number: 1R-3672 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Dark area
Testis/Epididymis	-Left testis small.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, basophilic, focal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
Thyroid	-Cyst, colloid

The following tissues were found to be within normal limits:
Spleen, Heart, Prostate, Stomach, Urinary Bladder, Adrenal, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3673 Sex: Male Group: (6) FC-143 30 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, multifocal, mild Megalocytosis, minimal
Lung	-Vascular mineralization, mild Perivascular mononuclear infiltrate, mild
Pancreas	-Hyperplasia, acinar cell, nodular, mild
Salivary Gland	-Sialadenitis, chronic, moderate

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary.

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Animal Number: 1R-3674 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Heart	-Myocardial fibrosis, multifocal, mild Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, mild Hepatocyte alteration, vacuolated, multifocal, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3675 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Skin	-Raised area of thickening, 1.5 cm dia., in neck area; possibly inflammation or tumor; perineal lesion appears to be inflamed area of subcutaneous fat.
Pituitary	-Slightly enlarged due to hemorrhagic area, 0.4 cm dia.
Microscopic Observations:	
Heart	-Myocarditis, chronic nonsuppurative, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Cystoid degeneration, multifocal, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild
Pancreas	-Hyperplasia, islet cell, nodular, mild
Pituitary	-Adenoma
Skin	-Fibrosarcoma, subcutaneous
Testis/Epididymis	-Vascular mineralization, mild

The following tissues were found to be within normal limits:
Spleen, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Mammary Gland.

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Animal Number: 1R-3676 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Soft Tissues (leg)	-Swollen right and left hind feet.
Mesentery	-Vessels thickened
Kidney	-Pale, pitted, enlarged.
Lymph Node (mesenteric)	-Enlarged
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, mild
	Medullary cell hyperplasia, multifocal, mild
Bone	-Arthritis, synovitis; joints, moderate
Heart	-Myocardial fibrosis, local areas, mild
Kidney	-Chronic progressive nephropathy, marked
Lung	-Vascular mineralization, mild
Mesentery	-Polyarteritis, marked
Pancreas	-Polyarteritis, moderate
Pituitary	-Cyst, pars distalis
Salivary Gland	-Sialadenitis, chronic, marked
Spleen	-Polyarteritis, moderate
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked
	Polyarteritis, marked

The following tissues were found to be within normal limits:
Liver, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-3677 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Cystoid degeneration, focal, mild
	Hepatocyte alteration, vacuolated, multifocal, mild
	Megalocytosis, minimal
	Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, multifocal, mild
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-3677 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Testis/Epididymis	-Polyarteritis, mild
	Leydig cell adenoma, unilateral

The following tissues were found to be within normal limits:
Spleen, Heart, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Trachea, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3678 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 69) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 1 x 0.7 cm dia.
Liver	-Possibly slightly pale.
Microscopic Observations:	
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Hepatocyte vacuolation, diffuse, moderate
Lung	-Vascular mineralization, mild
	Hemorrhage, multifocal, mild
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild
Stomach	-Ulcer, marked

The following tissues were found to be within normal limits:
Heart, Testis/Epididymis, Prostate, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3679 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Heart	-Myocardial fibrosis, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, mild
	Hemorrhage, local areas, moderate
Pancreas	-Hyperplasia, acinar cell, nodular, moderate

The following tissues were found to be within normal limits:
Spleen, Liver, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid,

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Animal Number: 1R-3679 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary.

Animal Number: 1R-3680 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Eye	-Opacity, left eye.
Abdomen (internal)	-Soft fatty tumor, 3 x 3 cm, attached to right wall.

Microscopic Observations:

Eye	-Cataract, unilateral
Kidney	-Chronic progressive nephropathy, moderate Pyelitis, acute, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Salivary Gland	-Sialadenitis, chronic, marked
Soft Tissues (abdomen)	-Fibrosa

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary, Pancreas.

Animal Number: 1R-3681 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Skin	-Raised ulcerated inflammatory lesions, right and left hind footpads.
Pituitary	-Small raised hemorrhagic lesion, 0.2 cm dia.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Perivascular mononuclear infiltrate, mild
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, mild
Skin	-Pododermatitis, ulcerative, bilateral, hindleg, marked

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Animal Number: 1R-3681 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Thyroid	-Follicular hyperplasia, cystic, unilateral, marked

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Stomach, Urinary Bladder, Adrenal, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3682 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Liver	-Mottled

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, mild Nodular hyperplasia, cortex, focal, moderate
Kidney	-Chronic progressive nephropathy, mild Calculus, pelvic
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, local areas, moderate
Testis/Epididymis	-Leydig cell hyperplasia, multifocal, mild
Thyroid	-Hyperplasia, C cell, focal, mild Follicular adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Stomach, Urinary Bladder, Parathyroid, Prostate, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3683 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte alteration, vacuolated, local areas, moderate
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild

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Animal Number: 1R-3683 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Parathyroid	-Not examined, not in plane of section

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-3684 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Heart	-Endocarditis, chronic, diffuse, marked
Kidney	-Chronic progressive nephropathy, mild
	Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, multifocal, mild
Salivary Gland	-Sialadenitis, chronic, moderate

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary, Pancreas.

Animal Number: 1R-3685 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 104) Sacrificed in extremis

Macroscopic Observations:

Skin	-Raised ulcerated lesion on left hind footpad.
Pituitary	-Small dark area.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
	Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pituitary	-Adenoma
Prostate	-Prostatitis, acute, mild
Salivary Gland	-Not examined, missing
Skin	-Pododermatitis, ulcerative, marked

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Animal Number: 1R-3685 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 104) Sacrificed in extremis

Microscopic Observations (continued):

Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

The following tissues were found to be within normal limits:
Heart, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Spleen, Pancreas.

Animal Number: 1R-3686 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Cystoid degeneration, focal, minimal Hepatocyte alteration, vacuolated, focal, mild
Pituitary	-Cyst, pars intermedia
Salivary Gland	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Lung, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas.

Animal Number: 1R-3687 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 98) Sacrificed in extremis

Macroscopic Observations:

Thorax (internal)	-Filled with blood tinged fluid.
Heart	-Appears enlarged
Lung	-Possible areas of consolidation.
Liver	-Mottled and possible congestion.
Kidney	-Pale and pitted.
Testis/Epididymis	-One testis appears small.
Mesentery	-Nodular mesenteric blood vessels.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, marked Sinusoidal ectasia, cortex, moderate
Heart	-Myocardial fibrosis, multifocal, mild Myocarditis, chronic nonsuppurative, multifocal, mild

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Animal Number: 1R-3687 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 98) Sacrificed in extremis

Microscopic Observations (continued):

Kidney	-Chronic progressive nephropathy, marked
	Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
	Cystoid degeneration, focal, mild
	Hepatocyte vacuolation, diffuse, mild
Lung	-Vascular mineralization, mild
	Alveolar macrophages, multifocal, mild
	Atelectasis, diffuse, moderate
	Pneumonia, interstitial, acute, local areas, moderate
Mesentery	-Polyarteritis, marked
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Prostate	-Not examined, missing
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, moderate
	Polyarteritis, moderate
	Leydig cell hyperplasia, focal, moderate
	Granuloma, spermatic

The following tissues were found to be within normal limits:
Spleen, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Eye, Pituitary.

Animal Number: 1R-3688 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 89) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged due to raised 1 cm dia. mass.
Thyroid	-One thyroid appeared slightly enlarged.
Liver	-Slightly pale
Kidney	-Pale and slightly enlarged.
Testis/Epididymis	-Appear small

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, moderate
Liver	-Hepatocyte vacuolation, local areas, mild
	Necrosis, local areas, moderate
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

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Table: 2

Animal Number: 1R-3688 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 89) Sacrificed in extremis

Microscopic Observations (continued):

Testis/Epididymis	-Tubule atrophy, aspermatogenesis, bilateral, mild
Thyroid	-Follicular hyperplasia, cystic, unilateral, marked
	Ultimobranchial cyst

The following tissues were found to be within normal limits:
Heart, Prostate, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3689 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Thyroid	-C cell adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3690 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Testis/Epididymis	-Left testis somewhat small.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, minimal
Heart	-Myocarditis, chronic nonsuppurative, local areas, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
	Megalocytosis, minimal
Parathyroid	-Not examined, not in plane of section

Animal Number: 1R-3690 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):

Pituitary	-Cyst, pars intermedia
Testis/Epididymis	-Tubule atrophy, aspermatogenesis, unilateral, marked

The following tissues were found to be within normal limits:
Spleen, Lung, Prostate, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3691 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Subcutaneous, multilobular mass, 5.5 x 4 x 5 cm, left.

Microscopic Observations:

Heart	-Myocardial fibrosis, local areas, mild Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pancreas	-Acinar atrophy, minimal
Parathyroid	-Not examined, not in plane of section
Skin	-Fibrosarcoma, subcutaneous

The following tissues were found to be within normal limits:
Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Spleen.

Animal Number: 1R-3692 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:

-No visible lesions.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Adrenal, Thyroid,

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Animal Number: 1R-3692 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-3693 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Raised ulcerated inflammed lesion, right hind footpad.
Liver	-Appears mottled
Microscopic Observations:	
Adrenal	-Cortical degeneration, focal, moderate Pheochromocytoma, benign, bilateral
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, moderate Pelvic mineralization, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Cystoid degeneration, multifocal, mild Hepatocyte alteration, vacuolated, focal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, multifocal, mild
Pancreas	-Acinar atrophy, mild
Salivary Gland	-Sialadenitis, chronic, moderate
Skin	-Pododermatitis, ulcerative, marked

The following tissues were found to be within normal limits:
Spleen, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary.

Animal Number: 1R-3694 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Reddish mass, 0.5 cm dia.
Microscopic Observations:	
Adrenal	-Pheochromocytoma, benign, unilateral
Kidney	-Chronic progressive nephropathy, mild

Animal Number: 1R-3694 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Microscopic Observations (continued):	
Liver	-Portal mononuclear cell infiltrate, mild
	Portal bile duct proliferation, mild
Lung	-Alveolar macrophages, mild
Pancreas	-Hyperplasia, islet cell, nodular, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-3695 Sex: Male Group: (6) FC-143 30 ppm
Fate: (Week= 106) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Medullary cell hyperplasia, focal, mild
	One of pair present
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative,
	multifocal, mild
Liver	-Portal mononuclear cell infiltrate, mild
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, focal, mild
Pituitary	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Kidney, Testis/Epididymis, Prostate, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Salivary Gland, Pancreas.

Animal Number: 1R-4706 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 72) Sacrificed in extremis

Macroscopic Observations:	
Mammary Gland	-Large ulcerated mass, 1.5 x 3.5 cm dia. in
	left inguinal area
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, minimal
Kidney	-Chronic progressive nephropathy, minimal
Liver	-Hematopoiesis, extramedullary, mild
Lung	-Vascular mineralization, minimal

Animal Number: 1R-4706 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 72) Sacrificed in extremis

Microscopic Observations (continued):

Mammary Gland	-Adenocarcinoma
Pancreas	-Acinar atrophy, minimal
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, marked

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4707 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 90) Found Dead

Macroscopic Observations:

Mammary Gland	-Large cystic mass, 8 x 4.5 x 2.5 cm, filled with blood, in perineal and right inguinal areas.
Pituitary	-Hemorrhagic lesion, 1.5 x 1 cm.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild
Mammary Gland	-Adenocarcinoma
Ovary	-Within normal limits One of pair present
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Lung, Uterus, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4708 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Raised mass, 0.5 cm dia.
Mammary Gland	-Small nodular mass, 1 cm dia., in left axilla; large mass, 5 x 5 x 3 cm, in right inguinal area.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate

Animal Number: 1R-4708 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Mammary Gland	-Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:
Spleen, Liver, Kidney, Heart, Lung, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4709 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Enlarged, 0.7 cm dia.
Abdomen (internal)	-Gastrointestinal tract distended with gas.
Liver	-Yellowish focal lesion, 0.9 x 0.3 cm, in fissure of median lobe; liver possibly slightly pale.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Pelvic mineralization, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, vacuolated, focal, marked
Lung	-Vascular mineralization, mild
Mammary Gland	-Galactocele
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4710 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.6 cm dia.
Mammary Gland	-Large multilobular mass, 9 x 7.5 x 3 cm, in left inguinal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, moderate
Lung	-Vascular mineralization, mild
Mammary Gland	-Fibroadenoma Extensive necrosis of tumor.
Ovary	-Cyst
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, marked Leiomyoma

The following tissues were found to be within normal limits:
Spleen, Liver, Kidney, Heart, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pancreas, Thyroid.

Animal Number: 1R-4711 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Large mass, 10 x 10 x 4 cm, in right inguinal/perineal area.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, minimal
Mammary Gland	-Fibroadenoma
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Table: 2

Animal Number: 1R-4712 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 1.3 x 1 cm.
Mammary Gland	-Cystic multilobular mass, 5 x 5 x 3 cm, in left inguinal area, filled with dark fluid; small cystic mass, 2 x 1 cm, in right inguinal area.
Pancreas	-Small nodule, 0.3 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Galactocele Adenocarcinoma
Ovary	-Cyst
Pancreas	-Islet cell adenoma
Pituitary	-Adenoma
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:
Spleen, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4713 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Found Dead

Macroscopic Observations:	
Liver	-Slightly pale
Uterus	-Left uterine horn has small clear spherical mass, 0.5 cm dia.; right uterine horn greatly enlarged and filled with dark bloody fluid.
Microscopic Observations:	
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, multifocal, mild
Lung	-Vascular mineralization, mild
Lymph Node	-Hyperplasia, reactive, moderate
Mammary Gland	-Not examined, missing

Animal Number: 1R-4713 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Found Dead

Microscopic Observations (continued):

Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild
Uterus	-Cystic glands, marked Hemangioma

The following tissues were found to be within normal limits:
Kidney, Heart, Ovary, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4714 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Milk cyst, left axilla; large mass, 8.5 x 7 x 4 cm, in left inguinal area.
Lymph Node (abdominal)	-Renal lymph nodes enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate Adenoma, cortical Tumor described as enlarged renal lymph node at necropsy.
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hegalocytosis, minimal
Lung	-Vascular mineralization, mild
Mammary Gland	-Fibroadenoma Galactocele Adenocarcinoma
Pancreas	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, mild
Uterus	-Polyp

The following tissues were found to be within normal limits:
Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary.

Animal Number: 1R-4715 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
	-No visible lesions.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, unilateral, marked
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Pelvic mineralization, moderate Polyarteritis, minimal
Liver	-Hepatocyte vacuolation, multifocal, minimal
Lung	-Vascular mineralization, mild
Ovary	-Cyst, unilateral
Pancreas	-Polyarteritis, minimal
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Spleen	-Hemosiderosis, mild

The following tissues were found to be within normal limits:
Uterus, Mammary Gland, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4716 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Hair thinning on head.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, focal, mild
Lung	-Vascular mineralization, minimal
Ovary	-Cyst, unilateral
Pituitary	-Cyst, pars intermedia

The following tissues were found to be within normal limits:
Spleen, Liver, Kidney, Heart, Uterus, Mammary Gland, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas, Skin.

Table: 2

Animal Number: 1R-4717 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 1 cm dia.
Mammary Gland	-Lobular mass, 4 x 3 x 2.5 cm, in left axilla; cystic lobular mass, 2.5 x 2 x 1.2 cm, in perineal area.
Adrenal	-Left adrenal enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Enlargement of left adrenal due to massive sinusoidal ectasia.
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, moderate
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, mild Alveolar macrophages, multifocal, mild Hemorrhage, local areas, moderate
Mammary Gland	-Fibroadenoma Galactocele Adenocarcinoma
Pituitary	-Adenoma
Uterus	-Cystic glands, mild

The following tissues were found to be within normal limits:
Spleen, Heart, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4718 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised mass, 1.3 cm dia.
Mammary Gland	-Cystic mass, 4 x 3 cm, left axilla; milk cyst in the perineal area.
Adrenal	-Right adrenal enlarged.
Kidney	-Possibly pale
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Enlargement of right adrenal due to massive sinusoidal ectasia.
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, minimal
Lung	-Hemorrhage, local areas, mild Pneumonia, foreign body, local areas, marked

Animal Number: 1R-4718 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Microscopic Observations (continued):

Mammary Gland	-Fibroadenoma
	Galactocele
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Uterus	-Cystic glands, moderate

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Salivary Gland, Pancreas.

Animal Number: 1R-4719 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 96) Sacrificed in extremis

Macroscopic Observations:

Eye	-Left eye dark, possible hemorrhage.
Pituitary	-Small hemorrhagic lesion.
Soft Tissues (neck)	-Irregular cystic subcutaneous mass, 6 x 4 x 2 cm, in neck area, possibly mammary gland or salivary gland.
Liver	-Slightly pale
Kidney	-Slightly pale and pitted.

Microscopic Observations:

Adrenal	-Cortical vacuolation, local areas, moderate
Eye	-Keratitis, acute, unilateral, marked
Kidney	-Chronic progressive nephropathy, mild
Liver	-Hepatocyte vacuolation, diffuse, mild
	Hepatocyte alteration, basophilic, focal, mild
Lung	-Hemorrhage, local areas, marked
	Metastatic neoplasm
Mammary Gland	-Adenocarcinoma
Ovary	-Cyst, unilateral
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Spleen	-Hemosiderosis, moderate

The following tissues were found to be within normal limits:
Heart, Uterus, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Pancreas.

Animal Number: 1R-4720 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass in right inguinal area appears to be inflamed milk cyst.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, focal, mild
Lung	-Alveolar macrophages, multifocal, mild Perivascular mononuclear infiltrate, mild
Mammary Gland	-Adenocarcinoma
Pancreas	-Acinar atrophy, moderate
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4721 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 95) Found Dead

Macroscopic Observations:	
Mammary Gland	-Mass, 8 x 7.5 x 3.5 cm, multilobular, right inguinal area; multilobular mass in left inguinal area.
Uterus	-Hemorrhagic lesion, 0.7 x 1 cm, left uterine horn.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Hematopoiesis, extramedullary, cortical, marked
Liver	-Hematopoiesis, extramedullary, minimal
Mammary Gland	-Fibroadenoma Adenocarcinoma
Ovary	-Within normal limits One of pair present
Pancreas	-Not examined, missing
Parathyroid	-Not examined, not in plane of section
Pituitary	-Not examined, missing
Salivary Gland	-Not examined, missing
Spleen	-Hematopoiesis, extramedullary, increased, marked

Animal Number: 1R-4721 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 95) Found Dead

Microscopic Observations (continued):

Stomach	-Hemorrhage, focal, mucosal, mild
Uterus	-Polyp

The following tissues were found to be within normal limits:
Kidney, Heart, Lung, Urinary Bladder, Thyroid, Trachea, Esophagus.

Animal Number: 1R-4722 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 83) Found Dead

Macroscopic Observations:

Mammary Gland	-Large necrotic mass, 11 x 8 x 3.5 cm, left axillary region.
Liver	-Pale
Pituitary	-Hemorrhagic mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Liver	-Necrosis, multifocal, marked
Lung	-Vascular mineralization, minimal Alveolar macrophages, multifocal, mild
Mammary Gland	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Not examined, missing
Skin	-Fibroma
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:
Kidney, Heart, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Pancreas.

Animal Number: 1R-4723 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Perineal mass appears to be inflamed milk cyst: large mass, 9 x 5 x 2 cm, in throat area.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Nephrosis, tubular, moderate

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Animal Number: 1R-4723 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Lung	-Vascular mineralization, minimal
Mammary Gland	-Adenocarcinoma, papillary
Ovary	-Tubular hyperplasia, moderate
Pituitary	-Adenoma
Uterus	-Cystic glands, marked Hyperplasia, endometrial, papillary, moderate

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4724 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Small Intestine	-Ulcerated outpouching filled with ingesta in jejunum.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Cortical degeneration, focal, mild
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild
Lung	-Vascular mineralization, minimal
Lymph Node	-Hyperplasia, reactive, moderate
Mammary Gland	-Not examined, missing
Ovary	-Tubular hyperplasia, bilateral, mild
Parathyroid	-Not examined, not in plane of section
Small Intestine	-Leiomyosarcoma, jejunum Large infiltrative tumor with mucosal surface ulcerated.
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Stomach, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas, Pituitary.

Animal Number: 1R-4725 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 94) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised red mass, 1 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Lung	-Vascular mineralization, mild Hemorrhage, multifocal, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Ovary, Mammary Gland, Stomach, Urinary Bladder, Uterus, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4726 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 0.6 cm dia.
Mammary Gland	-Small mass, appears to be milk cyst, in throat area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Nodular hyperplasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, minimal
Lung	-Vascular mineralization, minimal Hemorrhage, local areas, moderate
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Urinary Bladder	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Mammary Gland, Stomach, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4727 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Skin	-Hair loss on head and neck.
Pituitary	-Raised dark mass, 0.5 cm dia.
Mammary Gland	-Mass, 4 x 3 cm, right axillary and throat areas; mass, 3 cm dia., left side.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Pelvic mineralization, minimal
Lung	-Vascular mineralization, mild Hemorrhage, diffuse, marked
Mammary Gland	-Fibroadenoma
Ovary	-Cyst
Pancreas	-Acinar atrophy, minimal
Pituitary	-Adenoma
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Eye.

Animal Number: 1R-4728 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 84) Sacrificed in extremis

Macroscopic Observations:	
Abdomen (internal)	-Abdominal cavity filled with bloody fluid; mesentary and omentum extensively involved with nodular, granular tissue, possibly tumor or chronic inflammation.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild Cortical degeneration, focal, mild Metastatic neoplasm
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild Metastatic neoplasm
Liver	-Hepatocyte vacuolation, multifocal, minimal Hematopoiesis, extramedullary, minimal
Lung	-Vascular mineralization, mild
Mesentery	-Mesothelioma, malignant
Pancreas	-Metastatic neoplasm
Pituitary	-Adenoma
Spleen	-Metastatic neoplasm

Animal Number: 1R-4728 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 84) Sacrificed in extremis

Microscopic Observations (continued):

Stomach	-Ulcer
	Metastatic neoplasm
Urinary Bladder	-Metastatic neoplasm
Uterus	-Cystic glands, mild

The following tissues were found to be within normal limits:
Heart, Ovary, Mammary Gland, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4729 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Small raised dark mass, 1 cm dia.
Mammary Gland	-Multilobular mass, 3.5 x 3 cm, in right axilla; large multilobular mass, 9 x 6 x 3 cm, in throat area.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
	Cortical degeneration, local areas, moderate
Kidney	-Pelvic mineralization, minimal
Liver	-Portal mononuclear cell infiltrate, minimal
	Hepatocyte vacuolation, multifocal, minimal
Lung	-Vascular mineralization, mild
	Pneumonia, interstitial, chronic, local areas, mild
	Hemorrhage, multifocal, minimal
	Granuloma, multifocal, mild
Mammary Gland	-Fibroadenoma
	Fibroadenoma
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4730 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 74) Found Dead

Macroscopic Observations:	
Mammary Gland	-Multilobular ulcerated subcutaneous mass, 4 x 3 x 2.5 cm, right axilla; cystic mammary gland, 1.2 cm dia., filled with milky white fluid, in left inguinal area.
Adrenal	-Right adrenal enlarged.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, local areas, moderate
Kidney	-Chronic progressive nephropathy, mild Mineralization, intersititial, cortical, moderate
Liver	-Portal mononuclear cell infiltrate, mild Necrosis, multifocal, mild
Lung	-Vascular mineralization, minimal
Mammary Gland	-Adenocarcinoma Galactocele
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild
Uterus	-Polyp

The following tissues were found to be within normal limits:
Heart, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4731 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:	
Mammary Gland	-Circular mass, 3 cm dia., in right axilla.
Liver	-Pale and slightly enlarged.
Small Intestine	-Area of ulceration with adhesions.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, diffuse, moderate Hemosiderosis, diffuse, cortical, mild
Kidney	-Protein resorption droplets, marked
Liver	-Hepatocyte vacuolation, diffuse, marked Malignant lymphoma, histiocytic
Lung	-Malignant lymphoma, histiocytic Atelectasis, local areas, mild

Species: Rat
Project Number: 02B1CR0012

Animal Number: 1R-4731 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 99) Sacrificed in extremis

Microscopic Observations (continued):

Lymph Node (thoracic)	-Malignant lymphoma, histiocytic
Mammary Gland	-Fibroadenoma
Mesentery	-Malignant lymphoma, histiocytic
Ovary	-Malignant lymphoma, histiocytic
Pancreas	-Acinar atrophy, marked Malignant lymphoma, histiocytic
Salivary Gland	-Not examined, missing
Small Intestine	-Ulcer, marked
Spleen	-Malignant lymphoma, histiocytic
Stomach	-Ulcer, multifocal, mild
Urinary Bladder	-Malignant lymphoma, histiocytic

The following tissues were found to be within normal limits:
Uterus, Thyroid, Parathyroid, Trachea, Esophagus, Pituitary, Heart.

Animal Number: 1R-4732 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 99) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Raised mass, 0.5 cm dia.
Mammary Gland	-Cystic mass, 4 cm dia., possibly inflamed milk cyst, left inguinal area; firm cystic mass, 4 cm dia., possibly tumor, in right inguinal area; large mass, 12 x 10 x 3 cm, left and right axilla.
Adrenal	-Right adrenal enlarged; left adrenal pale mass, 0.7 cm dia.
Liver	-Appears swollen and enlarged.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, moderate Carcinoma, cortical, unilateral
Kidney	-Pelvic mineralization, marked Nephrosis, tubular, marked
Liver	-Cystoid degeneration, focal, mild Hematopoiesis, extramedullary, mild Necrosis, focal, minimal
Lung	-Vascular mineralization, minimal Alveolar macrophages, mild Metastatic neoplasm

Animal Number: 1R-4732 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 99) Sacrificed in extremis

Microscopic Observations (continued):

Mammary Gland	-Fibroadenoma
	Fibroadenoma
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4733 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Vascular mineralization, minimal
	Alveolar macrophages, multifocal, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Mammary Gland, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4734 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 95) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Hemorrhagic multilobular mass, 1.2 x 0.8 cm.
Mammary Gland	-Cystic mass, 3 x 3 x 1.5 cm, in left inguinal area.
Liver	-Possibly slightly pale.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Liver	-Hepatocyte vacuolation, periportal, moderate
Lung	-Hemorrhage, multifocal, mild
Mammary Gland	-Lobular hyperplasia, cystic
Pituitary	-Adenoma

Animal Number: 1R-4734 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 95) Sacrificed in extremis

Microscopic Observations (continued):

Spleen	-Hemosiderosis, marked
Stomach	-Ulcer, multifocal, mild

The following tissues were found to be within normal limits:
Kidney, Heart, Uterus, Ovary, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4735 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 50) Sacrificed in extremis

Macroscopic Observations:

Mammary Gland	-Large firm mass, 9 x 6.5 x 4.5 cm, ulcerated skin surface, right axilla; circular mass, 2.5 cm dia., left axilla.
Liver	-Pale areas on all lobes.

Microscopic Observations:

Adrenal	-Cortical vacuolation, focal, mild Sinusoidal ectasia, cortex, mild
Liver	-Necrosis, centrilobular, marked
Lung	-Vascular mineralization, minimal
Parathyroid	-Not examined, not in plane of section
Skin	-Fibroma Fibrosarcoma
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:
Kidney, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas, Mammary Gland.

Animal Number: 1R-4736 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

	-No visible lesions.

Microscopic Observations:

Liver	-Hepatocyte alteration, vacuolated, focal, minimal
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Thyroid	-Not examined, missing

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Animal Number: 1R-4736 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

The following tissues were found to be within normal limits:
Spleen, Kidney, Heart, Lung, Uterus, Ovary, Mammary Gland, Stomach, Urinary Bladder, Adrenal, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4737 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised mass, 0.6 cm dia.
Mammary Gland	-Mass, 2 x 1.5 cm, in perineal area; mass, 5 x 4 x 1 cm, in right inguinal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, periportal, mild
Lung	-Vascular mineralization, minimal
Mammary Gland	-Fibroadenoma Fibroadenoma
Ovary	-Tubular hyperplasia, bilateral, moderate
Pancreas	-Not examined, missing
Pituitary	-Adenoma
Salivary Gland	-Sialadenitis, chronic, mild
Uterus	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Heart, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus.

Animal Number: 1R-4738 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 101) Sacrificed in extremis

Macroscopic Observations:	
Mammary Gland	-Large subcutaneous mass, 9 x 12 x 5 cm, in right axilla.
Adrenal	-Left adrenal slightly enlarged.
Microscopic Observations:	
Adrenal	-Cortical vacuolation, local areas, moderate Sinusoidal ectasia, cortex, moderate Nodular hyperplasia, cortex, focal, moderate
Kidney	-Pelvic mineralization, mild

Animal Number: 1R-4738 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 101) Sacrificed in extremis

Microscopic Observations (continued):

Liver	-Hepatocyte alteration, basophilic, focal, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Not examined, missing
Pituitary	-No diagnosis, inadequate section
Skin	-Fibroma
Stomach	-Necrosis, focal, mucosal, mild
Thyroid	-Hyperplasia, C cell, focal, mild

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Urinary Bladder, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4739 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Very large multilobular mass, 14.5 x 10 x 6.5 cm, in the axillary and lateral area.
Spleen	-Enlarged

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate Hematopoiesis, extramedullary, cortical, moderate
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Protein resorption droplets, tubular, mild Pigment, conv. tub. epithelium, moderate Nephrosis, tubular, mild
Liver	-Hematopoiesis, extramedullary, mild
Lung	-Vascular mineralization, mild Hyperplasia, septal cell, focal, mild
Mammary Gland	-Not examined, missing
Skin	-Fibrosarcoma Extensive necrosis and ulceration. No mammary tissue in tumor.
Spleen	-Hematopoiesis, extramedullary, increased, marked

The following tissues were found to be within normal limits:
Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus,

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Animal Number: 1R-4739 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-4740 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Mammary Gland	-Mass, 4 x 3 x 1 cm, in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
	Medullary cell hyperplasia, multifocal, mild
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte alteration, vacuolated, mild
	Hepatocyte alteration, basophilic, mild
Lung	-Vascular mineralization, mild
	Perivascular mononuclear infiltrate, mild
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma
Thyroid	-Ultimobranchial cyst

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4741 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Raised dark mass, 1.3 cm dia.
Mammary Gland	-Nodular lesion, 1 cm dia., in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild
Lung	-Vascular mineralization, minimal
	Hemorrhage, focal, mild
Mammary Gland	-Lobular hyperplasia
Parathyroid	-Not examined, not in plane of section
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Trachea, Esophagus,

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Animal Number: 1R-4741 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Sacrificed in extremis

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Salivary Gland, Pancreas.

Animal Number: 1R-4742 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 83) Found Dead

Macroscopic Observations:

Mammary Gland	-Large multilobular mass, 10 x 9 x 3 cm, in right axilla; necrotic mass, 4 x 3 cm, in left inguinal area.
Adrenal	-Possibly slightly enlarged.
Pituitary	-Hemorrhagic mass, 0.5 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Kidney	-Pelvic mineralization, mild
Liver	-Necrosis, multifocal, mild Atrophy, hepatocytes, centrilobular, moderate
Lung	-Vascular mineralization, mild
Mammary Gland	-Fibroadenoma Fibroadenoma
Pancreas	-Not examined, missing
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Spleen	-Not examined, missing
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Salivary Gland.

Animal Number: 1R-4743 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Sacrificed in extremis

Macroscopic Observations:

Pituitary	-Raised hemorrhagic mass, 1 cm dia.
Mammary Gland	-Circular mass, 2 cm dia, in perineal area.
Lung	-Areas of consolidation in right anterior and apical lobes.
Liver	-Possibly mottled

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Animal Number: 1R-4743 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Sacrificed in extremis

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Pelvic mineralization, marked
Liver	-Hepatocyte vacuolation, periportal, moderate Hepatocyte alteration, basophilic, focal, mild
Lung	-Vascular mineralization, mild Pneumonia, acute exudative, local areas, mild Hemorrhage, multifocal, mild
Mammary Gland	-Fibroadenoma
Pancreas	-Acinar atrophy, mild
Pituitary	-Adenoma
Urinary Bladder	-Epithelial hyperplasia, simple, diffuse, mild
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:
Spleen, Heart, Ovary, Stomach, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Skin.

Animal Number: 1R-4744 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 48) Found Dead

Macroscopic Observations:

Mammary Gland	-Mass, 8.5 x 7.5 x 4.5 cm, hollow cavity filled with brown matter, in left inguinal area.
Heart	-Possibly slightly enlarged.
Lung	-Multiple grayish tan raised nodules, 0.1 - 0.3 cm dia.; 2 nodules in left lobe; 3 nodules in right cardiac lobe; 2 nodules in right intermediate lobe; 3 nodules in right diaphragmatic lobe.

Microscopic Observations:

Kidney	-Chronic progressive nephropathy, minimal
Lung	-Metastatic neoplasm Hemorrhage, local areas, mild
Mammary Gland	-Adenocarcinoma Extensive necrosis in tumor; areas highly anaplastic. Locally invasive. Multiple lung metastases.
Pituitary	-No diagnosis, inadequate section
Spleen	-Hematopoiesis, extramedullary, increased, moderate

Animal Number: 1R-4744 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 48) Found Dead

Microscopic Observations (continued):

The following tissues were found to be within normal limits:
Liver, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4745 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Small raised dark mass, 0.4 cm dia.
Mammary Gland	-Mass, 5 x 4 x 2 cm, in perineal area.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Fibroadenoma
Ovary	-Tubular hyperplasia, unilateral, moderate Granulosa cell tumor, benign, unilateral
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Uterus, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Salivary Gland, Pancreas.

Animal Number: 1R-4746 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 87) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Enlarged with 0.7 cm dia. mass.
Mammary Gland	-Multilobular mass, 11 x 6 x 3 cm, in left inguinal area.
Spleen	-Slightly enlarged
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Pelvic mineralization, minimal
Liver	-Hepatocyte vacuolation, multifocal, minimal Hepatocyte alteration, basophilic, multifocal, mild Hematopoiesis, extramedullary, multifocal, minimal

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Table: 2

Animal Number: 1R-4746 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 87) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild
Mammary Gland	-Adenocarcinoma
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:
Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas.

Animal Number: 1R-4747 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Lobular mass, 5 x 4 x 3 cm, in throat area; lobular mass, 5 x 2.6 x 1.5 cm, in left axilla; lobular mass, 7 x 4.5 x 3 cm, in right inguinal area.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild Medullary cell hyperplasia, multifocal, mild
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hematopoiesis, extramedullary, minimal Hepatocyte alteration, basophilic, multifocal, mild
Lung	-Vascular mineralization, minimal Alveolar macrophages, mild
Mammary Gland	-Fibroadenoma Fibroadenoma
Ovary	-Cyst, unilateral
Pancreas	-Not examined, missing
Skin	-Fibroma
Spleen	-Hematopoiesis, extramedullary, increased, mild

The following tissues were found to be within normal limits:
Kidney, Heart, Uterus, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary.

Animal Number: 1R-4748 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 81) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Enlarged due to red mass, 1.3 x 1.2 x 0.8 cm.
Mammary Gland	-Subcutaneous mass, 3.5 x 3.9 cm, left axillary; subcutaneous mass, 1.5 x 2 cm, left inguinal.
Adrenal	-Right adrenal darkened and enlarged, 1.4 cm dia., filled with reddish liquid.
Kidney	-Small cyst, 0.4 cm dia., on surface of left kidney.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked Cortical degeneration, moderate
Esophagus	-Not examined, missing
Kidney	-Chronic progressive nephropathy, mild
Liver	-Portal mononuclear cell infiltrate, mild Hepatocyte alteration, basophilic, multifocal, mild
Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild
Mammary Gland	-Fibroadenoma Adenocarcinoma Galactocele
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Thyroid	-Not examined, missing
Trachea	-Not examined, missing
Urinary Bladder	-Epithelial hyperplasia, simple, local areas, mild

The following tissues were found to be within normal limits:
Spleen, Heart, Uterus, Ovary, Stomach, Salivary Gland, Pancreas.

Animal Number: 1R-4749 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 82) Sacrificed in extremis

Macroscopic Observations:	
Pituitary	-Hemorrhagic mass, 1 x 0.5 cm dia.
Mammary Gland	-Small milk cyst present.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, marked
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, mild

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Animal Number: 1R-4749 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 82) Sacrificed in extremis

Microscopic Observations (continued):

Lung	-Vascular mineralization, mild Hemorrhage, local areas, mild
Mammary Gland	-Galactocele
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Uterus, Ovary, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pancreas, Eye, Skin.

Animal Number: 1R-4750 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 97) Found Dead

Macroscopic Observations:

Mammary Gland	-Multilobular mass, 0.3 x 2 cm, in right inguinal area; multilobular mass, 8.5 x 5 x 4 cm, in right axilla.
Pituitary	-Enlarged, 0.9 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, mild
Harderian Gland	-Adenocarcinoma Not described at necropsy. Probably from clinically described atrophic right eye.
Kidney	-Pelvic mineralization, mild
Liver	-Hepatocyte vacuolation, multifocal, mild
Lung	-Edema, local areas, mild
Mammary Gland	-Fibroadenoma Galactocele Fibroadenoma
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Thyroid	-Not examined, missing
Uterus	-Cystic glands, marked

The following tissues were found to be within normal limits:
Spleen, Heart, Ovary, Stomach, Urinary Bladder, Trachea, Esophagus, Salivary Gland, Pancreas.

Table: 2

Animal Number: 1R-4751 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 42) Found Dead

Macroscopic Observations:	
Mammary Gland	-Subcutaneous mass, 8 x 5.5 x 4.5 cm., right axilla
Microscopic Observations:	
Kidney	-Pelvic mineralization, minimal
Lung	-Vascular mineralization, minimal
Skin	-Fibroma
Spleen	-Hematopoiesis, extramedullary, increased, moderate
Stomach	-Ulcer

The following tissues were found to be within normal limits:
Liver, Heart, Uterus, Ovary, Mammary Gland, Urinary Bladder, Adrenal, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland, Pituitary, Pancreas.

Animal Number: 1R-4752 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Raised hemorrhagic mass, 0.4 cm dia.
Microscopic Observations:	
Adrenal	-Sinusoidal ectasia, cortex, moderate Nodular hyperplasia, cortex, moderate
Kidney	-Chronic progressive nephropathy, mild Pelvic mineralization, minimal
Lung	-Vascular mineralization, mild
Ovary	-Cyst, bilateral Tubular hyperplasia, bilateral, moderate
Pancreas	-Hyperplasia, islet cell, mild
Pituitary	-Adenoma

The following tissues were found to be within normal limits:
Spleen, Liver, Heart, Uterus, Mammary Gland, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus, Salivary Gland.

Animal Number: 1R-4753 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:	
Pituitary	-Enlarged with small dark lesions, 0.2 cm dia.
Skin	-Hair loss on head.
Mammary Gland	-Lobular mass, 4 x 3 x 2 cm, in perineal area.

Animal Number: 1R-4753 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):

Adrenal	-Sinusoidal ectasia, cortex, mild
Kidney	-Pelvic mineralization, unilateral, marked
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild
Mammary Gland	-Fibroadenoma
Ovary	-Tubular hyperplasia, bilateral, moderate
Pituitary	-Adenoma
Spleen	-Not examined, missing

The following tissues were found to be within normal limits:
Heart, Uterus, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus,
Salivary Gland, Pancreas.

Animal Number: 1R-4754 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Mammary Gland	-Lobulated mass, 8 x 6 x 3 cm, in inguinal and perineal areas; mass is quite necrotic and cystic.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Kidney	-Pigment, conv. tub. epithelium, brown, moderate
Liver	-Portal mononuclear cell infiltrate, mild Portal bile duct proliferation, mild Hepatocyte vacuolation, multifocal, mild Hepatocyte alteration, vacuolated, mild
Lung	-Vascular mineralization, mild Pneumonia, interstitial, chronic, multifocal, mild Alveolar macrophages, multifocal, mild
Mammary Gland	-Adenocarcinoma
Ovary	-Cyst, unilateral
Pituitary	-Adenoma
Spleen	-Hematopoiesis, extramedullary, increased, moderate

The following tissues were found to be within normal limits:
Heart, Uterus, Stomach, Urinary Bladder, Thyroid, Parathyroid, Trachea, Esophagus,

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Animal Number: 1R-4754 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Microscopic Observations (continued):
The following tissues were found to be within normal limits (continued):
Salivary Gland, Pancreas.

Animal Number: 1R-4755 Sex: Female Group: (6) FC-143 30 ppm
Fate: (Week= 105) Terminal Sacrifice

Macroscopic Observations:

Pituitary	-Hemorrhagic mass, 0.7 cm dia.

Microscopic Observations:

Adrenal	-Sinusoidal ectasia, cortex, moderate
Esophagus	-Not examined, missing
Heart	-Myocarditis, chronic nonsuppurative, multifocal, mild
Kidney	-Chronic progressive nephropathy, minimal Pelvic mineralization, mild
Liver	-Hepatocyte alteration, basophilic, focal, mild
Lung	-Alveolar macrophages, focal, minimal
Ovary	-Tubular hyperplasia, bilateral, moderate
Parathyroid	-Not examined, missing
Pituitary	-Adenoma
Thyroid	-Not examined, missing
Trachea	-Not examined, missing

The following tissues were found to be within normal limits:
Spleen, Uterus, Mammary Gland, Stomach, Urinary Bladder, Salivary Gland, Pancreas, Skin.

Tissue Inventory

Table: 3

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name \ Animal Numbers	1R-3516	1R-3517	1R-3520	1R-3522	1R-3527	1R-3535	1R-3543	1R-3546	1R-3550	1R-3551	1R-3559	1R-3568	1R-3570	1R-3575	1R-3580	1R-4578	1R-4582	1R-4585	1R-4588	1R-4589	1R-4590	1R-4601	1R-4608	1R-4610	1R-4620
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	c	+	+
Mammary Gland	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
Ovary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	c	c	c	c	+	c	+	+	+	+	+	c	c	+	c	c	c	c	+	c	+	+	+	c	+
Pituitary	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-
Salivary Gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-
Thyroid	c	c	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	c
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
-------------------- The following tissue(s) were not required by protocol ------------------																									
Mesentary	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Skin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-
Ureter	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012
Species: Rat

Tissue Name	Sex	Dose Group Name: CONTROL 0 ppm Animal Numbers	1 1 1 1 1 R R R R R - - - - - 4 4 4 4 4 6 6 6 6 6 2 3 3 3 4 9 0 1 2 0 F F F F F
Adrenal			+ + + + +
Aorta			c + + + +
Bone Marrow			+ + + + +
Brain			+ + + + +
Esophagus			+ + + + +
Eye			+ + + + +
Heart			+ + + + +
Kidney			+ + + + +
Large Intestine			+ + + + +
Liver			+ + + + +
Lung			+ + + + +
Lymph Node (mesenteric)			+ + c + +
Mammary Gland			+ + + + +
Ovary			+ + + + +
Pancreas			+ + + + +
Parathyroid			c c c + c
Pituitary			+ + + + +
Prostate			- - - - -
Salivary Gland			+ + + + +
Small Intestine			+ + + + +
Spinal Cord			+ + + + +
Spleen			+ + + + +
Stomach			+ + + + +
Testis/Epididymis			- - - - -
Thyroid			+ c + + +
Trachea			+ + + + +
Urinary Bladder			+ + c + +
Uterus			+ + + + +
---------- The following tissue(s) were not required by protocol ----------			
Mesentary			- - - - -
Skin			+ - - - -
Ureter			- - - - -

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Animal Numbers	1R-3584	1R-3588	1R-3589	1R-3592	1R-3598	1R-3604	1R-3613	1R-3617	1R-3620	1R-3622	1R-3626	1R-3627	1R-3638	1R-3642	1R-3643	1R-4642	1R-4652	1R-4655	1R-4656	1R-4664	1R-4666	1R-4669	1R-4671	1R-4674	1R-4676
Tissue Name / Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	c	+	c	+	+	c	+	+	c	+	+	+	+	+	+	+	+	c	+	+	+	+	+	c	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	+	+	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	c	+	+	+	+	+	+
Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	c	+	+	+
Ovary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	c	+	c	c	c	c	c	+	c	c	c	c	+	c	c	c	c	+	+	+	+	+	c	c	+
Pituitary	+	+	+	+	c	+	+	+	+	+	c	+	c	+	+	+	+	c	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	c	+	+	c	+	+	-	-	-	-	-	-	-	-	-	-
Salivary Gland	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-
Thyroid	+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	+	c	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+
---- The following tissue(s) were not required by protocol ----																									
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ureter	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

		Dose Group Name: FC-143 300 ppm				
		1	1	1	1	1
		R	R	R	R	R
	Animal Numbers	-	-	-	-	-
		4	4	4	4	4
		6	6	6	6	7
		8	8	9	9	0
		7	9	2	9	4
Tissue Name	Sex	F	F	F	F	F
Adrenal		+	+	+	+	+
Aorta		+	+	+	+	+
Bone Marrow		+	+	+	+	+
Brain		+	+	+	+	+
Esophagus		c	+	+	+	+
Eye		+	+	+	+	+
Heart		+	+	+	+	+
Kidney		+	+	+	+	+
Large Intestine		+	+	+	+	+
Liver		+	+	+	+	+
Lung		+	+	+	+	+
Lymph Node (mesenteric)		+	+	c	+	+
Mammary Gland		c	+	+	+	+
Ovary		+	+	+	+	+
Pancreas		+	+	+	+	+
Parathyroid		c	c	+	+	+
Pituitary		+	+	+	+	+
Prostate		-	-	-	-	-
Salivary Gland		+	+	+	+	+
Small Intestine		+	+	+	+	+
Spinal Cord		+	+	+	+	+
Spleen		+	+	+	+	+
Stomach		+	+	+	+	+
Testis/Epididymis		-	-	-	-	-
Thyroid		+	c	+	+	c
Trachea		+	+	+	+	+
Urinary Bladder		+	+	+	+	+
Uterus		+	+	+	+	+
---------- The following tissue(s) were not required by protocol ----------						
Mesentary		-	-	-	-	-
Skin		-	-	-	-	-
Ureter		+	-	-	-	-

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Tissue Inventory

Table: 4

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name	Animal Numbers	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R
		3518	3519	3521	3523	3524	3525	3526	3528	3529	3530	3531	3532	3533	3534	3536	3537	3538	3539	3540	3541	3542	3544	3545	3547	3548
	Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Adrenal		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone Marrow		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+
Brain		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus		+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Eye		+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	c	+	+	+	+	+	+	c	+	+
Heart		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)		+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+
Mammary Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovary		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+
Parathyroid		c	+	c	+	c	c	+	+	c	+	+	+	+	c	+	c	c	c	+	+	+	c	+	+	c
Pituitary		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate		+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	+
Salivary Gland		+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small Intestine		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+
Spleen		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+
Thyroid		c	+	+	+	+	+	+	+	+	+	+	+	+	c	+	c	+	+	+	+	c	+	+	+	+
Trachea		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	+
Uterus		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
---------- The following tissue(s) were not required by protocol ----------																										
Bone		-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name	Animal Numbers	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
		R R R R R R R R R R R R R R R R R R R R R R R R
		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
		5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
		1 1 2 2 2 2 2 2 3 3 3 3 3 3 3 3 4 4 4 4 4 4 4 4
		8 9 1 3 4 5 6 8 9 0 1 2 3 4 6 7 8 9 0 1 2 4 5 7 8
	Sex	M M M M M M M M M M M M M M M M M M M M M M M M
Preputial Gland		- -
Skin		+ - + + - - - - + - - - - - + + - - - + - - + - -
Soft Tissues (abdomen)		- -
Soft Tissues (head)		- -
Soft Tissues (leg)		- -
Soft Tissues (neck)		- -
Soft Tissues (thorax)		- -
Thymus		- - - - - - - - - - - - - - + - - - - - - - - - -
Unidentified Tissue		- -
General Comment		- -

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000772

Table: 4

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name	Animal Numbers	1R 3549M	1R 3552M	1R 3553M	1R 3554M	1R 3555M	1R 3556M	1R 3557M	1R 3558M	1R 3560M	1R 3561M	1R 3562M	1R 3563M	1R 3564M	1R 3565M	1R 3566M	1R 3567M	1R 3569M	1R 3571M	1R 3572M	1R 3573M	1R 3574M	1R 3576M	1R 3577M	1R 3578M	1R 3579M
Adrenal		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Aorta		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Bone Marrow		+	+	+	+	+	+	+	+	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Brain		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Eye		+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Heart		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine		+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Liver		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)		+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	c	+	+	+	+
Mammary Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovary		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas		+	+	c	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	+	+	+	+	+	+	+
Parathyroid		c	c	+	c	c	c	+	c	+	c	c	+	c	c	c	+	+	c	c	c	c	c	+	+	c
Pituitary		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+
Prostate		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Salivary Gland		+	+	c	+	+	+	+	+	+	+	c	+	c	c	+	+	+	+	+	+	c	+	+	+	+
Small Intestine		+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord		+	+	+	+	+	+	+	+	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Spleen		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+
Testis/Epididymis		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid		c	+	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Trachea		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder		+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	c	+	+	+
Uterus		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
---------- The following tissue(s) were not required by protocol ----------																										
Bone		-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-

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000773

Tissue Inventory (continued)

Table: 4

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name	Animal Numbers	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R
		3549	3552	3553	3554	3555	3556	3557	3558	3560	3561	3562	3563	3564	3565	3566	3567	3569	3571	3572	3573	3574	3576	3577	3578	3579
	Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Preputial Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin		-	-	-	-	-	-	-	-	-	-	+	+	-	+	-	+	-	-	-	-	+	-	-	+	+
Soft Tissues (abdomen)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

Tissue Inventory (continued)

Table: 4

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: CONTROL 0 ppm

Animal Numbers	1R4576	1R4577	1R4579	1R4580	1R4581	1R4583	1R4584	1R4586	1R4587	1R4591	1R4592	1R4593	1R4594	1R4595	1R4596	1R4597	1R4598	1R4599	1R4600	1R4602	1R4603	1R4604	1R4605	1R4606	1R4607
Tissue Name / Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	c	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	c	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	c
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	c	c	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	c	c	c	+	+	+	+	+	c	c	+	c	+	c	c	+	+	+	+	+	+	+	+	+
Mammary Gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivary Gland	c	+	+	+	+	+	+	+	c	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	c
Small Intestine	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
------ The following tissue(s) were not required by protocol ------																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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Tissue Inventory (continued)

Table: 4

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name	Animal Numbers	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R
		4576	4577	4579	4580	4581	4583	4584	4586	4587	4591	4592	4593	4594	4595	4596	4597	4598	4599	4600	4602	4603	4604	4605	4606	4607
	Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Preputial Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin		-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-
Soft Tissues (abdomen)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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Tissue Inventory (continued)

Table: 4

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name / Animal Numbers	1R-4609	1R-4611	1R-4612	1R-4613	1R-4614	1R-4615	1R-4616	1R-4617	1R-4618	1R-4619	1R-4621	1R-4622	1R-4623	1R-4624	1R-4625	1R-4626	1R-4627	1R-4628	1R-4633	1R-4634	1R-4635	1R-4636	1R-4637	1R-4638	1R-4639
Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	+	+	c	+	+	+	+	+	c	+	+	+	+	+	+	c	+	+	+	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	c	+	+	+	+	c	c	c	+	c	+	c	+	+	c	c	c	c	+	+	c	+
Eye	+	+	c	+	+	+	+	+	+	c	+	+	+	+	c	+	+	+	+	+	c	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mammary Gland	+	+	+	+	+	+	c	c	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	c	c	c	c	c	c	c	c	c	c	c	c	+	c	c	c	c	c	c	c	c	c	+	c	+
Pituitary	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+	+	c	+	+	c	+
Prostate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivary Gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	c	+	+	+	c
Small Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
-------------------- The following tissue(s) were not required by protocol ------------------																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

389

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
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Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: CONTROL 0 ppm

Tissue Name / Animal Numbers	1R4609	1R4611	1R4612	1R4613	1R4614	1R4615	1R4616	1R4617	1R4618	1R4619	1R4621	1R4622	1R4623	1R4624	1R4625	1R4626	1R4627	1R4628	1R4633	1R4634	1R4635	1R4636	1R4637	1R4638	1R4639
Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Preputial Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-
Soft Tissues (abdomen)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

390

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Tissue Inventory (continued)

Table: 4

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 300 ppm

Tissue Name / Animal Numbers	1R3581	1R3582	1R3583	1R3585	1R3586	1R3587	1R3590	1R3591	1R3593	1R3594	1R3595	1R3596	1R3597	1R3599	1R3600	1R3601	1R3602	1R3603	1R3605	1R3606	1R3607	1R3608	1R3609	1R3610	1R3611
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	c	+	+	+	c	c	+	c	c	+	+	+	+	+	+	+	c	+	c	+	+	c	+	c
Pituitary	+	+	+	+	+	+	c	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary Gland	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small Intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	c	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
The following tissue(s) were not required by protocol																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

391

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Animal Numbers	1R-3581	1R-3582	1R-3583	1R-3585	1R-3586	1R-3587	1R-3590	1R-3591	1R-3593	1R-3594	1R-3595	1R-3596	1R-3597	1R-3599	1R-3600	1R-3601	1R-3602	1R-3603	1R-3605	1R-3606	1R-3607	1R-3608	1R-3609	1R-3610	1R-3611
Tissue Name / Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Preputial Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-
Soft Tissues (abdomen)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

392

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Animal Numbers	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	R R R R R R R R R R R R R R R R R R R R R R R R R
	3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
	1 1 1 1 1 2 2 2 2 2 3 3 3 3 3 3 3 4 4 4 4 4 4 4 4
	2 4 5 6 8 9 1 3 4 5 8 9 0 1 2 3 4 5 6 7 9 0 1 4 5
Tissue Name Sex	M M M M M M M M M M M M M M M M M M M M M M M M M
Adrenal	+ +
Aorta	+ +
Bone Marrow	+ +
Brain	+ +
Esophagus	+ +
Eye	+ +
Heart	+ +
Kidney	+ +
Large Intestine	+ +
Liver	+ +
Lung	+ +
Lymph Node (mesenteric)	+ +
Mammary Gland	- -
Ovary	- -
Pancreas	+ + + + + + + + + + + + + + + + + + c + + + +
Parathyroid	+ + c + + + c + + + c + + + + + c + + + c + + + +
Pituitary	+ + + + + + + c + + + + c + + + + + + + + + + +
Prostate	+ c +
Salivary Gland	+ + + c + c + + + + + + + + + + + + c + + + + +
Small Intestine	+ +
Spinal Cord	+ +
Spleen	+ +
Stomach	+ +
Testis/Epididymis	+ +
Thyroid	+ +
Trachea	+ +
Urinary Bladder	+ +
Uterus	- -
---------- The following tissue(s) were not required by protocol ----------	
Bone	- - - - - - - - - - - - - - - - - - + - - - - - -
Clitoral Gland	- -
Harderian Gland	- -
Lymph Node	- -
Lymph Node (abdominal)	- -
Lymph Node (thoracic)	- -
Mesentary	- -

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CC0781

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Tissue Name	Animal Numbers / Sex	1 1 1 1 1-1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
		R R R R R-R R R R R R R R R R R R R R R R R R R R R
		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
		6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
		1 1 1 1 1 1 2 2 2 2 2 2 3 3 3 3 3 3 3 3 4 4 4 4 4
		2 4 5 6 8 9 1 3 4 5 8 9 0 1 2 3 4 5 6 7 9 0 1 4 5
	Sex	M M M M M M M M M M M M M M M M M M M M M M M M M
Preputial Gland		- -
Skin		- -
Soft Tissues (abdomen)		- -
Soft Tissues (head)		- -
Soft Tissues (leg)		- -
Soft Tissues (neck)		- -
Soft Tissues (thorax)		- +
Thymus		- + - - - - -
Unidentified Tissue		- -
General Comment		- -

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000782

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Tissue Name / Animal Numbers	1R-4641	1R-4643	1R-4644	1R-4645	1R-4646	1R-4647	1R-4648	1R-4649	1R-4650	1R-4651	1R-4653	1R-4654	1R-4657	1R-4658	1R-4659	1R-4660	1R-4661	1R-4662	1R-4663	1R-4665	1R-4667	1R-4668	1R-4670	1R-4672	1R-4673
Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	c	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	c	c	+	+	+	c	+	+	+	c	c	c	+	c	c	c	c	c	+	c	c	+	+	c	+
Eye	+	+	+	+	+	+	c	+	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	+	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	c	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+
Mammary Gland	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	c	c	c	+	+
Ovary	c	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	c	+	c	c	c	c	c	c	c	+	+	+	c	+	c	c	+	c	+	c	c	+	c	c
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivary Gland	c	+	+	+	c	+	+	c	+	c	+	+	+	c	+	+	+	+	+	+	c	+	+	+	+
Small Intestine	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroid	+	+	+	+	+	c	+	+	+	c	+	+	+	c	+	+	+	+	+	+	+	c	+	c	c
Trachea	+	+	+	+	+	c	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	c	+
Urinary Bladder	+	+	c	+	+	c	+	+	+	c	+	+	c	+	+	+	+	+	+	+	+	c	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
------- The following tissue(s) were not required by protocol -------																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 300 ppm

Tissue Name / Animal Numbers	1R-4641	1R-4643	1R-4644	1R-4645	1R-4646	1R-4647	1R-4648	1R-4649	1R-4650	1R-4651	1R-4653	1R-4654	1R-4657	1R-4658	1R-4659	1R-4660	1R-4661	1R-4662	1R-4663	1R-4665	1R-4667	1R-4668	1R-4670	1R-4672	1R-4673
Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Preputial Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (abdomen)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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Tissue Inventory (continued)

Table: 4

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 300 ppm

Animal Numbers	1R-4675	1R-4677	1R-4678	1R-4679	1R-4680	1R-4681	1R-4682	1R-4683	1R-4684	1R-4685	1R-4686	1R-4688	1R-4690	1R-4691	1R-4693	1R-4694	1R-4695	1R-4696	1R-4697	1R-4698	1R-4700	1R-4701	1R-4702	1R-4703	1R-4705
Tissue Name / Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Adrenal	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+
Bone Marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	c	c	+	c	+	c	c	c	c	c	c	+	+	+	+	+	+	+	+	+	+	+	c	c	c
Eye	+	+	+	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	+	+	+	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	+	+	+	+	c	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+
Mammary Gland	+	+	+	+	+	+	+	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+
Parathyroid	c	+	c	+	c	c	c	c	c	+	+	+	c	+	+	c	+	+	+	+	c	c	+	+	+
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivary Gland	+	+	+	+	+	+	c	+	c	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Small Intestine	+	+	+	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal Cord	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thyroid	+	+	+	+	+	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	c	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Uterus	+	+	+	+	c	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
-------------------- The following tissue(s) were not required by protocol ------------------																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: FC-143 300 ppm

Tissue Name	Animal Numbers	Sex	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
			R R R R R R R R R R R R R R R R R R R R R R R R R
			4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
			6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 7 7 7 7 7
			7 7 7 7 8 8 8 8 8 8 8 8 9 9 9 9 9 9 9 9 0 0 0 0 0
			5 7 8 9 0 1 2 3 4 5 6 8 0 1 3 4 5 6 7 8 0 1 2 3 5
Preputial Gland		F	- -
Skin		F	- -
Soft Tissues (abdomen)		F	- -
Soft Tissues (head)		F	- -
Soft Tissues (leg)		F	- -
Soft Tissues (neck)		F	- -
Soft Tissues (thorax)		F	- -
Thymus		F	- -
Unidentified Tissue		F	- - - - - - - - + - - - - - - - - - - - - - - - -
General Comment		F	- -

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
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000786

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name / Animal Numbers	1R3646	1R3647	1R3648	1R3649	1R3650	1R3651	1R3652	1R3653	1R3654	1R3655	1R3656	1R3657	1R3658	1R3659	1R3660	1R3661	1R3662	1R3663	1R3664	1R3665	1R3666	1R3667	1R3668	1R3669	1R3670
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Esophagus	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Eye	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	+	-	-	-	-
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+
Mammary Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas	c	+	c	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	+	+	+	+	+	+	c	+	c	+	+	c	c	+	c	+	+	c	+	+	+	c	+
Pituitary	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary Gland	+	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	+	+	+	+	+	+	+	c	+
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
Spinal Cord	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	c	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
---- The following tissue(s) were not required by protocol ----																									
Bone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

399

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
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Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name / Animal Numbers	1R-3646	1R-3647	1R-3648	1R-3649	1R-3650	1R-3651	1R-3652	1R-3653	1R-3654	1R-3655	1R-3656	1R-3657	1R-3658	1R-3659	1R-3660	1R-3661	1R-3662	1R-3663	1R-3664	1R-3665	1R-3666	1R-3667	1R-3668	1R-3669	1R-3670
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Preputial Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	+	-
Soft Tissues (abdomen)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

400

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Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name / Animal Numbers	1R3671	1R3672	1R3673	1R3674	1R3675	1R3676	1R3677	1R3678	1R3679	1R3680	1R3681	1R3682	1R3683	1R3684	1R3685	1R3686	1R3687	1R3688	1R3689	1R3690	1R3691	1R3692	1R3693	1R3694	1R3695
Sex	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brain	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Esophagus	c	+	+	+	+	+	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c
Eye	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph Node (mesenteric)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mammary Gland	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ovary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+
Parathyroid	c	c	+	c	+	+	c	+	+	+	+	+	c	+	+	+	c	c	c	c	c	+	+	+	+
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	c
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	c	+	+	+	+	+	+	+	+
Salivary Gland	c	+	+	+	+	+	+	+	+	+	+	+	+	+	c	c	+	+	+	+	+	+	+	+	+
Small Intestine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spinal Cord	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testis/Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
The following tissue(s) were not required by protocol																									
Bone	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clitoral Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Harderian Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (abdominal)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lymph Node (thoracic)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mesentary	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name	Animal Numbers	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
		R R R R R R R R R R R R R R R R R R R R R R R R R
		3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
		6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
		7 7 7 7 7 7 7 7 8 8 8 8 8 8 8 8 8 9 9 9 9 9 9 9 9
		1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5
	Sex	M M M M M M M M M M M M M M M M M M M M M M M M M
Preputial Gland		- -
Skin		- - - - + - - - - - + - - - + - - - - - + - + - -
Soft Tissues (abdomen)		- - - - - - - - - + - - - - - - - - - - - - - - -
Soft Tissues (head)		- -
Soft Tissues (leg)		- -
Soft Tissues (neck)		- -
Soft Tissues (thorax)		- -
Thymus		- -
Unidentified Tissue		- -
General Comment		- -

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
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000790

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name	Animal Numbers	1 1 1 1 1-1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
		R R R R R-R R R R R R R R R R R R R R R R R R R R R
		4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
		7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
		0 0 0 0 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 3
		6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0
	Sex	F F F F F F F F F F F F F F F F F F F F F F F F F
Adrenal		+ +
Aorta		- -
Bone Marrow		- -
Brain		- -
Esophagus		+ + + + + + + + + + + c + + + + + + + + + + + + +
Eye		- - - - - - - - - - - - - + - - - - - - - + - - -
Heart		+ +
Kidney		+ +
Large Intestine		- -
Liver		+ +
Lung		+ +
Lymph Node (mesenteric)		- -
Mammary Gland		+ + + + + + + c + + + + + + + + c + c + + + + + +
Ovary		+ +
Pancreas		+ + + c + + + + c + + + + + + c + + + + + + + + +
Parathyroid		c c c c c + + + + c + + c c + c + + c + c + + c +
Pituitary		+ + + + + + + + + + + + + + + + c + + + + + + + +
Prostate		- -
Salivary Gland		+ + + + + + + + + + + + + c + c c + + + + + + + +
Small Intestine		- - - - - - - - - - - - - - - - - - - + - - - - - -
Spinal Cord		- -
Spleen		+ +
Stomach		+ +
Testis/Epididymis		- -
Thyroid		+ +
Trachea		+ +
Urinary Bladder		+ + + + + + + + + + + + + + + + + + c + c + + + +
Uterus		+ +
---------- The following tissue(s) were not required by protocol ----------		
Bone		- -
Clitoral Gland		- -
Harderian Gland		- -
Lymph Node		- - - - - - - + - - - - - - - - - - + - - - - - - -
Lymph Node (abdominal)		- -
Lymph Node (thoracic)		- -
Mesentary		- + - -

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
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Table: 4

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

Project Number: 0281CR0012
Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name	Animal Numbers	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R	1R
		4706	4707	4708	4709	4710	4711	4712	4713	4714	4715	4716	4717	4718	4719	4720	4721	4722	4723	4724	4725	4726	4727	4728	4729	4730
	Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Preputial Gland		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin		-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Soft Tissues (abdomen)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

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

Project Number: 02B1CR0012
Species: Rat

Dose Group Name: FC-143 30 ppm

Animal Numbers	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	R R R R R R R R R R R R R R R R R R R R R R R R R
	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
	7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
	3 3 3 3 3 3 3 3 4 4 4 4 4 4 4 4 4 5 5 5 5 5 5 5 5
	1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5
Tissue Name Sex	F F F F F F F F F F F F F F F F F F F F F F F F F
Adrenal	+ +
Aorta	- -
Bone Marrow	- -
Brain	- -
Esophagus	+ + + + + + + + + + c + + c + + c + + + + + + c
Eye	- - - - - - - - - - - - - - - - - - - + - - - - -
Heart	+ +
Kidney	+ +
Large Intestine	- -
Liver	+ +
Lung	+ +
Lymph Node (mesenteric)	- -
Mammary Gland	+ + + + + + + c c + + + + + + + + + + + + + + +
Ovary	+ +
Pancreas	+ + + + + + c + + + + c + + + + c + + + + + + +
Parathyroid	+ + + + c c + + + c c c + + + + c + c + + + + c
Pituitary	+ + + + + + + c + + + + + c + + + + + + + + + +
Prostate	- -
Salivary Gland	c +
Small Intestine	+ -
Spinal Cord	- -
Spleen	+ + + + + + + + + + c + + + + + + + + + + c + +
Stomach	+ +
Testis/Epididymis	- -
Thyroid	+ + + + + c + + + + + c + + + + + c + c + + + + c
Trachea	+ + + + + + + + + + c + + + + + c + + + + + + c
Urinary Bladder	+ +
Uterus	+ + + + + + c + + + + + + + + + + + + + + + + + +
---------- The following tissue(s) were not required by protocol ----------	
Bone	- -
Clitoral Gland	- -
Harderian Gland	- - - - - - - - - - - - - - - - - - - + - - - - -
Lymph Node	- -
Lymph Node (abdominal)	- -
Lymph Node (thoracic)	+ -
Mesentary	+ -

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

000793

Riker Laboratories, Inc. 3M

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

Project Number: 0281CR0012

Species: Rat

Dose Group Name: FC-143 30 ppm

Tissue Name	1R4731	1R4732	1R4733	1R4734	1R4735	1R4736	1R4737	1R4738	1R4739	1R4740	1R4741	1R4742	1R4743	1R4744	1R4745	1R4746	1R4747	1R4748	1R4749	1R4750	1R4751	1R4752	1R4753	1R4754	1R4755
Sex	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F	F
Preputial Gland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin	-	-	-	-	+	-	-	+	+	-	-	-	+	-	-	-	+	-	+	-	+	-	-	-	+
Soft Tissues (abdomen)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (head)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (leg)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (neck)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soft Tissues (thorax)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thymus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Unidentified Tissue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
General Comment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

406

A + indicates that a diagnosis was made. A - indicates that no diagnosis or comment was made.
A c indicates only a nondiagnostic comment was made. Please refer to the Single Tabulated Animal Report.

APPENDIX ITEM E

STATISTICAL METHODS

1. For memo dated February 11, 1985; see Tables 12-18
2. For memo dated September 24, 1985; see Tables 19 and 20

000795

Internal Correspondence

Appendix Item E

To: Chuck F. Chesney - Riker Path and Tox - 270-3S-05

From: Sally E. McCarville - Riker Res Data Ops - 270-3A-01

Subject: **Statistical Analysis for FC-143 in Rats**

Date: February 11, 1985

3M

The laboratory values and organ weight data for the study of fluorocarbon FC-143 in rats have been analyzed, and the results are presented in the attached tables. The statistical methods used to analyze the data are described in the following paragraphs.

Statistical Methods

The means and standard deviations for percent organ weight to body weight ratios, organ weight to brain weight ratios, and 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.

References

Bartlett's Test
Anderson, V.L. and McLean, R.A. (1974), Design of Experiments: A Realistic Approach, New York: Marcel Dekker, Inc., 16-22.

Dunnett's Test
Winer, B.J. (1971), Statistical Principles in Experimental Design, New York, McGraw-Hill Book Company, 201-204.

Rank Transformations

Conover, W.J., and Iman, R.L. (1981), "Rank Transformations as a Bridge Between Parametric and Nonparametric Statistics", The American Statistician, Vol.35, No. 3, 124-129.

If you have any questions regarding the analyses, please let me know.

Sem

SEM

:emr

Att.

c: Cathy E. Ludemann
Len J. Sibinski
MEE/RWH

Internal Correspondence

APPENDIX ITEM E

To: **L. J. Sibinski - Riker Path and Tox - 270-3S-05**

From: S. E. McCarville - Riker Res Data Ops - 270-3A-01

Subject: **Statistical Analysis of Microscopic Findings for FC-143 in Rats**

Date: September 24, 1985

3M

The major microscopic findings of the Two Year Oral (Diet) Toxicity-Oncogenicity Study of Fluorocarbon FC-143 in Rats were statistically analyzed. 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.

References

Fisher's Exact Test:

Conover, W. J., (1971), Practical Nonparametric Statistics, New York, John Wiley and Sons Inc., 162-164.

Yates' Corrected Chi-Square:

Fleiss, Joseph L., (1973), Statistical Methods for Rates and Porportions, New York, John Wiley and Sons Inc., 14-15, 19-20.

S. E. McCarville

:mjm

c: MEE/RWH

APPENDIX ITEM F

GROUP MEAN BODY WEIGHTS,
INDIVIDUAL BODY WEIGHTS AND FEED JAR WEIGHTS OF MALE
RATS RECEIVING FLUOROCHEMICAL FC-143
IN DIET FOR TWO YEARS

NOTES: Code 1 indicates a control group rat weight
Code 2 indicates a FC-143 - 300 ppm group rat weight
Code 3 indicates a FC-143 - 30 ppm group rat weight
Codes 11, 12, 13 indicates the total feed jar weight for the previous rat
All weights are in grams

000799

APPENDIX ITEM F

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

Group Mean Body Weights (g) ± Standard Deviation

Males

Study Week	Control - 0 ppm Mean BW ± SD	(N)	300 ppm Mean BW ± SD	(N)	30 ppm Mean BW ± SD	(N)
0	165.3 ± 10.5	(65)	162.1 ± 11.0	(65)	167.0 ± 9.8	(50)
2	270.9 ± 16.4	(65)	*234.3 ± 21.7	(65)	271.0 ± 14.7	(50)
4	334.0 ± 25.1	(65)	*276.7 ± 31.8	(65)	328.5 ± 22.9	(50)
6	390.7 ± 31.0	(65)	*308.6 ± 38.6	(65)	*369.4 ± 30.8	(50)
8	429.2 ± 37.3	(65)	*353.2 ± 39.7	(65)	*410.3 ± 37.1	(50)
10	456.2 ± 42.7	(65)	*380.1 ± 44.9	(65)	441.5 ± 44.2	(50)
12	475.5 ± 43.4	(65)	*398.0 ± 46.7	(65)	458.1 ± 47.5	(50)
14	493.2 ± 47.7	(65)	*412.8 ± 47.4	(65)	475.4 ± 48.6	(50)
16	502.9 ± 48.9	(65)	*425.4 ± 47.5	(65)	487.9 ± 52.5	(50)
18	515.3 ± 48.7	(65)	*436.0 ± 48.4	(65)	498.5 ± 52.8	(50)
20	526.8 ± 49.5	(65)	*447.4 ± 48.7	(64)	512.1 ± 53.6	(50)
22	542.3 ± 52.1	(65)	*456.1 ± 48.9	(64)	*519.4 ± 54.7	(50)
24	550.4 ± 53.0	(65)	*464.2 ± 49.4	(64)	*526.3 ± 56.7	(50)
26	561.0 ± 54.3	(65)	*475.0 ± 49.4	(64)	538.9 ± 59.7	(50)
28	567.5 ± 55.0	(65)	*484.9 ± 51.4	(63)	546.2 ± 61.8	(50)
30	576.3 ± 56.7	(65)	*497.2 ± 51.8	(63)	558.6 ± 61.3	(50)
32	580.6 ± 57.4	(65)	*505.7 ± 52.5	(63)	566.4 ± 62.3	(50)
34	582.9 ± 62.5	(65)	*511.8 ± 52.5	(63)	571.3 ± 63.3	(50)
36	591.0 ± 59.7	(64)	*514.2 ± 53.1	(63)	575.4 ± 64.6	(50)
38	599.4 ± 59.4	(64)	*524.8 ± 53.2	(63)	584.0 ± 65.6	(50)
40	608.4 ± 61.6	(64)	*535.2 ± 56.0	(63)	592.5 ± 69.0	(49)
42	612.9 ± 61.2	(64)	*540.9 ± 57.9	(63)	600.5 ± 69.1	(49)
44	619.8 ± 62.3	(64)	*550.8 ± 58.0	(63)	610.4 ± 69.7	(49)
46	623.5 ± 64.3	(64)	*552.0 ± 61.2	(63)	612.1 ± 71.0	(49)
48	626.1 ± 63.4	(64)	*558.5 ± 64.0	(63)	618.9 ± 72.3	(49)
50	639.2 ± 67.0	(64)	*566.7 ± 64.7	(63)	627.1 ± 74.2	(49)
52	638.6 ± 70.1	(64)	*570.1 ± 66.2	(63)	633.6 ± 76.2	(49)

[a] Number of animals weighed

* Significant difference from Control at the 5% level (Dunnett's t Test; $\alpha = 0.05$)

000800

APPENDIX ITEM F

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

Group Mean Body Weights (g) ± Standard Deviation

Males

Study Week	Control - 0 ppm Mean BW ± SD	(N)	300 ppm Mean BW ± SD	(N)	30 ppm Mean BW ± SD	(N)
54	654.3 ± 75.3	(49)	*577.6 ± 69.8	(48)	641.9 ± 76.9	(49)
56	661.6 ± 73.3	(48)	*583.1 ± 71.2	(48)	646.4 ± 78.6	(49)
58	668.0 ± 76.4	(48)	*587.9 ± 73.9	(48)	652.7 ± 78.2	(49)
60	673.2 ± 75.4	(48)	*590.8 ± 75.9	(48)	656.8 ± 79.5	(49)
62	674.4 ± 77.4	(48)	*593.2 ± 74.9	(48)	655.7 ± 82.1	(49)
64	664.5 ± 77.6	(47)	*596.8 ± 80.8	(48)	658.3 ± 84.7	(49)
66	650.8 ± 78.1	(47)	*598.2 ± 80.8	(48)	662.5 ± 82.0	(47)
68	656.6 ± 82.9	(47)	*604.9 ± 83.0	(48)	666.5 ± 84.0	(47)
70	661.9 ± 84.7	(47)	*608.2 ± 79.9	(48)	666.2 ± 86.8	(45)
72	658.3 ± 86.3	(47)	*608.5 ± 76.5	(46)	664.4 ± 86.3	(45)
74	660.8 ± 81.7	(46)	*601.1 ± 76.5	(46)	659.2 ± 83.9	(45)
76	667.7 ± 84.9	(46)	*605.4 ± 76.6	(46)	663.8 ± 86.0	(45)
78	668.8 ± 83.8	(46)	*604.6 ± 77.5	(46)	661.7 ± 89.3	(45)
80	670.6 ± 85.2	(46)	*611.8 ± 76.7	(46)	669.2 ± 88.0	(45)
82	663.1 ± 85.5	(46)	*610.0 ± 77.1	(46)	666.9 ± 87.0	(45)
84	668.1 ± 88.8	(45)	*617.5 ± 79.1	(46)	662.3 ± 92.6	(45)
86	675.6 ± 86.8	(42)	*617.4 ± 78.8	(46)	664.5 ± 95.7	(44)
88	678.9 ± 86.4	(41)	*614.7 ± 83.0	(46)	654.7 ± 102.3	(44)
90	690.0 ± 93.9	(41)	*624.6 ± 87.3	(45)	662.4 ± 100.5	(43)
92	686.0 ± 91.6	(40)	*621.8 ± 85.6	(45)	652.9 ± 103.5	(43)
94	678.3 ± 90.3	(40)	*627.6 ± 80.8	(45)	660.0 ± 86.1	(40)
96	677.5 ± 95.1	(38)	*621.0 ± 84.6	(45)	653.4 ± 87.0	(39)
98	675.7 ± 98.6	(38)	627.2 ± 80.8	(45)	659.7 ± 88.8	(38)
100	671.1 ± 94.4	(37)	625.5 ± 87.5	(44)	660.0 ± 94.8	(38)
102	665.9 ± 101.2	(36)	629.4 ± 88.0	(44)	664.0 ± 93.2	(37)
104	642.0 ± 99.5	(35)	613.3 ± 88.1	(44)	650.8 ± 95.0	(36)

[a] Number of animals weighed

* Significant difference from Control at the 5% level (Dunnett's t Test; $\alpha = 0.05$)

000801

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 02810R0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 4/21/81
SEX OF RATS:S MALES
ROOM NUMBER:S D-340
WEIGHT OF FULL FOOD JAR:S 500GRAMS

WEEK 0

1R03516	01S	007101167.80	1	167.8
FOODJAR	11S	007201000.00	11	0
1R03517	01S	007301162.70	1	162.7
FOODJAR	11S	007401000.00	11	0
1R03518	01S	007501157.00	1	157
FOODJAR	11S	007601000.00	11	0
1R03519	01S	007701178.70	1	178.7
FOODJAR	11S	007801000.00	11	0
1R03520	01S	007901168.00	1	168
FOODJAR	11S	010001000.00	11	0
1R03521	01S	010101157.40	1	157.4
FOODJAR	11S	010201000.00	11	0
1R03522	01S	010301172.90	1	172.9
FOODJAR	11S	010401000.00	11	0
1R03523	01S	010501169.10	1	169.1
FOODJAR	11S	010601000.00	11	0
03524	01S	010701148.00	1	148
FOODJAR	11S	010801000.00	11	0
1R03525	01S	010901157.60	1	157.6
FOODJAR	11S	011001000.00	11	0
1R03526	01S	011101159.40	1	159.4
FOODJAR	11S	011201000.00	11	0
1R03527	01S	011301157.60	1	157.6
FOODJAR	11S	011401000.00	11	0
1R03528	01S	011501173.80	1	173.8
FOODJAR	11S	011601000.00	11	0
1R03529	01S	011701155.20	1	155.2
FOODJAR	11S	011801000.00	11	0
1R03530	01S	011901180.50	1	180.5
FOODJAR	11S	012001000.10	11	0.1
1R03531	01S	012101160.50	1	160.5
FOODJAR	11S	012201000.00	11	0
1R03532	01S	012301163.10	1	163.1
FOODJAR	11S	012401000.00	11	0
1R03533	01S	012501178.00	1	178
FOODJAR	11S	012601000.00	11	0
1R03534	01S	012701162.50	1	162.5
FOODJAR	11S	012801000.00	11	0
1R03535	01S	012901162.80	1	162.8
FOODJAR	11S	013001000.00	11	0
1R03536	01S	013101156.90	1	156.9
FOODJAR	11S	013201000.00	11	0
03537	01S	013301173.20	1	173.2
FOODJAR	11S	013401000.00	11	0
1R03538	01S	013501164.30	1	164.3
FOODJAR	11S	013601000.00	11	0
1R03539	01S	013701165.10	1	165.1
FOODJAR	11S	013801000.00	11	0
1R03540	01S	013901152.50	1	152.5
FOODJAR	11S	014001000.00	11	0

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1R0[illegible]41	01S	014101176.90	1	176.9
FOODJAR	11S	014201000.00	11	0
1R0[illegible]42	01S	014301160.10	1	160.1
FOODJAR	11S	014401000.00	11	0
1R03543	01S	014501169.70	1	169.7
FOODJAR	11S	014601000.00	11	0
1R03544	01S	014701167.70	1	167.7
FOODJAR	11S	014801000.00	11	0
1R03545	01S	014901169.30	1	169.3
FOODJAR	11S	015001000.00	11	0
1R03546	01S	015101149.60	1	149.6
FOODJAR	11S	015201000.00	11	0
1R03547	01S	015301168.50	1	168.5
FOODJAR	11S	015401000.00	11	0
1R03548	01S	015501176.70	1	176.7
FOODJAR	11S	015601000.00	11	0
1R03549	01S	015701173.00	1	173
FOODJAR	11S	015801000.00	11	0
1R03550	01S	015901168.40	1	168.4
FOODJAR	11S	016001000.00	11	0
1R03551	01S	016101149.10	1	149.1
FOODJAR	11S	016201000.00	11	0
1R03552	01S	016301162.70	1	162.7
FOODJAR	11S	016401000.00	11	0
1R03553	01S	016501173.60	1	173.6
FOODJAR	11S	016601000.00	11	0
1R03554	01S	016701147.30	1	147.3
FOODJAR	11S	016801000.00	11	0
1R03555	01S	016901154.30	1	154.3
FOODJAR	11S	017001000.00	11	0
1R03556	01S	017101168.60	1	168.6
FOODJAR	11S	017201000.00	11	0
1R03557	01S	017301171.70	1	171.7
FOODJAR	11S	017401000.00	11	0
1R03558	01S	017501174.90	1	174.9
FOODJAR	11S	017601000.00	11	0
1R03559	01S	017701161.90	1	161.9
FOODJAR	11S	017801000.00	11	0
1R03560	01S	017901186.50	1	186.5
FOODJAR	11S	018001000.00	11	0
1R03561	01S	018101155.30	1	155.3
FOODJAR	11S	018201000.00	11	0
1R03562	01S	018301147.80	1	147.8
FOODJAR	11S	018401000.00	11	0
1R03563	01S	018501182.40	1	182.4
FOODJAR	11S	018601000.00	11	0
1R03564	01S	018701144.50	1	144.5
FOODJAR	11S	018801000.00	11	0
1R03565	01S	018901174.70	1	174.7
FOODJAR	11S	019001000.00	11	0
1R03566	01S	019101153.40	1	153.4
FOODJAR	11S	019201000.00	11	0
1R03567	01S	019301163.20	1	163.2
FOODJAR	11S	019401000.00	11	0
1R03568	01S	019501185.40	1	185.4
FOODJAR	11S	019601000.00	11	0
1R03569	01S	019701157.70	1	157.7
FOODJAR	11S	019801000.00	11	0
1R03570	01S	019901163.60	1	163.6
FOODJAR	11S	020001000.00	11	0
1R03571	01S	020101159.70	1	159.7
FOODJAR	11S	020201000.00	11	0
1R03572	01S	020301172.40	1	172.4
FOODJAR	11S	020401000.00	11	0
1R03573	01S	020501181.90	1	181.9
FOODJAR	11S	020601000.00	11	0

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1R03574	01S	020701177.30	1	
FOODJAR	11S	020801000.10	11	0.1
1R03575	01S	020901165.80	1	165.8
FOODJAR	11S	021001000.30	11	0.3
1R03576	01S	021101160.20	1	160.2
FOODJAR	11S	021201000.00	11	0
1R03577	01S	021301177.30	1	177.3
FOODJAR	11S	021401000.00	11	0
1R03578	01S	021501183.80	1	183.8
FOODJAR	11S	021601000.00	11	0
1R03579	01S	021701149.90	1	149.9
FOODJAR	11S	021801000.00	11	0
1R03580	01S	021901154.00	1	154
FOODJAR	11S	022001000.00	11	0
1R03581	02S	007101167.70	2	167.7
FOODJAR	12S	007201000.00	12	0
1R03582	02S	007301160.70	2	160.7
FOODJAR	12S	007401000.00	12	0
1R03583	02S	007501141.20	2	141.2
FOODJAR	12S	007601000.00	12	0
1R03584	02S	007701142.50	2	142.5
FOODJAR	12S	007801000.00	12	0
1R03585	02S	007901159.40	2	159.4
FOODJAR	12S	010001000.00	12	0
1R03586	02S	010101168.50	2	168.5
FOODJAR	12S	010201000.00	12	0
1R03587	02S	010301151.10	2	151.1
FOODJAR	12S	010401000.00	12	0
1R03588	02S	010501168.10	2	168.1
FOODJAR	12S	010601000.00	12	0
1R03589	02S	010701149.10	2	149.1
FOODJAR	12S	010801000.00	12	0
03590	02S	010901178.30	2	178.3
FOODJAR	12S	011001000.00	12	0
1R03591	02S	011101157.20	2	157.2
FOODJAR	12S	011201000.00	12	0
1R03592	02S	011301156.70	2	156.7
FOODJAR	12S	011401000.00	12	0
1R03593	02S	011501160.70	2	160.7
FOODJAR	12S	011601000.00	12	0
1R03594	02S	011701158.60	2	158.6
FOODJAR	12S	011801000.00	12	0
1R03595	02S	011901168.80	2	168.8
FOODJAR	12S	012001000.00	12	0
1R03596	02S	012101173.90	2	173.9
FOODJAR	12S	012201000.10	12	0.1
1R03597	02S	012301154.60	2	154.6
FOODJAR	12S	012401000.00	12	0
1R03598	02S	012501185.60	2	185.6
FOODJAR	12S	012601000.00	12	0
1R03599	02S	012701166.80	2	166.8
FOODJAR	12S	012801000.00	12	0
1R03600	02S	012901162.70	2	162.7
FOODJAR	12S	013001000.00	12	0
1R03601	02S	013101170.70	2	170.7
FOODJAR	12S	013201000.00	12	0
1R03602	02S	013301151.10	2	151.1
FOODJAR	12S	013401000.00	12	0
1R03603	02S	013501168.30	2	168.3
FOODJAR	12S	013601000.00	12	0
1R03604	02S	013701166.60	2	166.6
FOODJAR	12S	013801000.00	12	0
1R03605	02S	013901170.20	2	170.2
FOODJAR	12S	014001000.00	12	0
1R03606	02S	014101155.80	2	155.8
FOODJAR	12S	014201000.00	12	0

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1R01607	02S	014201168.00	2	168
FOODJAR	12S	014001000.00	12	0
1R01608	02S	014501158.90	2	158.9
FOODJAR	12S	014601000.00	12	0
1R01609	02S	014701150.30	2	150.3
FOODJAR	12S	014801000.00	12	0
1R01610	02S	014901171.50	2	171.5
FOODJAR	12S	015001000.00	12	0
1R01611	02S	015101178.80	2	178.8
FOODJAR	12S	015201000.00	12	0
1R01612	02S	015301169.40	2	169.4
FOODJAR	12S	015401000.00	12	0
1R01613	02S	015501178.00	2	178
FOODJAR	12S	015601000.00	12	0
1R01614	02S	015701174.00	2	174
FOODJAR	12S	015801000.00	12	0
1R01615	02S	015901150.40	2	150.4
FOODJAR	12S	016001000.00	12	0
1R01616	02S	016101156.80	2	156.8
FOODJAR	12S	016201000.00	12	0
1R01617	02S	016301148.80	2	148.8
FOODJAR	12S	016401000.00	12	0
1R01618	02S	016501157.50	2	157.5
FOODJAR	12S	016601000.00	12	0
1R01619	02S	016701152.70	2	152.7
FOODJAR	12S	016801000.00	12	0
1R01620	02S	016901147.90	2	147.9
FOODJAR	12S	017001000.00	12	0
1R01621	02S	017101143.40	2	143.4
FOODJAR	12S	017201000.00	12	0
1R01622	02S	017301140.90	2	140.9
FOODJAR	12S	017401000.00	12	0
1R01623	02S	017501169.10	2	169.1
FOODJAR	12S	017601000.00	12	0
1R01624	02S	017701148.60	2	148.6
FOODJAR	12S	017801000.00	12	0
1R01625	02S	017901177.20	2	177.2
FOODJAR	12S	018001000.00	12	0
1R01626	02S	018101186.50	2	186.5
FOODJAR	12S	018201000.10	12	0.1
1R01627	02S	018301175.50	2	175.5
FOODJAR	12S	018401000.00	12	0
1R01628	02S	018501165.20	2	165.2
FOODJAR	12S	018601000.00	12	0
1R01629	02S	018701157.80	2	157.8
FOODJAR	12S	018801000.00	12	0
1R01630	02S	018901172.70	2	172.7
FOODJAR	12S	019001000.00	12	0
1R01631	02S	019101171.30	2	171.3
FOODJAR	12S	019201000.00	12	0
1R01632	02S	019301160.40	2	160.4
FOODJAR	12S	019401000.00	12	0
1R01633	02S	019501172.20	2	172.2
FOODJAR	12S	019601000.00	12	0
1R01634	02S	019701158.30	2	158.3
FOODJAR	12S	019801000.00	12	0
1R01635	02S	019901146.90	2	146.9
FOODJAR	12S	020001000.00	12	0
1R01636	02S	020101169.00	2	169
FOODJAR	12S	020201000.00	12	0
1R01637	02S	020301171.00	2	171
FOODJAR	12S	020401000.00	12	0
1R01638	02S	020501159.50	2	159.5
FOODJAR	12S	020601000.00	12	0
1R01639	02S	020701151.50	2	151.5
FOODJAR	12S	020801000.00	12	0

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1R03640	035	020901148.30	2	148.3
FOODJAR	135	0.1001000.00	12	0
1R03641	035	021101168.70	2	168.7
FOODJAR	135	021201000.00	12	0
1R03642	035	021301167.20	2	167.2
FOODJAR	135	021401000.10	12	0.1
1R03643	035	021501155.60	2	155.6
FOODJAR	135	021601000.00	12	0
1R03644	035	021701171.80	2	171.8
FOODJAR	135	021801000.00	12	0
1R03645	035	021901151.60	2	151.6
FOODJAR	135	022001000.00	12	0
1R03646	035	022101149.70	3	149.7
FOODJAR	135	022201000.00	13	0
1R03647	035	022301180.20	3	180.2
FOODJAR	135	022401000.00	13	0
1R03648	035	022501167.40	3	167.4
FOODJAR	135	022601000.00	13	0
1R03649	035	022701165.20	3	165.2
FOODJAR	135	022801000.00	13	0
1R03650	035	022901167.40	3	167.4
FOODJAR	135	023001000.00	13	0
1R03651	035	023101148.20	3	148.2
FOODJAR	135	023201000.00	13	0
1R03652	035	023301178.50	3	178.5
FOODJAR	135	023401000.00	13	0
1R03653	035	023501162.50	3	162.5
FOODJAR	135	023601000.00	13	0
1R03654	035	023701170.60	3	170.6
FOODJAR	135	023801000.00	13	0
1R03655	035	023901166.50	3	166.5
FOODJAR	135	024001000.00	13	0
03656	035	024101164.10	3	164.1
FOODJAR	135	024201000.00	13	0
1R03657	035	024301164.50	3	164.5
FOODJAR	135	024401000.00	13	0
1R03658	035	024501156.90	3	156.9
FOODJAR	135	024601000.00	13	0
1R03659	035	024701180.20	3	180.2
FOODJAR	135	024801000.00	13	0
1R03660	035	024901156.40	3	156.4
FOODJAR	135	025001000.00	13	0
1R03661	035	025101175.70	3	175.7
FOODJAR	135	025201000.00	13	0
1R03662	035	025301161.00	3	161
FOODJAR	135	025401000.00	13	0
1R03663	035	025501171.20	3	171.2
FOODJAR	135	025601000.00	13	0
1R03664	035	025701162.80	3	162.8
FOODJAR	135	025801000.00	13	0
1R03665	035	025901176.50	3	176.5
FOODJAR	135	026001000.00	13	0
1R03666	035	026101187.40	3	187.4
FOODJAR	135	026201000.00	13	0
1R03667	035	026301165.10	3	165.1
FOODJAR	135	026401000.00	13	0
1R03668	035	026501157.80	3	157.8
FOODJAR	135	026601000.00	13	0
03669	035	026701153.80	3	153.8
FOODJAR	135	026801000.00	13	0
1R03670	035	026901171.00	3	171
FOODJAR	135	027001000.00	13	0
1R03671	035	027101168.50	3	168.5
FOODJAR	135	027201000.00	13	0
1R03672	035	027301174.60	3	174.6
FOODJAR	135	027401000.10	13	0.1

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1R03673	03S	027501185.50	3	185.5
FOODJAR	13S	027601000.00	13	0
1R03674	03S	027701152.90	3	152.9
FOODJAR	13S	027801000.00	13	0
1R03675	03S	027901168.90	3	168.9
FOODJAR	13S	028001000.00	13	0
1R03676	03S	028101179.40	3	179.4
FOODJAR	13S	028201000.00	13	0
1R03677	03S	028301172.50	3	172.5
FOODJAR	13S	028401000.00	13	0
1R03678	03S	028501171.80	3	171.8
FOODJAR	13S	028601000.00	13	0
1R03679	03S	028701159.60	3	159.6
FOODJAR	13S	028801000.00	13	0
1R03680	03S	028901144.40	3	144.4
FOODJAR	13S	029001000.00	13	0
1R03681	03S	029101172.30	3	172.3
FOODJAR	13S	029201000.00	13	0
1R03682	03S	029301169.90	3	169.9
FOODJAR	13S	029401000.10	13	0.1
1R03683	03S	029501153.80	3	153.8
FOODJAR	13S	029601000.00	13	0
1R03684	03S	029701168.70	3	168.7
FOODJAR	13S	029801000.00	13	0
1R03685	03S	029901178.40	3	178.4
FOODJAR	13S	030001000.00	13	0
1R03686	03S	030101153.90	3	153.9
FOODJAR	13S	030201000.00	13	0
1R03687	03S	030301171.40	3	171.4
FOODJAR	13S	030401000.00	13	0
1R03688	03S	030501174.40	3	174.4
FOODJAR	13S	030601000.00	13	0
1R03689	03S	030701164.90	3	164.9
FOODJAR	13S	030801000.00	13	0
1R03690	03S	030901156.20	3	156.2
FOODJAR	13S	031001000.00	13	0
1R03691	03S	031101172.50	3	172.5
FOODJAR	13S	031201000.00	13	0
1R03692	03S	031301160.10	3	160.1
FOODJAR	13S	031401000.00	13	0
1R03693	03S	031501161.70	3	161.7
FOODJAR	13S	031601000.00	13	0
1R03694	03S	031701176.90	3	176.9
FOODJAR	13S	031801000.00	13	0
1R03695	03S	031901177.50	3	177.5
FOODJAR	13S	032001000.00	13	0
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 4/28/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340
WEIGHT OF FULL FOOD JAR:S 500GRAMS

WEEK 1

1R03516 01S 010000218.7Q	1	218.7
FOODJAR 11S 010100338.9Q	11	338.9
1R03517 01S 010200216.6Q	1	216.6
FOODJAR 11S 010300349.1Q	11	349.1
1R03518 01S 010400211.1Q	1	211.1
FOODJAR 11S 010500345.4Q	11	345.4
1R03519 01S 010600234.6Q	1	234.6
FOODJAR 11S 010700324.6Q	11	324.6
1R03520 01S 010800220.6Q	1	220.6
FOODJAR 11S 010900339.6Q	11	339.6
1R03521 01S 011000204.9Q	1	204.9
FOODJAR 11S 011100354.7Q	11	354.7
1R03522 01S 011200219.8Q	1	219.8
FOODJAR 11S 011300341.0Q	11	341
1R03523 01S 011400214.5Q	1	214.5-
FOODJAR 11S 011500358.2Q	11	358.2
1R03524 01S 011600199.6Q	1	199.6
FOODJAR 11S 011700364.7Q	11	364.7
.03525 01S 011800206.8Q	1	206.8
FOODJAR 11S 011900359.8Q	11	359.8
1R03526 01S 012000207.4Q	1	207.4
FOODJAR 11S 012100341.0Q	11	341
1R03527 01S 012200215.1Q	1	215.1
FOODJAR 11S 012300344.9Q	11	344.9
1R03528 01S 012400226.4Q	1	226.4
FOODJAR 11S 012500339.1Q	11	339.1
1R03529 01S 012600213.1Q	1	213.1
FOODJAR 11S 012700338.8Q	11	338.8
1R03530 01S 012800230.0Q	1	230
FOODJAR 11S 012900344.9Q	11	344.9
1R03531 01S 013000211.4Q	1	211.4
FOODJAR 11S 013100348.2Q	11	348.2
1R03532 01S 013200215.7Q	1	215.7
FOODJAR 11S 013300342.2Q	11	342.2
1R03533 01S 013400234.6Q	1	234.6
FOODJAR 11S 013500325.4Q	11	325.4
1R03534 01S 013600215.9Q	1	215.9
FOODJAR 11S 013700344.3Q	11	344.3
1R03535 01S 013800198.5Q	1	198.5
FOODJAR 11S 013900369.4Q	11	369.4
1R03536 01S 014000197N0Q	1	197
FOODJAR 11S 014100362.1Q	11	362.1
1R03537 01S 014200226.2Q	1	226.2
`ODJAR 11S 014300342.9Q	11	342.9
_.03538 01S 014400220.9Q	1	220.9
FOODJAR 11S 014500340.0Q	11	340
1R03539 01S 014600210.4Q	1	210.4
FOODJAR 11S 014700355.5Q	11	355.5
1R03540 01S 014800203.1Q	1	203.1
FOODJAR 11S 014900352.7Q	11	352.7
1R03541 01S 015000227.3Q	1	227.3

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FOODJAR 11S 015100348.4Q	11	348.4
1R03542 01S 015200215.5Q	1	215.5
FOODJAR 11S 015300335.8Q	11	335.8
1R03543 01S 015400223.6Q	1	223.6
FOODJAR 11S 015500330.#Q	11	330
1R03544 01S 015600216.8Q	1	216.8
FOODJAR 11S 015700340.9Q	11	340.9
03545 01S 015800230.1Q	1	230.1
FOODJAR 11S 015900348.0Q	11	348
1R03546 01S 016000207.4Q	1	207.4
FOODJAR 11S 016100345.6Q	11	345.6
1R03547 01S 016200222.0Q	1	222
FOODJAR 11S 016300329.9Q	11	329.9
1R03548 01S 016400235.0Q	1	235
FOODJAR 11S 016500336.4Q	11	336.4
1R03549 01S 016600223.3Q	1	223.3
FOODJAR 11S 016700352.7Q	11	352.7
1R03550 01S 016800219.4Q	1	219.4
FOODJAR 11S 016900350.0Q	11	350
1R03551 01S 017000183.2Q	1	183.2
FOODJAR 11S 017100374.2Q	11	374.2
1R03552 01S 017200216.1Q	1	216.1
FOODJAR 11S 017300336.9Q	11	336.9
1R03553 01S 017400228.3Q	1	228.3
FOODJAR 11S 017500334.7Q	11	334.7
1R03554 01S 017600192.6Q	1	192.6
FOODJAR 11S 017700357.4Q	11	357.4
1R03555 01S 017800204.8Q	1	204.8
FOODJAR 11S 017900354.4Q	11	354.4
1R03556 01S 018000226.6Q	1	226.6-
FOODJAR 11S 018100339.1Q	11	339.1
1R03557 01S 018200233.2Q	1	233.2
FOODJAR 11S 018300334.8Q	11	334.8
1R03558 01S 018400217.7Q	1	217.7
FOODJAR 11S 018500351.1Q	11	351.1
1R03559 01S 018600218.7Q	1	218.7
FOODJAR11S	11	339.5
1R03560 01S 018800234.1Q	1	234.1
FOODJAR 11S 0189 0346.9Q	11	346.9
1R03561 01S 019000212.6Q	1	212.6
FOODJAR 11S 019100338.0Q	11	338
1R03562 01S 019200192.6Q	1	192.6
FOODJAR 11S 019300370.0Q	11	370
1R03563 01S 019400237.6Q	1	237.6
FOODJAR 11S 019500338.7Q	11	338.7
1R03564 01S 019600197.8Q	1	197.8
FOODJAR 11S 019700362.5Q	11	362.5
1R03565 01S 019800227.1Q	1	227.1
FOODJAR 11S 019900351.1Q	11	351.1
1R03566 01S 020000205.3Q	1	205.3
FOODJAR 11S 020100356.8Q	11	356.8
1R03567 01S 020200221.3Q	1	221.3
FOODJAR 11S 020300340.8Q	11	340.8
1R03568 01S 020400247.1Q	1	247.1
FOODJAR 11S 020500328.7Q	11	328.7
1R03569 01S 020600219.9Q	1	219.9
FOODJAR 11S 020700345.8Q	11	345.8
1R03570 01S 020800218.0Q	1	218
ODJAR 11S 020900320.6Q	11	320.6
1R03571 01S 021000217.8Q	1	217.8
FOODJAR 11S 021100336.8Q	11	336.8
1R03572 01S 021200219.3Q	1	219.3
FOODJAR 11S 021300345.0Q	11	345
1R03573 01S 021400234.2Q	1	234.2
FOODJAR 11S 021500334.9Q	11	334.9
1R03574 01S 021600237.4Q	1	237.4

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FOODJAR 11S 021700326.0Q      11          326
1R03575 01S 021800216.4Q      1           216.4
FOODJAR 11S 021900340.4Q      11          340.4
1R03576 01S 022000211.8Q      1           211.8
FOODJAR 11S 022100342.1Q      11          342.1
1R03577 01S 022200232.4Q      1           232.4
FOODJAR 11S 022300337.7Q      11          337.7
 03578 01S 022400226.0Q       1           226
JODJAR 11S 022500330.0Q       11          330
1R03579 01S 022600204.0Q      1           204
FOODJAR 11S 022700357.0Q      11          357
1R03580 01S 022800202.8Q      1           202.8
FOODJAR 11S 022900351.3Q      11          351.3
1R03581 02S 00?100206.4Q      2           206.4
FOODJAR 12S 00?200360.5Q      12          360.5
1R03582 02S 00?300204.9Q      2           204.9
FOODJAR 12S 00?400368.1Q      12          368.1
1R03583 02S 00?500160.9Q      2           160.9
FOODJAR 12S 00?600388.2Q      12          388.2
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1R03588 02S 010500202.7Q      2           202.7
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1R03589 02S 010700181.1Q      2           181.1
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FOODJAR 12S 011000348.5Q      12          348.5
  03591 02S 011100174.2Q      2           174.2
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1R03593 02S 011500187.2Q      2           187.2
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1R03594 02S 011700200.2Q      2           200.2
FOODJAR 12S 011800343.2Q      12          343.2
1R03595 02S 011900192.3Q      2           192.3
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1R03597 02S 012300199.0Q      2           199
FOODJAR 12S 012400366.5Q      12          366.5
1R03598 02S 012500227.6Q      2           227.6
FOODJAR 12S 012600365.7Q      12          365.7
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FOODJAR 12S 013000396.2Q      12          396.2
1R03601 02S 013100211.5Q      2           211.5
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FOODJAR 12S 013400374.2Q      12          374.2
1R03603 02S 013500210.5Q      2           210.5
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FOODJAR 12S 014200366.5Q      12          366.5
1R03607 02S 014300216.5Q      2           216.5
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FOODJAR 12S 014600349.3Q      12          349.3
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FOODJAR 12S 014800355.5Q      12          355.5
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FOODJAR 12S 015000350.4Q      12          350.4
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FOODJAR 12S 015200371.6Q      12          371.6
1R03612 02S 015300206.0Q      2           206
FOODJAR 12S 015400359.0Q      12          359
1R03613 02S 015500220.7Q      2           220.7
FOODJAR 12C     12            12          350.4
1R03614 02S015600208.3Q       2           208.3

FOODJAR 12S 015700334.0Q      12          334
1R03615 02S 015800194.7Q      2           194.7
FOODJAR 12S 015900349.6Q      12          349.6
1R03616 02S 016000191.0Q      2           191
FOODJAR 12S 016100362.3Q      12          362.3
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FOODJAR 12S 016900357.8Q      12          357.8
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FOODJAR 12S 017300385.7Q      12          385.7
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1R03627 02S 018200221.7Q      2           221.7
FOODJAR 12S 018300359.5Q      12          359.5
1R03628 02S 018400203.7Q      2           203.7
FOODJAR 12S 018500362.0Q      12          362
1R03629 02S 018600193.1Q      2           193.1
FOODJAR 12S 018700366.3Q      12          366.3
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FOODJAR 12S 018900407.2Q      12          407.2
1R03631 02S 019000211.9Q      2           211.9
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1R03632 02S 019200197.6Q      2           197.6
FOODJAR 12S 019300361.9Q      12          361.9
1R03633 02S 019400200.8Q      2           200.8
FOODJAR 12S 019500373.6Q      12          373.6
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FOODJAR 12S 019700388.9Q      12          388.9
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1R03637 02S 020200195.9Q      2           195.9
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1R03638 02S 020400186.3Q      2           186.3
FOODJAR 12S 020500358.7Q      12          358.7
1R03639 02S 020600180.7Q      2           180.7
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1R03642 02S 021200174.8Q     2          174.8
FOODJAR 12S 021300393.2Q     12         393.2
1R03643 02S 021400188.8Q     2          188.8
 ODJAR 12S 021500377.4Q      12         377.4
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1R03645 02S 021800187.2Q     2          187.2
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1R03647 03S 022200238.1Q     3          238.1
FOODJAR 13S 022300336.7Q     13         336.7
1R03648 03S 022400226.2Q     3          226.2
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1R03649 03S 022600213.2Q     3          213.2
FOODJAR 13S 022700346.1Q     13         346.1
1R03650 03S 022800214.9Q     3          214.9
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1R03651 03S 023000208.0Q     3          208
FOODJAR 13S 023100344.7Q     13         344.7
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1R03653 03S 023400221.6Q     3          221.6
FOODJAR 13S 023500336.6Q     13         336.6
1R03654 03S 023600222.4Q     3          222.4
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FOODJAR 13S 024700330.0Q     13         330
1R03660 03S 024800207.2Q     3          207.2
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FOODJAR 13S 025700337.6Q     13         337.6
1R03665 03S 025800230.6Q     3          230.6
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1R03666 03S 026000243.7Q     3          243.7
FOODJAR 13S 026100323.5Q     13         323.5
1R03667 03S 026200206.7Q     3          206.7
FOODJAR 13S 026300358.6Q     13         358.6
1R03668 03S 026400198.4Q     3          198.4
FOODJAR 13S 026500361.5Q     13         361.5
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 ODJAR 13S 026700334.7Q      13         334.7
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FOODJAR 13S 026900333.1Q     13         333.1
1R03671 03S 027000221.5Q     3          221.5
FOODJAR 13S 027100345.0Q     13         345
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FOODJAR 13S 027300326.3Q     13         326.3
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FOODJAR 13S 028100324.5Q      13         324.5
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FOODJAR 13S 028300327.5Q      13         327.5
1R03678 03S 028400227.9Q      3          227.9
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1R03682 03S 029200216.0Q      3          216
FOODJAR 13S 029300353.6Q      13         353.6-
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FOODJAR 13S 029700339.7Q      13         339.7
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1R03686 03S 030000208.4Q      3          208.4
FOODJAR 13S 030100345.9Q      13         345.9
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FOODJAR 13S 030300330.9Q      13         330.9
1R03688 03S 030400230.0Q      3          230
 OODJAR 13S 030500337.5Q      13         337.5
1R03689 03S 030600211.9Q      3          211.9
FOODJAR 13S 030700349.2Q      13         349.2
1R03690 03S 030800214.5Q      3          214.5
FOODJAR 13S 030900338.6Q      13         338.6
1R03691 03S 031000223.4Q      3          223.4
FOODJAR 13S 031100345.3Q      13         345.3
1R03692 03S 031200212.0Q      3          212
FOODJAR 13S 031300348.1Q      13         348.1
1R03693 03S 031400223.4Q      3          223.4
FOODJAR 13S 031500328.9Q      13         328.9
1R03694 03S 031600234.9Q      3          234.9
FOODJAR 13S 031700334.4Q      13         334.4
1R03695 03S 031800236.4Q      3          236.4
FOODJAR 13S 031900320.2Q      13         320.2
9999999999      99            0
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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 5/5/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 500GRAMS

WEEK 2

1R03516	01S	00?100284.0Q	1	284
FOODJAR	11S	00?200333.6Q	11	333.6
1R03517	01S	00?300270.0Q	1	270
FOODJAR	11S	00?400341.5Q	11	341.5
1R03518	01S	.0?500267.6Q	1	267.6
FOODJAR	11S	00?600342.0Q	11	342
1R03519	01S	.0?700293.7Q	1	293.7
FOODJAR	11S	00?800325.3Q	11	325.3
1R03520	01S	00?9.0280.6Q	1	280.6
FOODJAR	11S	010000332.3Q	11	332.3
1R03521	01S	010100255.6Q	1	255.6
FOODJAR	11S	010200349.9Q	11	349.9
1R03522	01S	010300273.6Q	1	273.6
FOODJAR	11S	010400338.6Q	11	338.6
1R03523	01S	.10500281.9Q	1	281.9
FOODJAR	11S	010600346.4Q	11	346.4
1R03524	01S	010700250.2Q	1	250.2
FOODJAR	11S	010800362.7Q	11	362.7
03525	01S	010900258.5Q	1	258.5
FOODJAR	11S	011000352.0Q	11	352
1R03526	01S	011100268.2Q	1	268.2
FOODJAR	11S	011200329.6Q	11	329.6
1R03527	01S	011/00266.2Q	1	266
FOODJAR	11S	011400345.2Q	11	345.2
1R03528	01S	.11500276.6Q	1	276.6
FOODJAR	11S	011600337.0Q	11	337
1R03529	01S	011700266.8Q	1	266.8
FOODJAR	11S	011800312.5Q	11	312.5
1R03530	01S	011900290.3Q	1	290.3
FOODJAR	11S	012000339.7Q	11	339.7
1R03531	01S	012100268.8Q	1	268.8
FOODJAR	11S	012200336.9Q	11	336.9
1R03532	01S	012/00271.0Q	1	271
FOODJAR	11S	012400337.5Q	11	337.5
1R03533	01S	.12500294.5Q	1	294.5
FOODJAR	11S	012600320.6Q	11	320.6
1R03534	01S	012700284.6Q	1	284.6
FOODJAR	11S	012800327.4Q	11	327.4
1R03535	01S	012900244.6Q	1	244.6
FOODJAR	11S	013000362.5Q	11	362.5
1R03536	01S	013100250.5Q	1	250.5
FOODJAR	11S	013200356.6Q	11	356.6
1R03537	01S	013300266.5Q	1	266.5
ODJAR	11S	013400338.4Q	11	338.4
1R03538	01S	013500283.0Q	1	283
FOODJAR	11S	013600332.1Q	11	332.1
1R03539	01S	013700247.5Q	1	247.5
FOODJAR	11S	013800358.6Q	11	358.6
1R03540	01S	.13900249.2Q	1	249.2
FOODJAR	11S	014000344.8Q	11	344.8
1R03541	01S	014100286.3Q	1	286.3

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FOODJAR 11S 014200339.5Q     11          339.5
1R03542 01S 014300274.8Q     1           274.8
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1R03543 01S 014500290.4Q     1           290.4
FOODJAR 11S 014600316.2Q     11          316.2
1R03544 01S 0147.0275.6Q     1           275.6
FOODJAR 11S 014800330.5Q     11          330.5
  03545 01S 014900286.3Q     1           286.3
FOODJAR 11S 015000330.9Q     11          330.9
1R03546 01S 015100269.6Q     1           269.6
FOODJAR 11S 015200337.4Q     11          337.4
1R03547 01S 015300266.6Q     1           266.6
FOODJAR 11S 015400321.0Q     11          321
1R03548 01S 015500300.4Q     1           300.4
FOODJAR 11S 015600327.4Q     11          327.4
1R03549 01S . 15700270.6Q    1           270.6
FOODJAR 11S 015800354.6Q     11          354.6
1R03550 01S 015900270.6Q     1           270.6
FOODJAR 11S 016000345.7Q     11          345.7
1R03551 01S 016100216.0Q     1           216
FOODJAR 11S 016200375.9Q     11          375.9
1R03552 01S 016300275.6Q     1           275.6
FOODJAR 11S 016400320.6Q     11          320.6
1R03553 01S 016500289.6Q     1           289.6
FOODJAR 11S 016600326.6Q     11          326.6
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1R03556 01S 017100264.3Q     1           264.3
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1R03557 01S 017300287.0Q     1           287
FOODJAR 11S 017400336.1Q     11          336.1
. 03558 01S . 17500252.0Q    1           252
FOODJAR 11S 017600359.1Q     11          359.1
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FOODJAR 11S 017800342.1Q     11          342.1
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1R03562 01S . 18300239.9Q    1           239.9
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FOODJAR 11S 018600337.8Q     11          337.8
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FOODJAR 11S 018800358.4Q     11          358.4
1R03565 01S 018900280.6Q     1           280.6
FOODJAR 11S 019000341.8Q     11          341.8
1R03566 01S 019100263.9Q     1           263.9
FOODJAR 11S 019200338.7Q     11          338.7
1R03567 01S 019300280.5Q     1           280.5
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1R03568 01S 019500303.7Q     1           303.7
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FOODJAR 11S 019800336.5Q     11          336.5
1R03570 01S 019900266.7Q     1           266.7
  ODJAR 11S 020000317.7Q     11          317.7
1R03571 01S 020100283.7Q     1           283.7
FOODJAR 11S 020200320.9Q     11          320.9
1R03572 01S 020300268.4Q     1           268.4
FOODJAR 11S 020400342.8Q     11          342.8
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1R03577 01S 021300283.8Q     1           283.8
FOODJAR 11S 021400330.6Q     11          330.6
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FOODJAR 11S 021600350.1Q     11          350.1
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FOODJAR 11S 021800344.1Q     11          344.1
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FOODJAR 11S 022000339.0Q     11          339
1R03581 02S .0?100248.7Q     2           248.7
FOODJAR 12S 00?200343.1Q     12          343.1
1R03582 02S 00?300245.0Q     2           245
FOODJAR 12S 00?400337.2Q     12          337.2
1R03583 02S 00?/00189.3Q     2           189.3
FOODJAR 12S 00?600366.8Q     12          366.8
1R03584 02S 00?7.0233.4Q     2           233.4
FOODJAR 12S 00?800350.7Q     12          350.7
1R03585 02S 00?900236.0Q     2           236
FOODJAR 12S 010000327.6Q     12          327.6
1R03586 02S 010100252.2Q     2           252.2
FOODJAR 12S 010200321.5Q     12          321.5
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FOODJAR 12S 010400370.5Q     12          370.5
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FOODJAR 12S 011400340.1Q     12          340.1
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FOODJAR 12S 011600346.8Q     12          346.8
1R03594 02S 011700251.8Q     2           251.8
FOODJAR 12S 011800318.7Q     12          318.7
1R03595 02S 011900237.6Q     2           237.6
FOODJAR 12S 012000332.6Q     12          332.6
1R03596 02S 012/00232.6Q     2           232.6
FOODJAR 12S 012200324.7Q     12          324.7
1R03597 02S 012300244.4Q     2           244.4
FOODJAR 12S 012400339.9Q     12          339.9
1R03598 02S 012500274.3Q     2           274.3
FOODJAR 12S 012600325.5Q     12          325.5
1R03599 02S 012700235.6Q     2           235.6
FOODJAR 12S 012800337.1Q     12          337.1
1R03600 02S 012900220.9Q     2           220.9
FOODJAR 12S 013000341.8Q     12          341.8
1R03601 02S .13100254.7Q     2           254.7
FOODJAR 12S 013200328.8Q     12          328.8
1R03602 02S .13300220.7Q     2           220.7
FOODJAR 12S 013400355.3Q     12          355.3
1R03603 02S .13500249.4Q     2           249.4
 ODJAR 12S 013600340.6Q      12          340.6
1R03604 02S .13700221.1Q     2           221.1
FOODJAR 12S 013800354.3Q     12          354.3
1R03605 02S 013900247.2Q     2           247.2
FOODJAR 12S 014000342.7Q     12          342.7
1R03606 02S .14100224.9Q     2           224.9
FOODJAR 12S 014200361.7Q     12          361.7
1R03607 02S .14300261.1Q     2           261.1
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FOODJAR 12S 014400329.2Q     12          329.2
1R03608 02S 014500246.6Q     2           246.6
FOODJAR 12S 014600325.7Q     12          325.7
1R03609 02S 014700217.0Q     2           217
FOODJAR 12S 014800338.2Q     12          338.2
1R03610 02S .14900277.9Q     2           277.9
FOODJAR 12S 015000343.4Q     12          343.4
  03611 02S .15100252.5Q     2           252.5
FOODJAR 12S 015200332.0Q     12          332
1R03612 02S 015300$8.2Q      2           248.2

FOODJAR 12S 015400334.1Q     12          334.1
1R03613 02S 015500.70.8Q     2           270.8

FOODJAR 12S 015600325.3Q     12          325.3
1R03614 02S .15700241.8Q     2           241.8
FOODJAR 12S 015800321.3Q     12          321.3
1R03615 02S 015900235.8Q     2           235.8
FOODJAR 12S 016000332.7Q     12          332.7
1R03616 02S 016100234.9Q     2           234.9
FOODJAR 12S 016200338.3Q     12          338.3
1R03617 02S 016300226.5Q     2           226.5
FOODJAR 12S 016400342.6Q     12          342.6
1R03618 02S 016500244.6Q     2           244.6
FOODJAR 12S 016600323.0Q     12          323
1R03619 02S 016700206.2Q     2           206.2
FOODJAR 12S 016800335.8Q     12          335.8
1R03620 02S .16900225.5Q     2           225.5
FOODJAR 12S 017000338.0Q     12          338
1R03621 02S 0171002.0.5Q     2           200.5

FOODJAR 12S 017200362.7Q     12          362.7
1R03622 02S .17300218.2Q     2           218.2
FOODJAR 12S 017400352.7Q     12          352.7
1R03623 02S 017500237.9Q     2           237.9
FOODJAR 12S 017600329.7Q     12          329.7
1R03624 02S 01/700212.6Q     2           212.6
FOODJAR 12S 017800340.5Q     12          340.5
1R03625 02S 017900201.1Q     2           201.1
FOODJAR 12S 018000364.3Q     12          364.3
1R03626 02S 018100263.0Q     2           263
FOODJAR 12S 018200331.3Q     12          331.3
1R03627 02S 018300261.6Q     2           261.6
FOODJAR 12S 018400344.6Q     12          344.6
1R03628 02S 0/8500248.4Q     2           248.4
FOODJAR 12S 018600339.7Q     12          339.7
1R03629 02S .18700237.8Q     2           237.8
FOODJAR 12S 018800339.2Q     12          339.2
1R03630 02S 018900211.8Q     2           211.8
FOODJAR 12S 019000364.1Q     12          364.1
1R03631 02S 019100264.4Q     2           264.4
FOODJAR 12S 019200342.6Q     12          342.6
1R03632 02S 019300239.8Q     2           239.8
FOODJAR 12S 019400345.5Q     12          345.5
1R03633 02S .19500249.1Q     2           249.1
FOODJAR 12S 019600319.7Q     12          319.7
1R03634 02S 019700177.4Q     2           177.4
FOODJAR 12S 019800370.0Q     12          370
  03635 02S 01990.187.5Q     2           187.5
FOODJAR 12S 020000354.2Q     12          354.2
1R03636 02S .20100240.9Q     2           240.9
FOODJAR 12S 020200347.7Q     12          347.7
1R03637 02S .20300225.0Q     2           225
FOODJAR 12S 020400352.7Q     12          352.7
1R03638 02S 020500223.2Q     2           223.2
FOODJAR 12S 020600332.8Q     12          332.8
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1R03639 02S 020700221.6Q     2          221.6
FOODJAR 12S 020800353.6Q     12         353.6
1R03640 02S 020900185.4Q     2          185.4
FOODJAR 12S 021000361.1Q     12         361.1
1R03641 02S . 21100251.1Q    2          251.1
FOODJAR 12S 021200339.6Q     12         339.6
1R03642 02S . 21300218.2Q    2          218.2
  OOJAR 12S 021400347.5Q     12         347.5
1R03643 02S . 21500239.5Q    2          239.5
FOODJAR 12S 021600342.2Q     12         342.2
1R03644 02S 021700229.9Q     2          229.9
FOODJAR 12S 021800337.2Q     12         337.2
1R03645 02S 021900234.6Q     2          234.6
FOODJAR 12S 022000341.6Q     12         341.6
1R03646 03S 022100245.1Q     3          245.1
FOODJAR 13S 022200353.7Q     13         353.7
1R03647 03S 022300284.4Q     3          284.4
FOODJAR 13S 022400331.5Q     13         331.5
1R03648 03S 022500274.3Q     3          274.3
FOODJAR 13S 022600322.7Q     13         322.7
1R03649 03S 022700255.2Q     3          255.2
FOODJAR 13S 022800342.0Q     13         342
1R03650 03S . 22900260.7Q    3          260.7
FOODJAR 13S 023000349.4Q     13         349.4
1R03651 03S 023100261.8Q     3          261.8
FOODJAR 13S 023200336.2Q     13         336.2
1R03652 03S 023300276.0Q     3          276
FOODJAR 13S 023400344.2Q     13         344.2
1R03653 03S . 23500275.9Q    3          275.9
FOODJAR 13S 023600335.3Q     13         335.3
1R03654 03S . 23700278.0Q    3          278
FOODJAR 13S 023800326.9Q     13         326.9
1R03655 03S 023900276.9Q     3          276.9
  OODJAR 13S 024000320.5Q    13         320.5
1R03656 03S 024100275.8Q     3          275.8
FOODJAR 13S 024200326.5Q     13         326.5
1R03657 03S . 24300266.1Q    3          266.1
FOODJAR 13S 024400345.3Q     13         345.3
1R03658 03S . 24500266.3Q    3          266.3
FOODJAR 13S 024600342.7Q     13         342.7
1R03659 03S 024700286.5Q     3          286.5
FOODAR 13S 024800328.0Q      13         328.0
1R03660 03S 024900266.0Q     3          266
FOODJAR 13S 025000336.2Q     13         336.2
1R03661 03S 025100272.0Q     3          272
FOODJAR 13S 025200340.3Q     13         340.3
1R03662 03S 025300242.2Q     3          242.2
FOODJAR 13S 025400354.8Q     13         354.8
1R03663 03S 025500290.3Q     3          290.3
FOODJAR 13S 025600314.1Q     13         314.1
1R03664 03S 025700274.8Q     3          274.8
BFOODJAR 13S 025800327.0Q    13         327
1R03665 03S 025900289.2Q     3          289.2
FOODJAR 13S 026000332.0Q     13         332
1R03666 03S 026100284.3Q     3          284.3
FOODJAR 13S 026200340.1Q     13         340.1
1R03667 03S 026300229.7Q     3          229.7
FOODJAR 13S 026400367.5Q     13         367.5
 03668 03S 026500232.5Q      3          232.5
FOODJAR 13S 026600362.4Q     13         362.4
1R03669 03S 026700272.0Q     3          272
FOODJAR 13S 026800323.6Q     13         323.6
1R03670 03S 026900272.7Q     3          272.7
FOODJAR 13S 027000317.6Q     13         317.6
1R03671 03S 027100273.0Q     3          273
FOODJAR 13S 027200331.1Q     13         331.1
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1R03672	03S	027300282.8Q	3	282.8
FOODJAR	13S	027400330.2Q	13	330.2
1R03673	03S	027500265.2Q	3	265.2
FOODJAR	13S	027600348.2Q	13	348.2
1R03674	03S	027700253.2Q	3	253.2
FOODJAR	13S	027800336.1Q	13	336.1
1R03675	03S	027900281.8Q	3	281.8
ODJAR	13S	028000318.9Q	13	318.9
1R03676	03S	028100296.1Q	3	296.1
FOODJAR	13S	028200328.5Q	13	328.5
1R03677	03S	028300278.8Q	3	278.8
FOODJAR	!3S	028400324.6Q	0	324.6
1R03678	03S	028500285.5Q	3	285.5
FOODJAR	13S	028600333.6Q	13	333.6
1R03679	03S	028700275.7Q	3	275.7
FOODJAR	13S	028800327.6Q	13	327.6
1R03680	03S	028900269.4Q	3	269.4
FOODJAR	13S	029000320.7Q	13	320.7
1R03681	03S	029100277.2Q	3	277.2
FOODJAR	13S	029200334.8Q	13	334.8
1R03682	03S	029300258.2Q	3	258.2
FOODJAR	13S	029400351.0Q	13	351
1R03683	03S	029500266.9Q	3	266.9
FOODJAR	13S	029600341.1Q	13	341.1
1R03684	03S	029700273.6Q	3	273.6
FOODJAR	13S	029800336.4Q	13	336.4
1R03685	03S	029900272.6Q	3	272.6
FOODJAR	13S	030000343.1Q	13	343.1
1R03686	03S	030100262.1Q	3	262.1
FOODJAR	13S	030200336.8Q	13	336.8
1R03687	03S	030300275.4Q	3	275.4
FOODJAR	13S	030400329.9Q	13	329.9
1R03688	03S	030500283.4Q	3	283.4
JODJAR	13S	030600333.1Q	13	333.1
1R03689	03S	030700256.1Q	3	256.1
FOODJAR	13S	030800349.6Q	13	349.6
1R03690	03S	030900265.3Q	3	265.3
FOODJAR	13S	031000331.0Q	13	331
1R03691	03S	031100264.0Q	3	264
FOODJAR	13S	031200339.8Q	13	339.8
1R03692	03S	031300252.8Q	3	252.8
FOODJAR	13S	031400349.3Q	13	349.3
1R03693	03S	031500290.8Q	3	290.8
FOODJAR	13S	031600321.8Q	13	321.8
1R03694	03S	031700291.2Q	3	291.2
FOODJAR	13S	031800321.7Q	13	321.7
1R03695	03S	031900292.6Q	3	292.6
FOODJAR	13S	032000322.0Q	13	322
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 5/12/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340D-338
WEIGHT OF FULL FOOD JAR:S 500GRAMS

WEEK 3

1R02516	01S	007100329.90	1	329.9
FOODJAR	11S	007200318.80	11	318.8
1R02517	01S	007300306.00	1	306
FOODJAR	11S	007400332.40	11	332.4
1R02518	01S	007500310.60	1	310.6
FOODJAR	11S	007600330.00	11	330
1R02519	01S	007700335.50	1	335.5
FOODJAR	11S	007800318.50	11	318.5
1R02520	01S	007900318.40	1	318.4
FOODJAR	11S	010000328.10	11	328.1
1R02521	01S	010100292.50	1	292.5
FOODJAR	11S	010200336.10	11	336.1
1R02522	01S	010300305.20	1	305.2
FOODJAR	11S	010400338.00	11	338
1R02523	01S	010500323.30	1	323.3
FOODJAR	11S	010600334.70	11	334.7
1R02524	01S	010700286.40	1	286.4
FOODJAR	11S	010800349.20	11	349.2
1R02525	01S	010900291.40	1	291.4
FOODJAR	11S	011000337.70	11	337.7
1R02526	01S	011100307.30	1	307.3
FOODJAR	11S	011200322.60	11	322.6
1R02527	01S	011300301.70	1	301.7
FOODJAR	11S	011400338.20	11	338.2
1R02528	01S	011500320.60	1	320.6
FOODJAR	11S	011600328.10	11	328.1
1R02529	01S	011700310.60	1	310.6
FOODJAR	11S	011800318.40	11	318.4
1R02530	01S	011900326.50	1	326.5
FOODJAR	11S	012000330.40	11	330.4
1R02531	01S	012100306.10	1	306.1
FOODJAR	11S	012200328.50	11	328.5
1R02532	01S	012300307.30	1	307.3
FOODJAR	11S	012400327.30	11	327.3
1R02533	01S	012500338.30	1	338.3
FOODJAR	11S	012600314.20	11	314.2
1R02534	01S	012700320.10	1	320.1
FOODJAR	11S	012800319.80	11	319.8
1R02535	01S	012900274.20	1	274.2
FOODJAR	11S	013000351.60	11	351.6
1R02536	01S	013100293.30	1	293.3
FOODJAR	11S	013200338.70	11	338.7
1R02537	01S	013300293.10	1	293.1
FOODJAR	11S	013400338.80	11	338.8
1R02538	01S	013500329.80	1	329.8
FOODJAR	11S	013600324.40	11	324.4
1R02539	01S	013700272.50	1	272.5
FOODJAR	11S	013800349.80	11	349.8
1R02540	01S	013900286.70	1	286.7
FOODJAR	11S	014000339.40	11	339.4

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1R03541	01S	014100306.20	1	306.2
FOODJAR	11S	014200315.60	11	315.6
1R03542	01S	014300311.90	1	311.9
FOODJAR	11S	014400322.30	11	322.3
1R03543	01S	014500316.50	1	316.5
FOODJAR	11S	014600312.00	11	312
1R03544	01S	014700314.50	1	314.5
FOODJAR	11S	014800322.60	11	322.6
1R03545	01S	014900329.60	1	329.6
FOODJAR	11S	015000320.70	11	320.7
1R03546	01S	015100317.30	1	317.3
FOODJAR	11S	015200326.30	11	326.3
1R03547	01S	015300294.50	1	294.5
FOODJAR	11S	015400314.90	11	314.9
1R03548	01S	015500339.10	1	339.1
FOODJAR	11S	015600324.10	11	324.1
1R03549	01S	015700301.00	1	301
FOODJAR	11S	015800345.00	11	345
1R03550	01S	015900308.10	1	308.1
FOODJAR	11S	016000335.80	11	335.8
1R03551	01S	016100240.90	1	240.9
FOODJAR	11S	016200370.20	11	370.2
1R03552	01S	016300306.80	1	306.8
FOODJAR	11S	016400318.40	11	318.4
1R03553	01S	016500317.80	1	317.8
FOODJAR	11S	016600316.00	11	316
1R03554	01S	016700275.70	1	275.7
FOODJAR	11S	016800343.10	11	343.1
1R03555	01S	016900290.80	1	290.8
FOODJAR	11S	017000341.60	11	341.6
1R03556	01S	017100310.00	1	310
FOODJAR	11S	017200318.00	11	318
1R03557	01S	017300314.30	1	314.3
FOODJAR	11S	017400335.00	11	335
1R03558	01S	017500278.10	1	278.1
FOODJAR	11S	017600354.30	11	354.3
1R03559	01S	017700321.30	1	321.3
FOODJAR	11S	017800333.40	11	333.4
1R03560	01S	017900304.90	1	304.9
FOODJAR	11S	018000348.90	11	348.9
1R03561	01S	018100311.80	1	311.8
FOODJAR	11S	018200312.30	11	312.3
1R03562	01S	018300272.00	1	272
FOODJAR	11S	018400353.60	11	353.6
1R03563	01S	018500308.30	1	308.3
FOODJAR	11S	018600340.20	11	340.2
1R03564	01S	018700284.00	1	284
FOODJAR	11S	018800340.90	11	340.9
1R03565	01S	018900316.40	1	316.4
FOODJAR	11S	019000335.10	11	335.1
1R03566	01S	019100300.00	1	300
FOODJAR	11S	019200331.00	11	331
1R03567	01S	019300322.50	1	322.5
FOODJAR	11S	019400324.00	11	324
1R03568	01S	019500336.70	1	336.7
FOODJAR	11S	019600329.40	11	329.4
1R03569	01S	019700322.10	1	322.1
FOODJAR	11S	019800323.00	11	323
1R03570	01S	019900296.60	1	296.6
FOODJAR	11S	020000317.60	11	317.6
1R03571	01S	020100319.20	1	319.2
FOODJAR	11S	020200312.40	11	312.4
1R03572	01S	020300302.00	1	302
FOODJAR	11S	020400336.30	11	336.3
1R03573	01S	020500327.80	1	327.8
FOODJAR	11S	020600327.70	11	327.7

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1R03574	01S	020700299.30	1	299.3
FOODJAR	11S	020800310.90	11	310.9
1R03575	01S	020900286.70	1	286.7
FOODJAR	11S	021000325.10	11	325.1
1R03576	01S	021100302.40	1	302.4
FOODJAR	11S	021200334.60	11	334.6
1R03577	01S	021300320.10	1	320.1
FOODJAR	11S	021400323.60	11	323.6
1R03578	01S	021500293.40	1	293.4
FOODJAR	11S	021600339.60	11	339.6
1R03579	01S	021700294.30	1	294.3
FOODJAR	11S	021800338.40	11	338.4
1R03580	01S	021900295.40	1	295.4
FOODJAR	11S	022000327.50	11	327.5
1R03581	02S	007100278.20	2	278.2
FOODJAR	12S	007200325.80	12	325.8
1R03582	02S	007300255.90	2	255.9
FOODJAR	12S	007400337.80	12	337.8
1R03583	02S	007500199.90	2	199.9
FOODJAR	12S	007600370.00	12	370
1R03584	02S	007700255.50	2	255.5
FOODJAR	12S	007800342.40	12	342.4
1R03585	02S	007900260.90	2	260.9
FOODJAR	12S	010000321.30	12	321.3
1R03586	02S	010100282.50	2	282.5
FOODJAR	12S	010200321.10	12	321.1
1R03587	02S	010300229.50	2	229.5
FOODJAR	12S	010400357.40	12	357.4
1R03588	02S	010500262.10	2	262.1
FOODJAR	12S	010600349.60	12	349.6
1R03589	02S	010700252.60	2	252.6
FOODJAR	12S	010800317.90	12	317.9
[illegible]3590	02S	010900293.70	2	293.7
FOODJAR	12S	011000317.10	12	317.1
1R03591	02S	011100228.80	2	228.8
FOODJAR	12S	011200357.30	12	357.3
1R03592	02S	011300275.20	2	275.2
FOODJAR	12S	011400328.70	12	328.7
1R03593	02S	011500267.20	2	267.2
FOODJAR	12S	011600340.80	12	340.8
1R03594	02S	011700256.20	2	256.2
FOODJAR	12S	011800318.80	12	318.8
1R03595	02S	011900263.80	2	263.8
FOODJAR	12S	012000333.00	12	333
1R03596	02S	012100259.70	2	259.7
FOODJAR	12S	012200333.80	12	333.8
1R03597	02S	012300266.70	2	266.7
FOODJAR	12S	012400338.90	12	338.9
1R03598	02S	012500302.00	2	302
FOODJAR	12S	012600334.40	12	334.4
1R03599	02S	012700265.50	2	265.5
FOODJAR	12S	012800330.40	12	330.4
1R03600	02S	012900245.40	2	245.4
FOODJAR	12S	013000344.00	12	344
1R03601	02S	013100283.80	2	283.8
FOODJAR	12S	013200317.30	12	317.3
1R03602	02S	013300248.10	2	248.1
FOODJAR	12S	013400343.30	12	43.3
[illegible]3603	02S	013500274.10	2	274.1
FOODJAR	12S	013600333.30	12	333.3
1R03604	02S	013700237.70	2	237.7
FOODJAR	12S	013800359.00	12	359
1R03605	02S	013900260.20	2	260.2
FOODJAR	12S	014000349.70	12	349.7
1R03606	02S	014100255.50	2	255.5
FOODJAR	12S	014200347.80	12	347.8

000822

1R03607	02S	014300288.90	2	288.9	
FOODJAR	12S	014400327.10	12	327.1	
1R03608	02S	014500272.10	2	272.1	
FOODJAR	12S	014600317.80	12	317.8	
1R03609	02S	014700237.30	2	237.3	
FOODJAR	12S	014800329.30	12	329.3	
1R03610	02S	014900305.90	2	305.9	
FOODJAR	12S	015000331.60	12	331.6	
1R03611	02S	015100273.40	2	273.4	
FOODJAR	12S	015200334.00	12	334	
1R03612	02S	015300267.60	2	267.6	
FOODJAR	12S	015400338.60	12	338.6	
1R03613	02S	015500304.90	2	304.9	
FOODJAR	12S	015600316.10	12	316.1	
1R03614	02S	015700261.70	2	261.7	
FOODJAR	12S	015800324.30	12	324.3	
1R03615	02S	015900255.90	2	255.9	
FOODJAR	12S	016000321.80	12	321.8	
1R03616	02S	016100264.90	2	264.9	
FOODJAR	12S	016200325.80	12	325.8	
1R03617	02S	016300252.20	2	252.2	
FOODJAR	12S	016400329.90	12	329.9	
1R03618	02S	016500273.10	2	273.1	
FOODJAR	12S	016600317.00	12	317	
1R03619	02S	016700219.60	2	219.6	
FOODJAR	12S	016800348.30	12	348.3	
1R03620	02S	016900242.90	2	242.9	
FOODJAR	12S	017000330.90	12	330.9	
1R03621	02S	017100217.90	2	217.9	
FOODJAR	12S	017200372.60	12	372.6	
1R03622	02S	017300240.10	2	240.1	
FOODJAR	12S	017400343.60	12	343.6	
1R03623	02S	017500244.20	2	244.2	
FOODJAR	12S	017600340.20	12	340.2	
1R03624	02S	017700242.50	2	242.5	
FOODJAR	12S	017800331.70	12	331.7	
1R03625	02S	017900199.90	2	199.9	
FOODJAR	12S	018000374.40	12	374.4	
1R03626	02S	018100280.50	2	280.5	
FOODJAR	12S	018200345.60	12	345.6	
1R03627	02S	018300279.10	2	279.1	
FOODJAR	12S	018400346.00	12	346	
1R03628	02S	018500262.70	2	262.7	
FOODJAR	12S	018600344.50	12	344.5	
1R03629	02S	018700267.60	2	267.6	
FOODJAR	12S	018800335.30	12	335.3	
1R03630	02S	018900224.20	2	224.2	
FOODJAR	12S	019000361.70	12	361.7	
1R03631	02S	019100278.80	2	278.8	
FOODJAR	12S	019200316.80	12	316.8	
1R03632	02S	019300262.80	2	262.8	
FOODJAR	12S	019400345.60	12	345.6	
1R03633	02S	019500269.50	2	269.5	
FOODJAR	12S	019600318.50	12	318.5	
1R03634	02S	019700192.70	2	192.7	
FOODJAR	12S	019800362.40	12	362.4	
1R03635	02S	019900191.70	2	191.7	
FOODJAR	12S	020000363.60	12	363.6	
1R03636	02S	020100265.20	2	265.2	
FOODJAR	12S	020200339.80	12	339.8	
1R03637	02S	020300244.70	2	244.7	
FOODJAR	12S	020400341.10	12	341.1	
1R03638	02S	020500243.50	2	243.5	
FOODJAR	12S	020600330.80	12	330.8	
1R03639	02S	020700239.80	2	239.8	
FOODJAR	12S	020800351.10	12	351.1	

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1R03640	02S	020900191.10	2	191.1
FOODJAR	12S	021000369.80	12	369.8
1R03641	02S	021100278.50	2	278.5
FOODJAR	12S	021200336.60	12	336.6
1R03642	02S	021300235.50	2	235.5
FOODJAR	12S	021400354.90	12	354.9
1R03643	02S	021500271.20	2	271.2
FOODJAR	12S	021600338.90	12	338.9
1R03644	02S	021700235.00	2	235
FOODJAR	12S	021800353.60	12	353.6
1R03645	02S	021900267.10	2	267.1
FOODJAR	12S	022000329.80	12	329.8
1R03646	03S	022100269.60	3	269.6
FOODJAR	13S	022200352.00	13	352
1R03647	03S	022300315.10	3	315.1
FOODJAR	13S	022400317.50	13	317.5
1R03648	03S	022500295.80	3	295.8
FOODJAR	13S	022600311.50	13	311.5
1R03649	03S	022700292.50	3	292.5
FOODJAR	13S	022800322.40	13	322.4
1R03650	03S	022900290.90	3	290.9
FOODJAR	13S	023000340.30	13	340.3
1R03651	03S	023100295.80	3	295.8
FOODJAR	13S	023200326.60	13	326.6
1R03652	03S	023300305.40	3	305.4
FOODJAR	13S	023400333.60	13	333.6
1R03653	03S	023500304.80	3	304.8
FOODJAR	13S	023600330.10	13	330.1
1R03654	03S	023700316.00	3	316
FOODJAR	13S	023800320.20	13	320.2
1R03655	03S	023900309.60	3	309.6
FOODJAR	13S	024000312.80	13	312.8
1R03656	03S	024100301.60	3	301.6
FOODJAR	13S	024200320.40	13	320.4
1R03657	03S	024300301.40	3	301.4
FOODJAR	13S	024400338.00	13	338
1R03658	03S	024500302.60	3	302.6
FOODJAR	13S	024600330.20	13	330.2
1R03659	03S	024700310.10	3	310.1
FOODJAR	13S	024800329.90	13	329.9
1R03660	03S	024900296.60	3	296.6
FOODJAR	13S	025000336.40	13	336.4
1R03661	03S	025100307.90	3	307.9
FOODJAR	13S	025200334.80	13	334.8
1R03662	03S	025300260.30	3	260.3
FOODJAR	13S	025400351.90	13	351.9
1R03663	03S	025500306.20	3	306.2
FOODJAR	13S	025600314.10	13	314.1
1R03664	03S	025700306.90	3	306.9
FOODJAR	13S	025800322.70	13	322.7
1R03665	03S	025900315.40	3	315.4
FOODJAR	13S	026000329.60	13	329.6
1R03666	03S	026100316.20	3	316.2
FOODJAR	13S	026200333.50	13	333.5
1R03667	03S	026300252.30	3	252.3
FOODJAR	13S	026400366.00	13	366
1R03668	03S	026500252.10	3	252.1
FOODJAR	13S	026600352.00	13	352
1R03669	03S	026700301.10	3	301.1
FOODJAR	13S	026800316.60	13	316.6
1R03670	03S	026900279.00	3	279
FOODJAR	13S	027000317.50	13	317.5
1R03671	03S	027100304.70	3	304.7
FOODJAR	13S	027200318.30	13	318.3
1R03672	03S	027300318.60	3	318.6
FOODJAR	13S	027400325.50	13	325.5

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1R03673 03S 027500291.80      3              291.8
FOODJAR 13S 027600349.10      13             349.1
1R03674 03S 027700291.30      3              291.3
FOODJAR 13S 027800326.40      13             326.4
1R03675 03S 027900313.20      3              313.2
FOODJAR 13S 028000316.60      13             316.8
1R03676 03S 028100340.00      3              340
 JDJAR 13S 028200311.30       13             311.3
1R03677 03S 028300310.30      3              310.3
FOODJAR 13S 028400320.10      13             320.1
1R03678 03S 028500315.80      3              315.8
FOODJAR 13S 028600338.10      13             338.1
1R03679 03S 028700307.90      3              307.9
FOODJAR 13S 028800320.40      13             320.4
1R03680 03S 028900295.40      3              295.4
FOODJAR 13S 029000319.00      13             319
1R03681 03S 029100313.00      3              313
FOODJAR 13S 029200325.30      13             325.3
1R03682 03S 029300289.90      3              289.9
FOODJAR 13S 029400345.30      13             345.3
1R03683 03S 029500315.20      3              315.2
FOODJAR 13S 029600319.70      13             319.7
1R03684 03S 029700316.80      3              316.8
FOODJAR 13S 029800318.90      13             318.9
1R03685 03S 029900298.70      3              298.7
FOODJAR 13S 030000345.90      13             345.9
1R03686 03S 030100291.20      3              291.2
FOODJAR 13S 030200324.80      13             324.8
1R03687 03S 030300299.40      3              299.4
FOODJAR 13S 030400327.50      13             327.5
1R03688 03S 030500315.70      3              315.7
FOODJAR 13S 030600330.40      13             330.4
  03689 03S 030700283.80      3              283.8
FOODJAR 13S 030800343.10      13             343.1
1R03690 03S 030900298.50      3              298.5
FOODJAR 13S 031000314.60      13             314.6
1R03691 03S 031100292.50      3              292.5
FOODJAR 13S 031200340.20      13             340.2
1R03692 03S 031300272.30      3              272.3
FOODJAR 13S 031400348.30      13             348.3
1R03693 03S 031500329.20      3              329.2
FOODJAR 13S 031600311.20      13             311.2
1R03694 03S 031700309.90      3              309.9
FOODJAR 13S 031800320.70      13             320.7
1R03695 03S 031900308.60      3              308.6
FOODJAR 13S 032000316.90      13             316.9
9999999999      99            0
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000825

TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 5/19/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 525GRAMS

WEEK 4

1R03516	01S	00?100355.20	1	355.2
FOODJAR	11S	00?200333.40	11	333.4
1R03517	01S	00?300331.40	1	331.4
FOODJAR	11S	00?400353.60	11	353.6
1R03518	01S	00?500329.30	1	329.3
FOODJAR	11S	00?600317.30	11	317.3
1R03519	01S	00?700366.50	1	366.5
FOODJAR	11S	00?800323.10	11	323.1
1R03520	01S	00?900351.30	1	351.3
FOODJAR	11S	010000337.90	11	337.9
1R03521	01S	010100313.40	1	313.4
FOODJAR	11S	010200357.60	11	357.6
1R03522	01S	010300330.90	1	330.9
FOODJAR	11S	010400357.10	11	357.1
1R03523	01S	010500351.60	1	351.6
FOODJAR	11S	010600351.30	11	351.3
1R03524	01S	010700316.60	1	316.6
FOODJAR	11S	010800361.60	11	361.6
1R03525	01S	010900320.20	1	320.2
FOODJAR	11S	011000336.90	11	336.9
1R03526	01S	011100325.90	1	325.9
FOODJAR	11S	011200349.40	11	349.4
1R03527	01S	011300333.90	1	333.9
FOODJAR	11S	011400362.90	11	362.9
1R03528	01S	011500351.80	1	351.8
FOODJAR	11S	011600342.80	11	342.8
1R03529	01S	011700339.30	1	339.3
FOODJAR	11S	011800343.50	11	343.5
1R03530	01S	011900346.70	1	346.7
FOODJAR	11S	012000345.60	11	345.6
1R03531	01S	012100330.70	1	330.7
FOODJAR	11S	012200353.90	11	353.9
1R03532	01S	012300335.20	1	335.2
FOODJAR	11S	012400349.90	11	349.9
1R03533	01S	012500363.20	1	363.2
FOODJAR	11S	012600338.60	11	338.6
1R03534	01S	012700373.60	1	373.6
FOODJAR	11S	012800321.50	11	321.5
1R03535	01S	012900296.00	1	296
FOODJAR	11S	013000370.60	11	370.6
1R03536	01S	013100317.40	1	317.4
FOODJAR	11S	013200360.70	11	360.7
1R03537	01S	013300302.80	1	302.8
FOODJAR	11S	013400353.00	11	353
1R03538	01S	013500361.80	1	361.8
FOODJAR	11S	013600336.10	11	336.1
1R03539	01S	013700284.70	1	284.7
FOODJAR	11S	013800381.10	11	381.1
1R03540	01S	013900309.80	1	309.8
FOODJAR	11S	014000361.50	11	361.5

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1R03541	01S	014100368.20	1	368.2
FOODJAR	11S	014200318.30	11	318.3
1R03542	01S	014300338.30	1	338.3
FOODJAR	11S	014400340.40	11	340.4
1R03543	01S	014500350.60	1	350.6
FOODJAR	11S	014600311.70	11	311.7
[illegible]03544	01S	014700335.90	1	335.9
[illegible]ODJAR	11S	014800349.80	11	349.8
1R03545	01S	014900361.80	1	361.8
FOODJAR	11S	015000335.20	11	335.2
1R03546	01S	015100346.30	1	346.3
FOODJAR	11S	015200346.00	11	346
1R03547	01S	015300346.00	1	346
FOODJAR	11S	015400319.10	11	319.1
1R03548	01S	015500373.20	1	373.2
FOODJAR	11S	015600341.30	11	341.3
1R03549	01S	015700320.10	1	320.1
FOODJAR	11S	015800372.00	11	372
1R03550	01S	015900333.90	1	333.9
FOODJAR	11S	016000354.40	11	354.4
1R03551	01S	016100259.00	1	259
FOODJAR	11S	016200395.80	11	395.8
1R03552	01S	016300318.00	1	318
FOODJAR	11S	016400347.20	11	347.2
1R03553	01S	016500369.60	1	369.6
FOODJAR	11S	016600315.00	11	315
1R03554	01S	016700286.40	1	286.4
FOODJAR	11S	016800349.90	11	349.9
1R03555	01S	016900312.30	1	312.3
FOODJAR	11S	017000333.70	11	333.7
1R03556	01S	017100366.40	1	366.4
FOODJAR	11S	017200329.30	11	329.3
1R03557	01S	017300341.00	1	341
FOODJAR	11S	017400363.70	11	363.7
1R03558	01S	017500294.70	1	294.7
FOODJAR	11S	017600372.90	11	372.9
1R03559	01S	017700349.90	1	349.9
FOODJAR	11S	017800353.80	11	353.8
1R03560	01S	017900319.30	1	319.3
FOODJAR	11S	018000374.00	11	374
1R03561	01S	018100348.90	1	348.9
FOODJAR	11S	018200317.30	11	317.3
1R03562	01S	018300291.60	1	291.6
FOODJAR	11S	018400384.70	11	384.7
1R03563	01S	018500321.40	1	321.4
FOODJAR	11S	018600356.30	11	356.3
1R03564	01S	018700310.90	1	310.9
FOODJAR	11S	018800352.00	11	352
1R03565	01S	018900348.00	1	348
FOODJAR	11S	019000341.10	11	341.1
1R03566	01S	019100325.10	1	325.1
FOODJAR	11S	019200356.40	11	356.4
1R03567	01S	019300359.10	1	359.1
FOODJAR	11S	019400332.40	11	332.4
1R03568	01S	019500362.20	1	362.2
FOODJAR	11S	019600352.40	11	352.4
1R03569	01S	019700349.20	1	349.2
[illegible]ODJAR	11S	019800341.00	11	341
[illegible]03570	01S	019900323.80	1	323.8
FOODJAR	11S	020000317.60	11	317.6
1R03571	01S	020100362.30	1	362.3
FOODJAR	11S	020200322.20	11	322.2
1R03572	01S	020300335.50	1	335.5
FOODJAR	11S	020400350.10	11	350.1
1R03573	01S	020500357.10	1	357.1
FOODJAR	11S	020600342.60	11	342.6

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1R03574 01S 020700375.50     1          375.5
FOODJAR 11S 020800329.30     11         329.3
1R03575 01S 020900305.80     1          305.8
FOODJAR 11S 021000346.30     11         346.3
1R03576 01S 021100336.70     1          336.7
FOODJAR 11S 021200348.80     11         348.8
1R03577 01S 021300336.40     1          336.4
 JDJAR 11S 021400358.40      11         358.4
1R03578 01S 021500315.50     1          315.5
FOODJAR 11S 021600358.50     11         358.5
1R03579 01S 021700317.10     1          317.1
FOODJAR 11S 021800365.40     11         365.4
1R03580 01S 021900300.70     1          300.7
FOODJAR 11S 022000317.40     11         317.4
1R03581 02S 00?100305.10     2          305.1
FOODJAR 12S 00?200345.90     12         345.9
1R03582 02S 00?300262.70     2          262.7
FOODJAR 12S 00?400379.10     12         379.1
1R03583 02S 00?500211.30     2          211.3
FOODJAR 12S 00?600390.00     12         390
1R03584 02S 00?700273.70     2          273.7
FOODJAR 12S 00?800367.60     12         367.6
1R03585 02S 00?900276.60     2          276.6
FOODJAR 12S 010000340.40     12         340.4
1R03586 02S 010100298.40     2          298.4
FOODJAR 12S 010200350.50     12         350.5
1R03587 02S 010300249.10     2          249.1
FOODJAR 12S 010400377.60     12         377.6
1R03588 02S 010500278.00     2          278
FOODJAR 12S 010600383.50     12         383.5
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FOODJAR 12S 010800344.30     12         344.3
1R03590 02S 010900350.30     2          350.3
FOODJAR 12S 011000319.50     12         319.5
1R03591 02S 011100241.10     2          241.1
FOODJAR 12S 011200388.60     12         388.6
1R03592 02S 011300291.80     2          291.8
FOODJAR 12S 011400359.20     12         359.2
1R03593 02S 011500295.30     2          295.3
FOODJAR 12S 011600363.20     12         363.2
1R03594 02S 011700305.50     2          305.5
FOODJAR 12S 011800320.20     12         320.2
1R03595 02S 011900283.00     2          283
FOODJAR 12S 012000359.10     12         359.1
1R03596 02S 012100288.90     2          288.9
FOODJAR 12S 012200352.90     12         352.9
1R03597 02S 012300275.50     2          275.5
FOODJAR 12S 012400377.30     12         377.3
1R03598 02S 012500325.00     2          325
FOODJAR 12S 012600356.50     12         356.5
1R03599 02S 012700283.60     2          283.6
FOODJAR 12S 012800353.50     12         353.5
1R03600 02S 012900249.50     2          249.5
FOODJAR 12S 013000387.00     12         387
1R03601 02S 013100306.20     2          306.2
FOODJAR 12S 013200340.10     12         340.1
1R03602 02S 013300267.50     2          267.5
FOODJAR 12S 013400371.30     12         371.3
 J3603 02S 013500284.40      2          284.4
FOODJAR 12S 013600366.70     12         366.7
1R03604 02S 013700248.20     2          248.2
FOODJAR 12S 013800380.70     12         380.7
1R03605 02S 013900268.80     2          268.8
FOODJAR 12S 014000381.40     12         381.4
1R03606 02S 014100279.40     2          279.4
FOODJAR 12S 014200376.00     12         376
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000828

1R03607	02S	014500317.00	2	317
FOODJAR	12S	014400350.60	12	350.6
1R03608	02S	014500302.00	2	302
FOODJAR	12S	014600330.60	12	330.6
1R03609	02S	014700264.30	2	264.3
FOODJAR	12S	014800354.30	12	354.3
[illegible]3610	02S	014900333.60	2	333.6
[illegible]JDJAR	12S	015000360.70	12	360.7
1R03611	02S	015100281.70	2	281.7
FOODJAR	12S	015200369.50	12	369.5
1R03612	02S	015300293.10	2	293.1
FOODJAR	12S	015400363.80	12	363.8
1R03613	02S	015500344.00	2	344
FOODJAR	12S	015600338.70	12	338.7
1R03614	02S	015700283.30	2	283.3
FOODJAR	12S	015800339.80	12	339.8
1R03615	02S	015900270.80	2	270.8
FOODJAR	12S	016000358.70	12	358.7
1R03616	02S	016100286.50	2	286.5
FOODJAR	12S	016200353.50	12	353.5
1R03617	02S	016300279.60	2	279.6
FOODJAR	12S	016400351.50	12	351.5
1R03618	02S	016500309.50	2	309.5
FOODJAR	12S	016600330.90	12	330.9
1R03619	02S	016700233.90	2	233.9
FOODJAR	12S	016800369.50	12	369.5
1R03620	02S	016900264.70	2	264.7
FOODJAR	12S	017000355.30	12	355.3
1R03621	02S	017100234.90	2	234.9
FOODJAR	12S	017200398.10	12	398.1
1R03622	02S	017300256.20	2	256.2
FOODJAR	12S	017400375.70	12	375.7
1R03623	02S	017500260.90	2	260.9
FOODJAR	12S	017600368.00	12	368
1R03624	02S	017700264.10	2	264.1
FOODJAR	12S	017800364.60	12	364.6
1R03625	02S	017900217.70	2	217.7
FOODJAR	12S	018000377.10	12	377.1
1R03626	02S		2	298.5
FOODJAR	12S	018200354.90	12	354.9
1R03627	02S	018300298.50	2	298.5
FOODJAR	12S	018400372.50	12	372.5
1R03628	02S	018500283.10	2	283.1
FOODJAR	12S	018600376.80	12	376.8
1R03629	02S	018700293.20	2	293.2
FOODJAR	12S	018800360.40	12	360.4
1R03630	02S	018900241.40	2	241.4
FOODJAR	12S	019000393.30	12	393.3
1R03631	02S	019100321.00	2	321
FOODJAR	12S	019200363.50	12	363.5
1R03632	02S	019300284.30	2	284.3
FOODJAR	12S	019400376.10	12	376.1
1R03633	02S	019500305.70	2	305.7
FOODJAR	12S	019600335.40	12	335.4
1R03634	02S	019700208.90	2	208.9
FOODJAR	12S	019800378.10	12	378.1
1R03635	02S	019900206.10	2	206.1
F[illegible]ODJAR	12S	020000376.20	12	376.2
[illegible]03636	02S	020100297.00	2	297
FOODJAR	12S	020200350.40	12	350.4
1R03637	02S	020300261.20	2	261.2
FOODJAR	12S	020400356.30	12	356.3
1R03638	02S	020500259.50	2	259.5
FOODJAR	12S	020600360.90	12	360.9
1R03639	02S	020700263.40	2	263.4
FOODJAR	12S	020800366.40	12	366.4

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1R03640	02S	020900198.60	2	198.6
FOODJAR	12S	021000383.90	12	383.9
1R03641	02S	021100306.00	2	306
FOODJAR	12S	021200359.20	12	359.2
1R03642	02S	021300256.00	2	256
FOODJAR	12S	021400371.30	12	371.3
1R03643	02S	021500294.30	2	294.3
FOODJAR	12S	021600358.20	12	358.2
1R03644	02S	021700251.90	2	251.9
FOODJAR	12S	021800367.00	12	367
1R03645	02S	021900296.60	2	296.6
FOODJAR	12S	022000348.00	12	348
1R03646	03S	022100288.40	3	288.4
FOODJAR	13S	022200366.60	13	366.6
1R03647	03S	022300338.00	3	338
FOODJAR	13S	022400358.80	13	358.8
1R03648	03S	022500354.10	3	354.1
FOODJAR	13S	022600313.10	13	313.1
1R03649	03S	022700322.10	3	322.1
FOODJAR	13S	022800346.00	13	346
1R03650	03S	022900308.00	3	308
FOODJAR	13S	023000366.70	13	366.7
1R03651	03S	023100325.80	3	325.8
FOODJAR	13S	023200355.10	13	355.1
1R03652	03S	023300327.30	3	327.3
FOODJAR	13S	023400360.60	13	360.6
1R03653	03S	023500320.50	3	320.5
FOODJAR	13S	023600357.20	13	357.2
1R03654	03S	023700349.00	3	349
FOODJAR	13S	023800341.80	13	341.8
1R03655	03S	023900335.10	3	335.1
FOODJAR	13S	024000328.00	13	328
1R03656	03S	024100333.10	3	333.1
FOODJAR	13S	024200350.10	13	350.1
1R03657	03S	024300324.20	3	324.2
FOODJAR	13S	024400359.60	13	359.6
1R03658	03S	024500328.90	3	328.9
FOODJAR	13S	024600360.20	13	360.2
1R03659	03S	024700331.10	3	331.1
FOODJAR	13S	024800349.70	13	349.7
1R03660	03S	024900325.00	3	325
FOODJAR	13S	025000352.20	13	352.2
1R03661	03S	025100336.90	3	336.9
FOODJAR	13S	025200349.00	13	349
1R03662	03S	025300277.60	3	277.6
FOODJAR	13S	025400388.30	13	388.3
1R03663	03S	025500362.20	3	362.2
FOODJAR	13S	025600314.50	13	314.5
1R03664	03S	025700326.10	3	326.1
FOODJAR	13S	025800357.20	13	357.2
1R03665	03S	025900338.00	3	338
FOODJAR	13S	026000353.70	13	353.7
1R03666	03S	026100339.40	3	339.4
FOODJAR	13S	026200349.10	13	349.1
1R03667	03S	026300264.30	3	264.3
FOODJAR	13S	026400388.60	13	388.6
1R03668	03S	026500268.70	3	268.7
FOODJAR	13S	026600379.70	13	379.7
1R03669	03S	026700330.40	3	330.4
FOODJAR	13S	026800338.50	13	338.5
1R03670	03S	026900339.60	3	339.6
FOODJAR	13S	027000317.30	13	317.3
1R03671	03S	027100325.80	3	325.8
FOODJAR	13S	027200335.70	13	335.7
1R03672	03S	027300339.50	3	339.5
FOODJAR	13S	027400346.80	13	346.8

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000830

1R03673	03S	027500317.80	3	317.8
FOODJAR	13S	027600364.00	13	364
1R03674	03S	027700319.00	3	319
FOODJAR	13S	027800352.80	13	352.8
1R03675	03S	027900351.80	3	351.8
FOODJAR	13S	028000324.50	13	324.5
1R03676	03S	028100374.10	3	374.1
FOODJAR	13S	028200336.60	13	336.6
1R03677	03S	028300337.70	3	337.7
FOODJAR	13S	028400335.10	13	335.1
1R03678	03S	028500342.00	3	342
FOODJAR	13S	028600358.20	13	358.2
1R03679	03S	028700338.90	3	338.9
FOODJAR	13S	028800340.80	13	340.8
1R03680	03S	028900340.00	3	340
FOODJAR	13S	029000323.70	13	323.7
1R03681	03S	029100345.00	3	345
FOODJAR	13S	029200336.70	13	336.7
1R03682	03S	029300310.40	3	310.4
FOODJAR	13S	029400372.20	13	372.2
1R03683	03S	029500346.90	3	346.9
FOODJAR	13S	029600340.00	13	340
1R03684	03S	029700342.70	3	342.7
FOODJAR	13S	029800332.60	13	332.6
1R03685	03S	029900319.10	3	319.1
FOODJAR	13S	030000358.80	13	358.8
1R03686	03S	030100311.60	3	311.6
FOODJAR	13S	030200341.60	13	341.6
1R03687	03S	030300320.70	3	320.7
FOODJAR	13S	030400346.70	13	346.7
1R03688	03S	030500332.80	3	332.8
FOODJAR	13S	030600347.00	13	347
1R03689	03S	030700302.90	3	302.9
FOODJAR	13S	030800362.70	13	362.7
1R03690	03S	030900335.00	3	335
FOODJAR	13S	031000326.50	13	326.5
1R03691	03S	031100317.30	3	317.3
FOODJAR	13S	031200361.30	13	361.3
1R03692	03S	031300287.60	3	287.6
FOODJAR	13S	031400384.60	13	384.6
1R03693	03S	031500372.20	3	372.2
FOODJAR	13S	031600318.50	13	318.5
1R03694	03S	031700340.70	3	340.7
FOODJAR	13S	031800318.00	13	318
1R03695	03S	031900358.90	3	358.9
FOODJAR	13S	032000329.10	13	329.1
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 5/26/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 5

1R03516	01S	00?000388.6Q	1	388.6
FOODJAR	11S	00?100358.0Q	11	358
1R03517	01S	00?200357.2Q	1	357.2
FOODJAR	11S	00?300386.8Q	11	386.8
1R03518	01S	00?400355.7Q	1	355.7
FOODJAR	11S	00?500389.6Q	11	389.6
1R03519	01S	00?600389.8Q	1	389.8
FOODJAR	11S	00?700361.8Q	11	361.8
1R03520	01S	00?800382.5Q	1	382.5
FOODJAR	11S	00?900364.2Q	11	364.2
1R03521	01S	010000345.9Q	1	345.9
FOODJAR	11S	010100335.7Q	11	335.7
1R03522	01S	010200354.9Q	1	354.9
FOODJAR	11S	010300394.2Q	11	394.2
1R03523	01S	010400388.7Q	1	388.7
FOODJAR	11S	010500377.4Q	11	377.4
1R03524	01S	010600340.9Q	1	340.9
FOODJAR	11S	010700385.8Q	11	385.8
1R03525	01S	010800357.6Q	1	357.6
FOODJAR	11S	010900377.3Q	11	377.3
1R03526	01S	011000353.5Q	1	353.5
FOODJAR	11S	011100383.6Q	11	383.6
1R03527	01S	011200361.7Q	1	361.7
FOODJAR	11S	011300389.9Q	11	389.9
1R03528	01S	011400379.2Q	1	379.2
FOODJAR	11S	011500378.7Q	11	378.7
1R03529	01S	011600365.6Q	1	365.6
FOODJAR	11S	011700376.1Q	11	376.1
1R03530	01S	011800377.3Q	1	377.3
FOODJAR	11S	011900377.0Q	11	377
1R03531	01S	012000353.8Q	1	353.8
FOODJAR	11S	012100392.4Q	11	392.4
1R03532	01S	012200363.8Q	1	363.8
FOODJAR	11S	012300363.7Q	11	363.7
1R03533	01S	012400370.4Q	1	370.4
FOODJAR	11S	012500382.2Q	11	382.2
1R03534	01S	012600396.9Q	1	396.9
FOODJAR	11S	012700360.1Q	11	360.1
1R03535	01S	012800320.0Q	1	320
FOODJAR	11S	012900350.7Q	11	350.7
1R03536	01S	013000339.3Q	1	339.3
FOODJAR	11S	013100398.8Q	11	398.8
1R03537	01S	013200325.7Q	1	325.7
FOODJAR	11S	013300369.8Q	11	369.8
1R03538	01S	013400386.4Q	1	386.4
FOODJAR	11S	013500375.2Q	11	375.2
1R03539	01S	013600295.8Q	1	295.8
FOODJAR	11S	013700407.0Q	11	407
1R03540	01S	013800339.2Q	1	339.2
FOODJAR	11S	013900384.5Q	11	384.5
1R03541	01S	014000369.7Q	1	369.7

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FOODJAR	11S	014100387.1Q	11	387.1
1R03542	01S	014200368.7Q	1	368.7
FOODJAR	11S	014300370.0Q	11	370
1R03543	01S	014400402.7Q	1	402.7
FOODJAR	11S	014500335.6Q	11	335.6
1R03544	01S	014600357.2Q	1	357.2
FOODJAR	11S	014700384.3Q	11	384.3
1R03545	01S	014800391.6Q	1	391.6
FOODJAR	11S	014900370.9Q	11	370.9
1R03546	01S	015000383.5Q	1	383.5
FOODJAR	11S	015100372.6Q	11	372.6
1R03547	01S	015200373.7Q	1	373.7
FOODJAR	11S	015300353.5Q	11	353.5
1R03548	01S	015400406.3Q	1	406.3
FOODJAR	11S	015500366.3Q	11	366.3
1R03549	01S	015600349.9Q	1	349.9
FOODJAR	11S	015700383.5Q	11	383.5
1R03550	01S	015800347.1Q	1	347.1
FOODJAR	11S	015900383.0Q	11	383
1R03551	01S	016000280.6Q	1	280.6
FOODJAR	11S	016100417.7Q	11	417.7
1R03552	01S	016200361.4Q	1	361.4
FOODJAR	11S	016300349.9Q	11	349.9
1R03553	01S	016400406.0Q	1	406
FOODJAR	11S	016500355.1Q	11	355.1
1R03554	01S	016600306.3Q	1	306.3
FOODJAR	11S	016700401.4Q	11	401.4
1R03555	01S	016800346.0Q	1	346
FOODJAR	11S	016900390.9Q	11	390.9
1R03556	01S	017000386.3Q	1	386.3
FOODJAR	11S	017100381.3Q	11	381.3
1R03557	01S	017200347.4Q	1	347.4
FOODJAR	11S	017300400.0Q	11	400
1R03558	01S	017400308.5Q	1	308.5
FOODJAR	11S	017500398.8Q	11	398.8
1R03559	01S	017600369.5Q	1	369.5
FOODJAR	11S	017700386.7Q	11	386.7
1R03560	01S	017800341.6Q	1	341.6
FOODJAR	11S	017900396.4Q	11	396.4
1R03561	01S	018000399.8Q	1	399.8
FOODJAR	11S	018100348.6Q	11	348.6
1R03562	01S	018200308.2Q	1	308.2
FOODJAR	11S	018300402.9Q	11	402.9
1R03563	01S	018400343.5Q	1	343.5
FOODJAR	11S	018500389.6Q	11	389.6
1R03564	01S	018600338.0Q	1	338
FOODJAR	11S	018700372.0Q	11	372
1R03565	01S	018800371.2Q	1	371.2
FOODJAR	11S	018900375.1Q	11	375.1
1R03566	01S	019000345.5Q	1	345.5
FOODJAR	11S	019100383.4Q	11	383.4
1R03567	01S	019200390.2Q	1	390.2
FOODJAR	11S	019300359.1Q	11	359.1
1R03568	01S	019400375.2Q	1	375.2
FOODJAR	11S	019500394.7Q	11	394.7
1R03569	01S	019600377.4Q	1	377.4
FOODJAR	11S	019700373.3Q	11	373.3
1R03570	01S	019800378.7Q	1	378.7
FOODJAR	11S	019900329.6Q	11	329.6
1R03571	01S	020000386.5Q	1	386.5
FOODJAR	11S	020100357.5Q	11	357.5
1R03572	01S	020200362.4Q	1	362.4
FOODJAR	11S	020300373.1Q	11	373.1
1R03573	01S	020400373.7Q	1	373.7
FOODJAR	11S	020500386.3Q	11	386.3
1R03574	01S	020600410.9Q	1	410.9

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FOODJAR	11S	020700337.7Q	11	337.7
1R03575	01S	020800324.0Q	1	324
FOODJAR	11S	020900382.0Q	11	382
1R03576	01S	021000364.9Q	1	364.9
FOODJAR	11S	021100376.7Q	11	376.7
1R03577	01S	021200371.2Q	1	371.2
FOODJAR	11S	021300369.2Q	11	369.2
1R03578	01S	021400349.3Q	1	349.3
FOODJAR	11S	021500366.1Q	11	366.1
1R03579	01S	021600345.7Q	1	345.7
FOODJAR	11S	021700386.0Q	11	386
1R03580	01S	021800341.6Q	1	341.6
FOODJAR	11S	021900367.3Q	11	367.3
1R03581	02S	007100334.3Q	2	334.3
FOODJAR	12S	007200370.7Q	12	370.7
1R03582	02S	007300271.5Q	2	271.5
FOODJAR	12S	007400406.9Q	12	406.9
1R03583	02S	007500234.9Q	2	234.9
FOODJAR	12S	007600407.1Q	12	407.1
1R03584	02S	007700301.2Q	2	301.2
FOODJAR	12S	007800393.9Q	12	393.9
1R03585	02S	007900297.6Q	2	297.6
FOODJAR	12S	010000370.5Q	12	370.5
1R03586	02S	010100320.6Q	2	320.6
FOODJAR	12S	010200379.7Q	12	379.7
1R03587	02S	010300268.9Q	2	268.9
FOODJAR	12S	010400407.1Q	12	407.1
1R03588	02S	010500303.5Q	2	303.5
FOODJAR	12S	010600400.5Q	12	400.5
1R03589	02S	010700282.5Q	2	282.5
FOODJAR	12S	010800348.5Q	12	348.5
1R03590	02S	010900378.3Q	2	378.3
FOODJAR	12S	011000356.4Q	12	356.4
1R03591	02S	011100254.5Q	2	254.5
FOODJAR	12S	011200411.9Q	12	411.9
1R03592	02S	011300325.4Q	2	325.4
FOODJAR	12S	011400376.0Q	12	376
1R03593	02S	011500324.0Q	2	324
FOODJAR	12S	011600391.5Q	12	391.5
1R03594	02S	011700333.4Q	2	333.4
FOODJAR	12S	011800358.2Q	12	358.2
1R03595	02S	011900292.2Q	2	292.2
FOODJAR	12S	012000398.8Q	12	398.8
1R03596	02S	012100319.5Q	2	319.5
FOODJAR	12S	012200368.7Q	12	368.7
1R03597	02S	012300289.6Q	2	289.6
FOODJAR	12S	012400407.1Q	12	407.1
1R03598	02S	012500355.7Q	2	355.7
FOODJAR	12S	012600384.2Q	12	384.2
1R03599	02S	012700314.5Q	2	314.5
FOODJAR	12S	012800371.0Q	12	371
1R03600	02S	012900260.4Q	2	260.4
FOODJAR	12S	013000416.6Q	12	416.6
1R03601	02S	013100338.8Q	2	338.8
FOODJAR	12S	013200362.3Q	12	362.3
1R03602	02S	013300285.0Q	2	285
FOODJAR	12S	013400405.1Q	12	405.1
1R03603	02S	013500308.0Q	2	308
FOODJAR	12S	013600388.9Q	12	388.9
1R03604	02S	013700268.0Q	2	268
FOODJAR	12S	013800414.2Q	12	414.2
1R03605	02S	013900286.5Q	2	286.5
FOODJAR	12S	014000398.6Q	12	398.6
1R03606	02S	014100304.3Q	2	304.3
FOODJAR	12S	014200397.9Q	12	397.9
1R03607	02S	014300343.6Q	2	343.6

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FOODJAR	12S	014400377.00	12	377
1R03608	02S	014500338.60	2	338.6
FOODJAR	12S	014600355.90	12	355.9
1R03609	02R	004600296.40	2	296.4
FOODJAR	12S	014800371.30	12	371.3
1R03610	02S	014900367.70	2	367.7
FOODJAR	12S	015000380.40	12	380.4
1[illegible]3611	02S	015100309.70	2	309.7
F[illegible]DJAR	12S	015200385.90	12	385.9
1R03612	02S	015300318.50	2	318.5
FOODJAR	12S	015400394.90	12	394.9
1R03613	02S	015500376.10	2	376.1
FOODJAR	12S	015600367.50	12	367.5
1R03614	02S	015700308.20	2	308.2
FOODJAR	12S	015800374.40	12	374.4
1R03615	02S	015900297.00	2	297
FOODJAR	12S	016000378.00	12	378
1R03616	02S	016100306.80	2	306.8
FOODJAR	12S	016200387.40	12	387.4
1R03617	02S	016300306.90	2	306.9
FOODJAR	12S	016400387.40	12	387.4
1R03618	02S	016500337.60	2	337.6
FOODJAR	12S	016600368.70	12	368.7
1R03619	02S	016700251.50	2	251.5
FOODJAR	12S	016800403.00	12	403
1R03620	02S	016900287.60	2	287.6
FOODJAR	12S	017000374.30	12	374.3
1R03621	02S	017100255.60	2	255.6
FOODJAR	12S	017200423.80	12	423.8
1R03622	02S	017300280.30	2	280.3
FOODJAR	12S	017400402.70	12	402.7
1R03623	02S	017500283.30	2	283.3
FOODJAR	12S	017600387.90	12	387.9
1[illegible]3624	02S	017700293.80	2	293.8
FOODJAR	12S	017800393.10	12	393.1
1R03625	02S	017900239.70	2	239.7
FOODJAR	12S	018000399.50	12	399.5
1R03626	02S	018100318.50	2	318.5
FOODJAR	12S	018200389.60	12	389.6
1R03627	02S	018300317.90	2	317.9
FOODJAR	12S	018400399.20	12	399.2
1R03628	02S	018500301.50	2	301.5
FOODJAR	12S	018600407.70	12	407.7
1R03629	02S	018700320.90	2	320.9
FOODJAR	12S	018800383.60	12	383.6
1R03630	02S	018900265.00	2	265
FOODJAR	12S	019000414.50	12	414.5
1R03631	02S	019100347.70	2	347.7
FOODJAR	12S	019200389.10	12	389.1
1R03632	02S	019300312.90	2	312.9
FOODJAR	12S	019400396.10	12	396.1
1R03633	02S	019500333.10	2	333.1
FOODJAR	12S	019600381.20	12	381.2
1R03634	02S	019700223.10	2	223.1
FOODJAR	12S	019800407.00	12	407
1R03635	02S	019900221.70	2	221.7
FOODJAR	12S	020000394.90	12	394.9
1R03636	02S	020100323.30	2	323.3
F[illegible]DJAR	12S	020200379.90	12	379.9
1[illegible]3637	02S	020300284.50	2	284.5
FOODJAR	12S	020400374.60	12	374.6
1R03638	02S	020500274.20	2	274.2
FOODJAR	12S	020600386.40	12	386.4
1R03639	02S	020700282.80	2	282.8
FOODJAR	12S	020800395.00	12	395
1R03640	02S	020900211.30	2	211.3

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FOODJAR	12S	021000414.8Q	12	414.8
1R03641	02S	021100330.6Q	2	330.6
FOODJAR	12S	021200381.6Q	12	381.6
1R03642	02S	021300269.3Q	2	269.3
FOODJAR	12S	021400386.6Q	12	386.6
1R03643	02S	021500327.6Q	2	327.6
FOODJAR	12S	021600375.6Q	12	375.6
1 3644	02S	021700269.6Q	2	269.6
FOODJAR	12S	021800351.9Q	12	351.9
1R03645	02S	021900331.2Q	2	331.2
FOODJAR	12S	022000371.8Q	12	371.8
1R03646	03S	022100312.5Q	3	312.5
FOODJAR	13S	022200396.3Q	13	396.3
1R03647	03S	022300365.0Q	3	365
FOODJAR	13S	022400384.8Q	13	384.8
1R03648	03S	022500393.0Q	3	393
FOODJAR	13S	022600341.2Q	13	341.2
1R03649	03S	022700359.8Q	3	359.8
FOODJAR	13S	022800369.4Q	13	369.4
1R03650	03S	022900333.7Q	3	333.7
FOODJAR	13S	023000393.2Q	13	393.2
1R03651	03S	023100354.5Q	3	354.5
FOODJAR	13S	023200375.9Q	13	375.9
1R03652	03S	023300353.8Q	3	353.8
FOODJAR	13S	023400386.6Q	13	386.6
1R03653	03S	023500341.8Q	3	341.8
FOODJAR	13S	023600379.3Q	13	379.3
1R03654	03S	023700373.5Q	3	373.5
FOODJAR	13S	023800377.0Q	13	377
1R03655	03S	023900370.6Q	3	370.6
FOODJAR	13S	024000342.4Q	13	342.4
1R03656	03S	024100358.3Q	3	358.3
FOODJAR	13S	024200378.0Q	13	378
1 3657	03S	024300352.9Q	3	352.9
FOODJAR	13S	024400388.7Q	13	388.7
1R03658	03S	024500360.3Q	3	360.3
FOODJAR	13S	024600385.8Q	13	385.8
1R03659	03S	024700347.3Q	3	347.3
FOODJAR	13S	024800379.1Q	13	379.1
1R03660	03S	024900363.8Q	3	363.8
FOODJAR	13S	025000369.2Q	13	369.2
1R03661	03S	025100360.2Q	3	360.2
FOODJAR	13S	025200379.4Q	13	379.4
1R03662	03S	025300302.4Q	3	302.4
FOODJAR	13S	025400396.2Q	13	396.2
1R03663	03S	025500403.6Q	3	403.6
FOODJAR	13S	025600343.4Q	13	343.4
1R03664	03S	025700347.6Q	3	347.6
FOODJAR	13S	025800386.4Q	13	386.4
1R03665	03S	025900359.7Q	3	359.7
FOODJAR	13S	026000379.0Q	13	379
1R03666	03S	026100364.8P	3	364.8
1R03667	03S	026300279.0Q	3	279
FOODJAR	13S	026400414.4Q	13	414.4
1R03668	03S	026500281.9Q	3	281.9
FOODJAR	13S	026600409.7Q	13	409.7
1R03669	03S	026700355.3Q	3	355.3
F DJAR	13S	026800374.1Q	13	374.1
1R03670	03S	026900365.5Q	3	365.5
FOODJAR	13S	027000360.8Q	13	360.8
1R03671	03S	027100350.9Q	3	350.9
FOODJAR	13S	027200377.5Q	13	377.5
1R03672	03S	027300358.6Q	3	358.6
FOODJAR	13S	027400366.6Q	13	366.6
1R03673	03S	027500339.6Q	3	339.6

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FOODJAR	13S	027600297.5Q	13	397.5
1R03674	03S	027700343.0Q	3	343
FOODJAR	13S	027800382.8Q	13	382.8
1R03675	03S	027900378.7Q	3	378.7
FOODJAR	13S	028000362.4Q	13	362.4
1R03676	03S	028100404.1Q	3	404.1
FOODJAR	13S	028200358.1Q	13	358.1
1 3677	03S	028300362.2Q	3	362.2
FOODJAR	13S	028400361.4Q	13	361.4
1R03678	03S	028500367.6Q	3	367.6
FOODJAR	13S	028600378.6Q	13	378.6
1R03679	03S	028700371.5Q	3	371.5
FOODJAR	13S	028800366.6Q	13	366.6
1R03680	03S	028900373.9Q	3	373.9
FOODJAR	13S	029000361.5Q	13	361.5
1R03681	03S	029100376.1Q	3	376.1
FOODJAR	13S	029200362.7Q	13	362.7
1R03682	03S	029300331.0Q	3	331
FOODJAR	13S	029400405.5Q	13	405.5
1R03683	03S	029500382.2Q	3	382.2
FOODJAR	13S	029600359.3Q	13	359.3
1R03684	03S	029700366.8Q	3	366.8
FOODJAR	13S	029800352.2Q	13	352.2
1R03685	03S	029900341.7Q	3	341.7
FOODJAR	13S	030000380.3Q	13	380.3
1R0286	03S	030100339.7Q	3	339.7
FOODJAR	13S	030200390.7Q	13	390.7
1R03687	03S	030300341.9Q	3	341.9
FOODJAR	13S	030400371.2Q	13	371.2
1R03688	03S		3	359.7
FOODJAR			13	367.4
1R03689	03S	030700321.1Q	3	321.1
FOODJAR	13S	030800391.3Q	13	391.3
1 3690	03S	030900371.8P	3	371.8
FOODJAR	13S	031000357.4Q	13	357.4
1R03691	03S	031100341.5Q	3	341.5
FOODJAR	13S	031200386.1Q	13	386.1
1R03692	03S	031300300.6Q	3	300.6
FOODJAR	13S	031400413.2Q	13	413.2
1R03693	03S	031500403.7Q	3	403.7
FOODJAR	13S	031600348.8Q	13	348.8
1R03694	03S	031700356.2Q	3	356.2
FOODJAR	13S	031800362.7Q	13	362.7
1R03695	03S	031900376.4Q	3	376.4
FOODJAR	13S	032000380.3Q	13	380.3
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 6/2/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 6

1R03516	01S	000000421.3Q	1	421.3
FOODJAR	11S	000100352.6Q	11	352.6
1R03517	01S	000200387.8Q	1	387.8
FOODJAR	11S	000300365.9Q	11	365.9
1R03518	01S	000400385.7Q	1	385.7
FOODJAR	11S	000500369.8Q	11	369.8
1R03519	01S	000600421.0Q	1	421
FOODJAR	11S	000700358.3Q	11	358.3
1R03520	01S	000800410.1Q	1	410.1
FOODJAR	11S	000900360.4Q	11	360.4
1R03521	01S	001000376.3Q	1	376.3
FOODJAR	11S	001100372.6Q	11	372.6
1R03522	01S	001200375.9Q	1	375.9
FOODJAR	11S	001300392.8Q	11	392.8
1R03523	01S	001400426.3Q	1	426.3
FOODJAR	11S	001500318.6Q	11	318.6
1R03524	01S	001600363.9Q	1	363.9
FOODJAR	11S	001700385.3Q	11	385.3
1 3525	01S	001800401.1Q	1	401.1
FOODJAR	11S	001900352.1Q	11	352.1
1R03526	01S	002000384.8Q	1	384.8
FOODJAR	11S	002100363.5Q	11	363.5
1R03527	01S	002200389.8Q	1	389.8
FOODJAR	11S	002300378.9Q	11	378.9
1R03528	01S	002400414.5Q	1	414.5
FOODJAR	11S	002500360.0Q	11	360
1R03529	01S	002600389.1Q	1	389.1
FOODJAR	11S	002700329.3Q	11	329.3
1R03530	01S	002800396.3Q	1	396.3
FOODJAR	11S	002900372.2Q	11	372.2
1R03531	01S	003000386.9Q	1	386.9
FOODJAR	11S	003100371.2Q	11	371.2
1R03532	01S	003200390.0Q	1	390
FOODJAR	11S	003300365.7Q	11	365.7
1R03533	01S	003400409.0Q	1	409
FOODJAR	11S	003500376.6Q	11	376.6
1R03534	01S	003600432.8Q	1	432.8
FOODJAR	11S	003700347.7Q	11	347.7
1R03535	01S	003800341.2Q	1	341.2
FOODJAR	11S	003900393.1Q	11	393.1
1R03536	01S	004000370.7Q	1	370.7
FOODJAR	11S	004100386.1Q	11	386.1
1R03537	01S	004200350.2Q	1	350.2
FOODJAR	11S	004300366.3Q	11	366.3
1 3538	01S	004400425.6Q	1	425.6
FOODJAR	11S	004500350.1Q	11	350.1
1R03539	01S	004600323.9Q	1	323.9
FOODJAR	11S	004700392.6Q	11	392.6
1R03540	01S	004800364.6Q	1	364.6
FOODJAR	11S	004900375.2Q	11	375.2
1R03541	01S	005000412.5Q	1	412.5

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FOODJAR 11S 005100328.5Q    11          328.5
1R03542 01S 005200397.2Q    1           397.2
FOODJAR 11S 005300365.2Q    11          365.2
1R03543 01S 005400443.8Q    1           443.8
FOODJAR 11S 005500335.2Q    11          335.2
1R03544 01S 005600384.6Q    1           384.6
FOODJAR 11S 005700367.0Q    11          367
1R03545 01S 005800422.1Q    1           422.1
FOODJAR 11S 005900359.6Q    11          359.6
1R03546 01S 006000420.2Q    1           420.2
FOODJAR 11S 006100371.1Q    11          371.1
1R03547 01S 006200407.1Q    1           407.1
FOODJAR 11S 006300347.0Q    11          347
1R03548 01S 006400441.1Q    1           441.1
FOODJAR 11S 006500359.4Q    11          359.4
1R03549 01S 006600371.0Q    1           371
FOODJAR 11S 006700382.3Q    11          382.3
1R03550 01S 006800382.1Q    1           382.1
FOODJAR 11S 006900379.7Q    11          379.7
1R03551 01S 007000301.1Q    1           301.1
FOODJAR 11S 007100408.8Q    11          408.8
1R03552 01S 007200403.2Q    1           403.2
FOODJAR 11S 007300363.9Q    11          363.9
1R03553 01S 007400442.7Q    1           442.7
FOODJAR 11S 007500348.9Q    11          348.9
1R03554 01S 007600329.8Q    1           329.8
FOODJAR 11S 007700385.0Q    11          385
1R03555 01S 007800374.0Q    1           374
FOODJAR 11S 007900385.9Q    11          385.9
1R03556 01S 008000421.0Q    1           421
FOODJAR 11S 008100380.0Q    11          380
1R03557 01S 008200383.5Q    1           383.5
F  DJAR 11S 008300392.7Q    11          392.7
1R03558 01S 008400326.9Q    1           326.9
FOODJAR 11S                 11          410.1
1R03559 01S 008600409.1Q    1           409.1
FOODJAR 11S 008700372.4Q    11          372.4
1R03560 01S 008800374.2Q    1           374.2
FNNDJ0R 00R 008900379.6Q    11          379.6
1R03561 01S 009000435.8Q    1           435.8
FOODJAR 11S 009100348.3Q    11          348.3
1R03562 01S 009200329.7Q    1           329.7
FOODJAR 11S 009300397.3Q    11          397.3
1R03563 01S 009400368.9Q    1           368.9
FOODJAR 11S 009500385.6Q    11          385.6
1R03564 01S 009600364.7Q    1           364.7
FOODJAR 11S 009700374.0Q    11          374
1R03565 01S 009800398.7Q    1           398.7
FOODJAR 11S 009900346.8Q    11          346.8
1R03566 01S 010000361.3Q    1           361.3
FOODJAR 11S                 11          397.2
1R03567                     1           427.0
FOODJAR 11S 010300358.1Q    11          358.1
1R03568 01S 010400404.9Q    1           404.9
FOODJAR 11S 010500388.7Q    11          388.7
1R03569 01S 010600409.0Q    1           409
FOODJAR 11S 010700362.2Q    11          362.2
1R03570 01S 010800414.2Q    1           414.2
   JDJAR 11S 010900319.0Q   11          319
1R03571 01S 011000424.6Q    1           424.6
FOODJAR 11S 011100340.0Q    11          340
1R03572 01S 011200396.7Q    1           396.7
FOODJAR 11S 011300350.9Q    11          350.9
1R03573 01S 011400398.5Q    1           398.5
FOODJAR 11S 011500368.1Q    11          368.1
1R03574 01S 011600407.4Q    1           407.4
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FOODJAR	11S	011700317.8Q	11	317.8
1R03575	01S	011800358.3Q	1	358.3
FOODJAR	11S	011900350.1Q	11	350.1
1R03576	01S	012000387.4Q	1	387.4
FOODJAR	11S	012100373.4Q	11	373.4
1R03577	01S	012200405.1Q	1	405.1
FOODJAR	11S	012300361.5Q	11	361.5
1R03578	01S	012400376.4Q	1	376.4
FOODJAR	11S	012500352.3Q	11	352.3
1R03579	01S	012600372.7Q	1	372.7
FOODJAR	11S	012700374.1Q	11	374.1
1R03580	01S	012800366.3Q	1	366.3
FOODJAR	11S	012900368.3Q	11	368.3
1R03581	02S	007100365.3Q	2	365.3
FOODJAR	12S	007200360.0Q	12	360
1R03582	02S	007300279.4Q	2	279.4
FOODJAR	12S	007400423.3Q	12	423.3
1R03583	02S	007500242.3Q	2	242.3
FOODJAR	12S	007600421.2Q	12	421.2
1R03584	02S	007700310.5Q	2	310.5
FOODJAR	12S	007800413.0Q	12	413
1R03585	02S	007900308.9Q	2	308.9
FOODJAR	12S	010000388.3Q	12	388.3
1R03586	02S	010100333.9Q	2	333.9
FOODJAR	12S	010200400.8Q	12	400.8
1R03587	02S	010300281.7Q	2	281.7
FOODJAR	12S	010400434.1Q	12	434.1
1R03588	02S	010500328.3Q	2	328.3
FOODJAR	12S	010600399.8Q	12	399.8
1R03589	02S	010700289.2Q	2	289.2
FOODJAR	12S	010800382.3Q	12	382.3
1R03590	02S	010900391.8Q	2	391.8
FOODJAR	12S	011000387.2Q	12	387.2
1R03591	02S	011100269.5Q	2	269.5
FOODJAR	12S	011200417.1Q	12	417.1
1R03592	02S	011300332.6Q	2	332.6
FOODJAR	12S	011400392.8Q	12	392.8
1R03593	02S	011500338.6Q	2	338.6
FOODJAR	12S	011600396.3Q	12	396.3
1R03594	02S	011700320.4Q	2	320.4
FOODJAR	12S	011800406.4Q	12	406.4
1R03595	02S	011900300.4Q	2	300.4
FOODJAR	12S	012000409.8Q	12	409.8
1R03596	02S	012100336.4Q	2	336.4
FOODJAR	12S	012200397.2Q	12	397.2
1R03597	02S	012300296.2Q	2	296.2
FOODJAR	12S	012400426.5Q	12	426.5
1R03598	02S	012500350.0Q	2	350
FOODJAR	12S	012600432.9Q	12	432.9
1R03599	02S	012700308.3Q	2	308.3
FOODJAR	12S	012800425.4Q	12	425.4
1R03600	02S	012900263.6Q	2	263.6
FOODJAR	12S	013000440.3Q	12	440.3
1R03601	02S	012100348.6Q	2	348.6
FOODJAR	12S	013200398.2Q	12	398.2
1R03602	02S	013300292.5Q	2	292.5
FOODJAR	12S	013400414.6Q	12	414.6
1R03603	02S	013500325.3Q	2	325.3
FOODJAR	12S	013600403.0Q	12	403
1R03604	02S	013700278.1Q	2	278.1
FOODJAR	12S	013800420.0Q	12	420
1R03605	02S	013900295.8Q	2	295.8
FOODJAR	12S	014000411.9Q	12	411.9
1R03606	02S	014100315.3Q	2	315.3
FOODJAR	12S	014200414.4Q	12	414.4
1R03607	02S	014300352.1Q	2	352.1

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FOODJAR	12S	014400398.10	12	398.1
1R03608	02S	014500353.10	2	353.1
FOODJAR	12S	014600376.30	12	376.3
1R03609	02S	014700307.50	2	307.5
FOODJAR	12S	014800388.20	12	388.2
1R03610	02S	014900374.50	2	374.5
FOODJAR	12S	015000392.80	12	392.8
1 2611	02S	015100315.20	2	315.2
FOODJAR	12S	015200344.70	12	344.7
1R03612	02S	015300323.00	2	323
FOODJAR	12S	015400403.60	12	403.6
1R03613	02S	015500391.20	2	391.2
FOODJAR	12S	015600391.60	12	391.6
1R03614	02S	01570326.60	2	326.6
FOODJAR	12S	015800382.50	12	382.5
1R03615	02S	015900309.30	2	309.3
FOODJAR	12S	016000393.10	12	393.1
1R03616	02S	016100308.80	2	308.8
FOODJAR	12S	016200416.90	12	416.9
1R03617	02S	016300317.90	2	317.9
FOODJ@R	12S	016400397.80	12	397.8
1R03618	02S	016500360.40	2	360.4
FOODJAR	12S	016600380.60	12	380.6
1R03619	02S	016700263.70	2	263.7
FOODJAR	12S	016800413.70	12	413.7
1R03620	02S	016900302.20	2	302.2
HOODJAR	12S	017000404.60	12	404.6
1R03621	02S	017100269.40	2	269.4
FOODJAR	12S	017200436.70	12	436.7
1R03622	02S	017300284.00	2	284
FOODJAR	12S	017400419.70	12	419.7
1R03623	02S	017500288.10	2	288.1
F DJAR	12S	017600411.60	12	411.6
1R03624	02S	017700295.60	2	295.6
FOODJAR	12S	017800415.80	12	415.8
1R03625	02S	017900250.70	2	250.7
FOODJAR	12S	018000426.90	12	426.9
1R03626	02S	018100333.40	2	333.4
FOODJAR	12S	018200407.60	12	407.6
1R03627	02S	018300328.60	2	328.6
FOODJAR	12S	018400409.70	12	409.7
1R03628	02S	018500306.60	2	306.6
FOODJAR	12S	018600431.10	12	431.1
1R03629	02S	018700331.00	2	331
FOODJAR	12S	018800404.70	12	404.7
1R03630	02S	018900271.50	2	271.5
FOODJAR	02S	019000439.80	12	439.8
1R03631	02S	019100337.70	2	337.7
FOODJAR	12S	019200439.30	12	439.3
1R03632	02S	019300226.00	2	226
FOODJAR	12S	019400409.00	12	409
1R03633	02S	019500346.80	2	346.8
FOODJAR	12S	019600411.40	12	411.4
1R03634	02S	019700239.30	2	239.3
FOODJAR	12S	019800415.80	12	415.8
1R03635	02S	019900220.60	2	220.6
FOODJAR	12S	020000442.00	12	442
1R03636	02S	020100341.40	2	341.4
JDJAR	12S	020200399.70	12	399.7
1R03637	02S	020300286.00	2	286
FOODJAR	12S	020400407.30	12	407.3
1R03638	02S	020500262.00	2	284.3
FOODJAR	12S	020600419.70	12	419.7
1R03639	02S	020700306.00	2	306
FOODJAR	12S	020800403.80	12	403.8
1R03640	02S	020900233.20	2	233.2

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FOODJAR	12S	021000417.8Q	12	417.8
1R03641	02S	021100350.0Q	2	350
FOODJAR	12S	021200395.9Q	12	395.9
1R03642	02S	021300268.6Q	2	268.6
FOODJAR	12S	021400432.1Q	12	432.1
1R03643	02S	021500338.3Q	2	338.3
FOODJAR	12S	021600405.9Q	12	405.9
1R03644	02S	021700263.0Q	2	263
FOODJAR	12S	021800421.3Q	12	421.3
1R03645	02S	021900348.3Q	2	348.3
FOODJAR	12S	022000378.8Q	12	378.8
1R03646	03S	022100321.4Q	3	321.4
FOODJAR	13S	022200407.6Q	13	407.6
1R03647	03S	022300381.9Q	3	381.9
FOODJAR	13S	022400393.2Q	13	393.2
0R03648	03S	022500413.1Q	3	413.1
FOODJAR	13S	022600358.8Q	13	358.8
1R03649	03S	022700370.1Q	3	370.1
FOODJAR	13S	022800382.4Q	13	382.4
1R03650	03S	022900350.3Q	3	350.3
FOODJAR	13S	023000394.5Q	13	394.5
1R03651	03S	023100378.3Q	3	378.3
FOODJAR	13S	023200374.9Q	13	374.9
1R03652	03S	023300365.0Q	3	365
FOODJAR	13S	023400385.0Q	13	385
1R03653	03S	023500373.3Q	3	373.3
FOODJAR	13S	023600380.8Q	13	380.8
1R03654	03S	023700403.6Q	3	403.6
FOODJAR	13S	023800374.9Q	13	374.9
1R03655	03S	023900384.3Q	3	384.3
FOODJAR	13S	024000372.1Q	13	372.1
1R03656	03S	024100395.2Q	3	395.2
FOODJAR	13S	024200372.3Q	13	372.3
1R03657	03S	024300369.6Q	3	369.6
FOODJAR	13S	024400392.8Q	13	392.8
1R03658	03S	024500370.8Q	3	370.8
FOODJAR	13S	024600407.5Q	13	407.5
1R03659	03S	024700348.7Q	3	348.7
FOODJAR	13S	024800416.6Q	13	416.6
1R03660	03S	024900386.0Q	3	386
FOODJAR	13S	025000379.2Q	13	379.2
1R03661	03S	025100365.2Q	3	365.2
FOODJAR	13S	025200402.6Q	13	402.6
1R03662	03S	025300314.2Q	3	314.2
FOODJAR	13S	025400417.2Q	13	417.2
1R03663	03S	025500427.1Q	3	427.1
FOODJAR	13S	025600371.9Q	13	371.9
1R03664	03S	025700371.4Q	3	371.4
FOODJAR	13S	025800391.2Q	13	391.2
1R03665	03S	025900377.0Q	3	377
FOODJAR	13S	026000398.8Q	13	398.8
1R03666	03S	026100380.2Q	3	380.2
FOODJAR	13S	026200384.6Q	13	384.6
1R03667	03S	026300292.9Q	3	292.9
FOODJAR	13S	026400420.5Q	13	420.5
1R03668	02S	026500289.9Q	3	289.9
FOODJAR	13S	026600421.1Q	13	421.1
1R03669	03S	026700371.2Q	3	371.2
FOODJAR	13S	026800289.1Q	13	289.1
1R03670	03S	026900375.0Q	3	375
FOODJAR	13S	027000383.6Q	13	383.6
1R03671	03S	027100369.1Q	3	369.1
FOODJAR	13S	027200377.6Q	13	377.6
1R03672	03S	027300378.8Q	3	378.8
FOODJAR	13S	027400390.9Q	13	390.9
1R03673	03S	027500336.8Q	3	336.8

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FOODJAR 13S 027600429.1Q      13          429.1
1R03674 03S 027700366.0Q      3           366
FOODJAR 12R 026800291.3Q      12          291.3
1R03675 03S 027900391.8Q      3           391.8
FOODJAR 13S 028000372.3Q      13          372.3
1R03676 03S 028100434.6Q      3           434.6
FOODJAR 13S 028200364.3Q      13          364.3
1R03677 03S 028300357.6Q      3           357.6
FOODJAR 13S 028400403.6Q      13          403.6
1R02678 03S 028500384.7Q      3           384.7
FOODJAR 13S 028600391.9Q      13          391.9
1R03679 03S 028700396.2Q      3           396.2
FOODJAR 13S 028800388.8Q      13          388.8
1R03680 03S 028900390.7Q      3           390.7
FOODJAR 13S 029000374.4Q      13          374.4
1R03681 03S 029100382.1Q      3           382.1
FOODJAR 13S 029200389.0Q      13          389
1R03682 03S 029300337.7Q      3           337.7
FOODJAR 13S 029400415.2Q      13          415.2
1R03683 03S 029500399.8Q      3           399.8
FOODJAR 13S 029600376.6Q      13          376.6
1R03684 03S 029700377.9Q      3.          377.9
FOODJAR 13S 029800371.5Q      13          371.5
1R03685 03S 029900351.9Q      3           351.9
FOODJAR 13S 030000399.0Q      13          399
1R03686 03S 030100355.5Q      3           355.5
FOODJAR 13S 030200394.6Q      13          394.6
1R03687 03S 030300357.9Q      3           357.9
FOODJAR 13S 020400384.5Q      13          384.5
1R03688 03S 030500366.6Q      3           366.6
FOODJ@R 02R 020600282.8P      13          383.8
1R03689
FOODJAR                       3           319.9
                              13          412.2

1R03690 03S 030900380.3Q      3           380.3
FOODJAR 13S 031000370.9Q      13          370.9
1R03691 03S 031100357.1Q      3           357.1
FOODJAR 13S 031200392.5Q      13          392.5
1R03692 03S 031300307.4Q      3           307.4
FOODJAR 13S 031400431.6Q      13          431.6
1R03693 03S 031500420.4Q      3           420.4
FOODJAR 13S 031600379.1Q      13          379.1
1R03694 03S 031700382.9Q      3           382.9
FOODJAR 13S 031800382.9Q      13          382.9
1R03695 03S 031900390.8Q      3           390.8
FOODJAR 13S 032000390.9Q      13          390.9
9999999999      99            0
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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 6/9/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 7

1R03516	01S	007100434.7Q	1	434.7
FOODJAR	11S	007200346.8Q	11	346.8
1R03517	01S	007300400.0Q	1	400
FOODJAR	11S	007400361.2Q	11	361.2
1R03518	01S	007500399.6Q	1	399.6
FOODJAR	11S	007600347.5Q	11	347.5
1R03519	01S	007700434.7Q	1	434.7
FOODJAR	11S	007800353.6Q	11	353.6
1R03520	01S	007900420.2Q	1	420.2
FOODJAR	11S	010000348.3Q	11	348.3
1R03521	01S	010100380.8Q	1	380.8
FOODJAR	11S	010200376.0Q	11	376
1R03522	01S	010300392.0Q	1	392
FOODJAR	11S	010400378.6Q	11	378.6
1R03523	01S	010500442.1Q	1	442.1
FOODJAR	11S	010600330.2Q	11	330.2
1R03524	01S	010700382.6Q	1	382.6
FOODJAR	11S	010800371.4Q	11	371.4
1 3525	01S	010900378.0Q	1	378
FOODJAR	11S	011000315.8Q	11	315.8
1R03526	01S	011100399.3Q	1	399.3
FOODJAR	11S	011200331.2Q	11	331.2
1R03527	01S	011300401.9Q	1	401.9
FOODJAR	11S	011400378.1Q	11	378.1
1R03528	01S	011500424.7Q	1	424.7
FOODJAR	11S	011600334.0Q	11	334
1R03529	01S	011700399.8Q	1	399.8
FOODJAR	11S	011800368.3Q	11	368.3
1R03530	01S	011900413.6Q	1	413.6
FOODJAR	11S	012000356.7Q	11	356.7
1R03531	01S	012100402.0Q	1	402
FOODJAR	11S	012200363.8Q	11	363.8
1R03532	01S	012300411.2Q	1	411.2
FOODJAR	11S	012400363.2Q	11	363
1R03533	01S	012500427.9Q	1	427.9
FOODJAR	11S	012600362.5Q	11	362.5
1R03534	01S	012700445.8Q	1	445.8
FOODJAR	11S	012800343.3Q	11	343.3
1R03535	01S	012900356.0Q	1	356
FOODJAR	11S	013000392.5Q	11	392.5
1R03536	01S	013100375.0Q	1	375
FOODJAR	11S	013200393.2Q	11	393.2
1R03537	01S	013300360.3Q	1	360.3
FOODJAR	11S	013400369.5Q	11	369.5
1R03538	01S	013500447.2Q	1	447.2
FOODJAR	11S	013600352.7Q	11	352.7
1R03539	01S	013700342.9Q	1	342.9
FOODJAR	11S	013800384.9Q	11	384.9
1R03540	01S	013900380.3Q	1	380.3
FOODJAR	11S	014000371.8Q	11	371.8
1R03541	01S	014100428.3Q	1	428.3
FOODJAR	11S	014200360.6Q	11	360.6

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1R03542 01S 014300408.00     1          408
FOODJAR 11S 014400360.90     11         360.9
1R03543 01S 014500453.20     1          453.2
FOODJAR 11S 014600336.40     11         336.4
1R03544 01S 014700402.20     1          402.2
FOODJAR 11S 014800362.70     11         362.7
1R03545 01S 014900432.50     1          432.5
FOODJAR 11S 015000356.30     11         356.3
1R03546 01S 015100434.90     1          434.9
FOODJAR 11S 015200370.00     11         370
1R03547 01S 015300426.50     1          426.5
FOODJAR 11S 015400313.60     11         313.6
1R03548 01S 015500457.60     1          457.6
FOODJAR 11S 015600328.30     11         328.3
1R03549 01S 015700384.00     1          384
FOODJAR 11S 015800388.30     11         388.3
1R03550 01S 015900399.00     1          399
FOODJAR 11S 016000366.70     11         366.7
1R03551 01S 016100312.20     1          312.2
FOODJAR 11S 016200408.50     11         408.5
1R03552 01S 016300416.20     1          416.2
FOODJAR 11S 016400355.30     11         355.3
1R03553 01S 016500456.90     1          456.9
FOODJAR 11S 016600317.40     11         317.4
1R03554 01S 016700333.90     1          333.9
FOODJAR 11S 016800352.80     11         352.8
1R03555 01S 016900390.20     1          390.2
FOODJAR 11S 017000355.90     11         355.9
1R03556 01S 017100427.30     1          427.3
FOODJAR 11S 017200313.60     11         313.6
1R03557 01S 017300397.40     1          397.4
FOODJAR 11S 017400384.60     11         384.6
1R03558 01S 017500338.70     1          338.7
FOODJAR 11S 017600368.10     11         368.1
1R03559 01S 017700422.40     1          422.4
FOODJAR 11S 017800373.60     11         373.6
1R03560 01S 017900380.40     1          380.4
FOODJAR 11S 018000377.60     11         377.6
1R03561 01S 018100452.90     1          452.9
FOODJAR 11S 018200327.40     11         327.4
1R03562 01S 018300343.90     1          343.9
FOODJAR 11S 018400389.50     11         389.5
1R03563 01S 018500379.10     1          379.1
FOODJAR 11S 018600382.00     11         382
1R03564 01S 018700373.90     1          373.9
FOODJAR 11S 018800351.10     11         351.1
1R03565 01S 018900412.00     1          412
FOODJAR 11S 019000373.70     11         373.7
1R03566 01S 019100373.20     1          373.2
FOODJAR 11S 019200375.70     11         375.7
1R03567 01S 019300434.30     1          434.3
FOODJAR 11S 019400353.80     11         353.8
1R03568 01S 019500428.40     1          428.4
FOODJAR 11S 019600361.90     11         361.9
1R03569 01S 019700421.30     1          421.3
FOODJAR 11S 019800354.20     11         354.2
1R03570 01S 019900432.20     1          432.2
FOODJAR 11S 020000325.60     11         325.6
1R03571 01S 020100445.50     1          445.5
FOODJAR 11S 020200342.00     11         342
1R03572 01S 020300414.80     1          414.8
FOODJAR 11S 020400353.10     11         353.1
1R03573 01S 020500421.50     1          421.5
FOODJAR 11S 020600361.30     11         361.3
1R03574 01S 020700417.90     1          417.9
FOODJAR 11S 020800313.30     11         313.3
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1R02575 01S 020900375.70     1          375.7
FOODJAR 11S 021000334.00     11         334
1R03576 01S 021100399.80     1          399.8
FOODJAR 11S 021200331.70     11         331.7
1R03577 01S 021300423.50     1          423.5
FOODJAR 11S 021400350.10     11         350.1
1R03578 01S 021500384.60     1          384.6
FOODJAR 11S 021600354.90     11         354.9
1R03579 01S 021700387.60     1          387.6
FOODJAR 11S 021800362.50     11         362.5
1R03580 01S 021900379.30     1          379.3
FOODJAR 11S 022000369.90     11         369.9
1R03581 02S 00?100387.30     2          387.3
FOODJAR 12S 00?200355.70     12         355.7
1R03582 02S 00?300294.40     2          294.4
FOODJAR 12S 00?400399.70     12         399.7
1R03583 02S 00?500258.00     2          258
FOODJAR 12S 00?600405.20     12         405.2
1R03584 02S 00?700328.90     2          328.9
FOODJAR 12S 00?800377.80     12         377.8
1R03585 02S 00?900325.30     2          325.3
FOODJAR 12S 010000381.20     12         381.2
1R03586 02S 010100348.20     2          348.2
FOODJAR 12S 010200385.40     12         385.4
1R03587 02S 010300297.70     2          297.7
FOODJAR 12S .10400411.20     12         411.2
1R03588 02S 010500346.20     2          346.2
FOODJAR 12S 010600383.00     12         383
1R03589 02S 010700305.60     2          305.6
FOODJAR 12S 010800358.10     12         358.1
1R03590 02S 010900407.10     2          407.1
FOODJAR 12S 011000370.00     12         370
1  3591 02S 011100277.10     2          277.1
FOODJAR 12S 011200400.60     12         400.6
1R03592 02S 011300365.30     2          365.3
FOODJAR 12S 011400379.00     12         379
1R03593 02S 011500354.20     2          354.2
FOODJAR 12S 011600381.20     12         381.2
1R03594 02S 011700350.90     2          350.9
FOODJAR 12S 011800377.20     12         377.2
1R03595 02S 011900310.80     2          310.8
FOODJAR 12S 012000393.80     12         393.8
1R03596 02S 012100359.20     2          359.2
FOODJAR 12S 012200363.60     12         363.6
1R03597 02S 012300318.70     2          318.7
FOODJAR 12S 012400392.10     12         392.1
1R03598 02S 012500378.80     2          378.8
FOODJAR 12S 012600363.60     12         363.6
1R03599 02S 012700339.60     2          339.6
FOODJAR 12S 012800361.30     12         361.3
1R03600 02S 012900285.50     2          285.5
FOODJAR 12S 013000407.00     12         407
1R03601 02S 013100365.30     2          365.3
FOODJAR 12S 013200373.00     12         373
1R03602 02S 013300315.10     2          315.1
FOODJAR 12S 013400406.90     12         406.9
1R03603 02S 013500345.00     2          345
FOODJAR 12S 013600380.60     12         380.6
1R03604 02S 013700288.90     2          288.9
FOODJAR 12S 013800416.10     12         416.1
1R03605 02S 013900304.70     2          304.7
FOODJAR 12S 014000400.50     12         400.5
1R03606 02S 014100327.50     2          327.5
FOODJAR 12S 014200407.60     12         407.6
1R03607 02S 014300354.70     2          354.7
FOODJAR 12S 014400396.50     12         396.5
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1R02608	02S	014500376.20	2	376.2
FOODJAR	12S	014600363.00	12	363
1R03609	02S	014700323.20	2	323.2
FOODJAR	12S	014800378.30	12	378.3
1R03610	02S	014900388.00	2	388
FOODJAR	12S	015000385.20	12	385.2
1R03611	02S	015100332.40	2	332.4
FOODJAR	12S	015200384.60	12	384.6
1R03612	02S	015300346.10	2	346.1
FOODJAR	12S	015400387.00	12	387
1R03613	02S	015500410.50	2	410.5
FOODJAR	12S	015600385.40	12	385.4
1R03614	02S	015700355.10	2	355.1
FOODJAR	12S	015800362.10	12	362.1
1R03615	02S	015900323.10	2	323.1
FOODJAR	12S	016000368.80	12	368.8
1R03616	02S	016100331.20	2	331.2
FOODJAR	12S	016200390.20	12	390.2
1R03617	02S	016300316.80	2	316.8
FOODJAR	12S	016400314.10	12	314.1
1R03618	02S	016500378.30	2	378.3
FOODJAR	12S	016600370.80	12	370.8
1R03619	02S	016700288.50	2	288.5
FOODJAR	12S	016800401.10	12	401.1
1R03620	02S	016900323.70	2	323.7
FOODJAR			12	357.3
1R03621	02S	017100292.10	2	292.1
FOODJAR	12S	017200405.70	12	405.7
1R03622	02S	017300302.70	2	302.7
FOODJAR	12S	017400410.60	12	410.6
1R03623	02S	017500317.00	2	317
FOODJAR	12S	017600375.50	12	375.5
1R03624	02S	017700331.50	2	331.5
FOODJAR	12S	017800392.90	12	392.9
1R03625	02S	017900244.10	2	244.1
FOODJAR	12S	018000396.60	12	396.6
1R03626	02S	018100351.50	2	351.5
FOODJAR	12S	018200391.70	12	391.7
1R03627	02S	018300344.20	2	344.2
FOODJAR	12S	018400388.60	12	388.6
1R03628	02S	018500333.50	2	333.5
FOODJAR	12S	018600393.70	12	393.7
1R03629	02S	018700357.50	2	357.5
FOODJAR	12S	018800382.10	12	382.1
1R03630	02S	018900275.60	2	275.6
FOODJAR	12S	019000434.00	12	434
1R03631	02S	019100379.70	2	379.7
FOODJAR	12S	019200346.70	12	346.7
1R03632	02S	019300345.70	2	345.7
FOODJAR	12S	019400383.10	12	383.1
1R03633	02S	19500375.90	2	375.9
FOODJAR	12S	019600361.60	12	361.6
1R03634	02S	019700262.90	2	262.9
FOODJAR	12S	019800400.80	12	400.8
1R03635	02S	019900255.90	2	255.9
FOODJAR	12S	020000385.60	12	385.6
1R03636	02S	20100360.50	2	360.5
FOODJAR	12S	020200382.00	12	382
1R03637	02S	020300313.70	2	313.7
FOODJAR	12S	020400378.10	12	378.1
1R03638	02S	020500303.30	2	303.3
FOODJAR	12S	020600391.70	12	391.7
1R03639	02S	020700328.40	2	328.4
FOODJAR	12S	020800387.50	12	387.5
1R03640	02S	020900246.20	2	246.2
FOODJAR	12S	021000409.20	12	409.2

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1R03641	02S	021100359.80	2	359.8
FOODJAR	12S	021200395.50	12	395.5
1R03642	02S	021300290.40	2	290.4
FOODJAR	12S	021400422.20	12	422.2
1R03643	02S	021500350.10	2	350.1
FOODJAR	12S	021600292.30	12	392.3
1R03644	02S	021700295.80	2	295.8
FOODJAR	12S	021800371.90	12	371.9
1R03645	02S	021900382.20	2	382.2
FOODJAR	12S	022000358.10	12	358.1
1R03646	03S	022100335.60	3	335.6
FOODJAR	13S	022200397.60	13	397.6
1R03647	03S	022300393.80	3	393.8
FOODJAR	13S	022400379.80	13	379.8
1R03648	03S	022500430.10	3	430.1
FOODJAR	13S	022600374.90	13	374.9
1R03649	03S	022700391.30	3	391.3
FOODJAR	13S	022800367.20	13	367.2
1R03650	03S	022900368.20	3	368.2
FOODJAR	13S	023000392.50	13	392.5
1R03651	03S	023100387.40	3	387.4
FOODJAR	13S	023200388.90	13	388.9
1R03652	03S	023300375.60	3	375.6
FOODJAR	13S	023400362.40	13	362.4
1R03653	03S	023500385.90	3	385.9
FOODJAR	13S	023600382.00	13	382
1R03654	03S	023700422.80	3	422.8
FOODJAR	13S	023800364.80	13	364.8
1R03655	03S	023900405.50	3	405.5
FOODJAR	13S	024000341.70	13	341.7
1R03656	03S	024100408.30	3	408.3
FOODJAR	13S	024200367.90	13	367.9
1 3657	03S	024300389.20	3	389.2
FOODJAR	13S	024400355.90	13	355.9
1R03658			3	380.5
FOODJAR	13S	024600387.60	13	387.6
1R03659	03S	024700357.40	3	357.4
FOODJAR	13S	024800384.10	13	384.1
1R03660	03S	024900410.00	3	410
FOODJAR	13S	025000371.70	13	371.7
1R03661	03S	025100389.30	3	389.3
FOODJAR	13S	025200374.80	13	374.8
1R03662	03S	025300320.50	3	320.5
FOODJAR	13S	025400406.60	13	406.6
1R03663	03S	025500445.00	3	445
FOODJAR	13S	025600369.90	13	369.9
1R03664	03S	025700379.80	3	379.8
FOODJAR	13S	025800385.70	13	385.7
1R03665	03S	025900398.50	3	398.5
FOODJAR	13S	026000373.90	13	373.9
1R03666	03S	026100389.40	3	389.4
FOODJAR	13S	026200377.60	13	377.6
1R03667	03S	.26300308.80	3	308.8
FOODJAR	13S	026400401.70	13	401.7
1R03668	03S	026500308.70	3	308.7
FOODJAR	13S	026600406.20	13	406.2
1R03669	03S	.26700368.50	3	368.5
FOODJAR	13S	026800380.70	13	380.7
1R03670	03S	026900385.70	3	385.7
FOODJAR	13S	027000374.20	13	374.2
1R03671	03S	027100368.90	3	368.9
FOODJAR	13S	027200376.50	13	376.5
1R03672	03S	027300392.90	3	392.9
FOODJAR	13S	027400380.60	13	380.6
1R03673	03S	027500350.60	3	350.6
FOODJAR	13S	027600390.60	13	390.6

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1R03674 03S 027700387.00     3              387
FOODJAR 13S 027800380.70     13             380.7
1R03675 03S 027900416.80     3              416.8
FOODJAR 13S 028000352.10     13             352.1
1R03676 03S 028100452.30     3              452.3
FOODJAR 13S 028200355.10     13             355.1
1?03677 03S .28300377.80     3              377.8
F. JDJAR 13S 028400384.60    13             384.6
1R03678 03S 028500404.50     3              404.5
FOODJAR 13S 028600394.40     13             394.4
1R03679 03S 028700415.20     3              415.2
FOODJAR 13S 028800375.50     13             375.5
1R03680 03S 028900407.20     3              407.2
FOODJAR                      13             365.1
1R03681 03S 029000403.20     3              403.2
FOODJAR 13S 029100366.50     13             366.5
1R03682 03S 029200348.90     3              348.9
FOODJAR 13S 029300407.50     13             407.5
1R03683 03S 029400423.40     3              423.4
FOODJAR 13S 029500359.20     13             359.2
1R03684 03S 029600401.50     3              401.5
FOODJAR 13S 029700371.50     13             371.5
1R03685 03S 029800367.80     3              367.8
FOODJAR 13S 029900380.80     13             380.8
1R03686 03S .30000368.60     3              368.6
FOODJAR 13S 030100403.10     13             403.1
1R03687 03S 030200375.60     3              375.6
FOODJAR 13S 030300365.70     13             365.7
1R03688 03S 030400385.20     3              385.2
FOODJAR 13S 030500376.20     13             376.2
1R03689 03S 030600335.10     3              335.1
FOODJAR 13S 030700403.30     13             403.3
1  3690 03S 030800389.00     3              389
FOODJAR 13S 030900390.30     13             390.3
1R03691 03S 031000357.20     3              357.2
FOODJAR 13S 031100364.20     13             364.2
1R03692 03S 031200312.10     3              312.1
FOODJAR 13S 031300372.50     13             372.5
1R03693 03S 031400438.00     3              438
FOODJAR 13S 031500358.50     13             358.5
1R03694 03S 031600400.80     3              400.8
FOODJAR 13S 031700366.90     13             366.9
1R03695 03S 031800412.30     3              412.3
FOODJAR 13S 031900381.50     13             381.5
9999999999      99           0
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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 6/16/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 8

1R03516	01S	007100463.90	1	463.9
FOODJAR	11S	007200358.00	11	358
1R03517	01S	007300426.20	1	426.2
FOODJAR	11S	007400376.20	11	376.2
1R03518	01S	007500419.00	1	419
FOODJAR	11S	007600366.90	11	366.9
1R03519	01S	007700455.60	1	455.6
FOODJAR	11S	007800372.40	11	372.4
1R03520	01S	007900437.90	1	437.9
FOODJAR	11S	010000380.20	11	380.2
1R03521	01S	010100400.80	1	400.8
FOODJAR	11S	010200374.30	11	374.3
1R03522	01S	010300408.20	1	408.2
FOODJAR	11S	010400387.50	11	387.5
1R03523	01S	010500473.70	1	473.7
FOODJAR	11S	010600367.60	11	367.6
1R03524	01S	010700412.50	1	412.5
FOODJAR	11S	010800371.70	11	371.7
1 3525	01S	010900422.40	1	422.4
FOODJAR	11S	011000352.20	11	352.2
1R03526	01S	011100428.70	1	428.7
FOODJAR	11S	011200363.80	11	363.8
1R03527	01S	011300420.10	1	420.1
FOODJAR	11S	011400382.60	11	382.6
1R03528	01S	011500451.70	1	451.7
FOODJAR	11S	011600358.50	11	358.5
1R03529	01S	011700419.30	1	419.3
FOODJAR	11S	011800363.10	11	363.1
1R03530	01S	011900444.90	1	444.9
FOODJAR	11S	012000360.20	11	360.2
1R03531	01S	012100427.90	1	427.9
FOODJAR	11S	012200371.60	11	371.6
1R03532	01S	012300422.80	1	422.8
FOODJAR	11S	012400378.20	11	378.2
1R03533	01S	012500464.80	1	464.8
FOODJAR	11S	012600352.10	11	352.1
1R03534	01S	012700477.40	1	477.4
FOODJAR	11S	012800341.30	11	341.3
1R03535	01S	012900380.00	1	380
FOODJAR	11S	.13000381.00	11	381
1R03536	01S	013100393.00	1	393
FOODJAR	11S	013200397.30	11	397.3
1R03537	01S	0133003/4.40	1	374.4
F. .JAR	11S	013400377.90	11	377.9
1R03538	01S	013500485.90	1	485.9
FOODJAR	11S	013600343.70	11	343.7
1R03539	01S	013700363.40	1	363.4
FOODJAR	11S	013800386.00	11	386
1R03540	01S	013900398.10	1	398.1
FOODJAR	11S	014000371.80	11	371.8
[illegible]				

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FOODJAR	11S	014200358.20	11	358.2
1R03542	01S	014300436.70	1	436.7
FOODJAR	11S	014400367.80	11	367.8
1R03543	01S	014500484.90	1	484.9
FOODJAR	11S	014600331.50	11	331.5
1R03544	01S	014700434.70	1	434.7
F DJAR	11S	014800332.40	11	332.4
1R03545	01S	014900463.30	1	463.3
FOODJAR	11S	015000346.10	11	346.1
1R03546	01S	015100457.60	1	457.6
FOODJAR	11S	015200347.10	11	347.1
1R03547	01S	015300457.90	1	457.9
FOODJAR	11S	015400337.80	11	337.8
1R03548	01S	015500487.30	1	487.3
FOODJAR	11S	015600351.40	11	351.4
1R03549	01S	015700403.40	1	403.4
FOODJAR	11S	015800390.20	11	390.2
1R03550	01S	015900417.50	1	417.5
FOODJAR	11S	016000375.50	11	375.5
1R03551	01S	016100326.00	1	326
FOODJAR	11S	016200410.80	11	410.8
1R03552	01S	016300447.10	1	447.1
FOODJAR	11S	016400351.60	11	351.6
1R03553	01S	016500494.20	1	494.2
FOODJAR	11S	016600333.00	11	333
1R03554	01S	016700353.60	1	353.6
FOODJAR	11S	016800393.60	11	393.6
1R03555	01S		1	409.3
FOODJAR	11S	017000378.80	11	378.8
1R03556	01S	017100467.10	1	467.1
FOODJAR	11S	017200364.80	11	364.8
1R03557	01S	017300422.60	1	422.6
F DJAR	11S	017400380.90	11	380.9
1R03558	01S	017500359.40	1	359.4
FOODJAR	11S	017600384.00	11	384
1R03559	01S	017700453.70	1	453.7
FOODJAR	11S	017800369.40	11	369.4
1R03560	01S	017900395.50	1	395.5
FOODJAR	11S	018000385.60	11	385.6
1R03561	01S	018100480.00	1	480
FOODJAR	11S	018200329.90	11	329.9
1R03562	01S	018300350.80	1	350.8
FOODJAR	11S	018400395.10	11	395.1
1R03563	01S	018500400.10	1	400.1
FOODJAR	11S	018600371.50	11	371.5
1R03564	01S	018700400.30	1	400.3
FOODJAR	11S	018800356.80	11	356.8
1R03565	01S	018900437.20	1	437.2
FOODJAR	11S	019000374.40	11	374.4
1R03566	01S	019100396.40	1	396.4
FOODJAR	11S	019200391.00	11	391
1R03567	01S	019300464.60	1	464.6
FOODJAR	11S	019400364.70	11	364.7
1R03568	01S	019500459.70	1	459.7
FOODJAR	11S	019600361.20	11	361.2
1R03569	01S	019700447.70	1	447.7
FOODJAR	11S	019800359.70	11	359.7
1 03570	01S	019900457.60	1	457.6
FOODJAR	11S	020000344.60	11	344.6
1R03571	01S	020100481.80	1	481.8
FOODJAR	11S	020200346.90	11	346.9
1R03572	01S	020300431.60	1	431.6
FOODJAR	11S	020400366.00	11	366
1R03573	01S	020500447.50	1	447.5
FOODJAR	11S	020600358.60	11	358.6
1R03574	01S	020700462.50	1	462.5

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FOODJAR 11S 020800318.60     11          318.6
1R03575 01S 020900389.50     1           389.5
FOODJAR 11S 021000337.70     11          337.7
1R03576 01S 021100428.60     1           428.6
FOODJAR 11S 021200373.40     11          373.4
1R03577 01S 021300452.10     1           452.1
F  DJAR 11S 021400349.20     11          349.2
1  03578 01S 021500397.70     1           397.7
FOODJAR 11S 021600370.40     11          370.4
1R03579 01S 021700410.50     1           410.5
FOODJAR 11S 021800368.50     11          368.5
1R03580 01S 021900403.70     1           403.7
FOODJAR 11S 022000369.70     11          369.7
1R03581 02S 007100408.80     2           408.8
FOODJAR 12S 007200350.90     12          350.9
1R03582 02S 007300309.90     2           309.9
FOODJAR 12S 007400392.90     12          392.9
1R03583 02S 007500269.60     2           269.6
FOODJAR 12S 007600403.20     12          403.2
1R03584 02S 007700348.10     2           348.1
FOODJAR 12S 007800379.40     12          379.4
1R03585 02S 007900352.90     2           352.9
FOODJAR 12S 010000361.20     12          361.2
1R03586 02S 010100369.50     2           369.5
FOODJAR 12S 010200374.10     12          374.1
1R03587 02S 010300311.40     2           311.4
FOODJAR 12S 010400404.30     12          404.3
1R03588 02S 010500357.90     2           357.9
FOODJAR 12S 010600396.60     12          396.6
1R03589 02S 010700329.00     2           329
FOODJAR 12S 010800346.30     12          346.3
1R03590 02S 010900433.60     2           433.6
F  DJAR 12S 011000360.50     12          360.5
1R03591 02S 011100288.20     2           288.2
FOODJAR 12S 011200403.10     12          403.1
1R03592 02S 011300397.60     2           397.6
FOODJAR 12S 011400361.50     12          361.5
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FOODJAR 12S 011600384.30     12          384.3
1R03594 02S 011700379.90     2           379.9
FOODJAR 12S 011800342.10     12          342.1
1R03595 02S 011900326.20     2           326.2
FOODJAR 12S 012000390.00     12          390
1R03596 02S 012100387.70     2           387.7
FOODJAR 12S 012200362.20     12          362.2
1R03597 02S 012300336.40     2           336.4
FOODJAR 12S 012400389.00     12          389
1R03598 02S 012500402.60     2           402.6
FOODJAR 12S 012600366.10     12          366.1
1R03599 02S 012700357.00     2           357
FOODJAR 12S 012800364.40     12          364.4
1R03600 02S 012900322.00     2           322
FOODJAR 12S 013000377.70     12          377.7
1R03601 02S 013100387.90     2           387.9
FOODJAR 12S 013200372.10     12          372.1
1R03602 02S 013300346.80     2           346.8
FOODJAR 12S 013400374.60     12          374.6
1  03603 02S 013500366.20     2           366.2
F  .OJAR 12S 013600373.90    12          373.9
1R03604 02S 013700304.40     2           304.4
FOODJAR 12S 013800409.40     12          409.4
1R03605 02S 013900333.10     2           333.1
FOODJAR 12S 014000385.00     12          385
1R03606 02S 014100340.70     2           340.7
FOODJAR 12S 014200401.70     12          401.7
1R03607 02S 014300374.90     2           374.9
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1R03608 02S 014500405.10     2           405.1
FOODJAR 12S 014600347.40     12          347.4
1R03609 02S 014700351.00     2           351
FOODJAR 12S 014800365.80     12          365.8
1R03610 02S 014900410.60     2           410.6
F  DJAR 12S 015000382.40     12          382.4
1R03611 02S 015100353.30     2           353.3
FOODJAR 12S 015200378.50     12          378.5
1R03612 02S 015300366.00     2           366
FOODJAR 12S 015400381.80     12          381.8
1R03613 02S 015500420.10     2           420.1
FOODJAR 12S 015600349.90     12          349.9
1R03614 02S 015700373.40     2           373.4
FOODJAR 12S 015800358.80     12          358.8
1R03615 02S 015900346.00     2           346
FOODJAR 12S 016000355.40     12          355.4
1R03616 02S 016100362.00     2           362
FOODJAR 12S 016200367.60     12          367.6
1R03617 02S 016300358.00     2           358
FOODJAR 12S 016400345.50     12          345.5
1R03618 02S 016500404.80     2           404.8
FOODJAR 12S 016600357.80     12          357.8
1R03619 02S 016700312.10     2           312.1
FOODJAR 12S 016800386.30     12          386.3
1R03620 02S 016900353.10     2           353.1
FOODJAR 12S 017000358.40     12          358.4
1R03621 02S 017100307.50     2           307.5
FOODJAR 12S 017200407.10     12          407.1
1R03622 02S 017300315.80     2           315.8
FOODJAR 12S 017400404.10     12          404.1
1R03623 02S                  2           339.4
F  DJAR 12S 017600363.00     12          363
1R03624 02S 017700353.90     2           353.9
FOODJAR 12S 017800384.60     12          384.6
1R03625 02S                  2           279.0
FOODJAR 12S 018000383.30     12          383.3
1R03626 02S 018100376.10     2           376.1
FOODJAR 12S 018200371.30     12          371.3
1R03627 02S 018300366.10     2           366.1
FOODJAR 12S 018400386.20     12          386.2
1R03628 02S 018500355.00     2           355
FOODJAR 12S 018600386.60     12          386.6
1R03629 02S 018700386.80     2           386.8
FOODJAR 12S 018800369.30     12          369.3
1R03630 02S 018900302.60     2           302.6
FOODJAR 12S 019000412.40     12          412.4
1R03631 02S 019100407.90     2           407.9
FOODJAR 12S 019200367.80     12          367.8
1R03632 02S 019300371.00     2           371
FOODJAR 12S 019400369.00     12          369
1R03633 02S 019500397.50     2           397.5
FOODJAR 12S 019600365.30     12          365.3
1R03634 02S 019700273.40     2           273.4
FOODJAR 12S 019800395.50     12          395.5
1R03635 02S 019900285.80     2           285.8
FOODJAR 12S 020000380.80     12          380.8
1  03636 02S 020100383.50     2           383.5
F  JDJAR 12S 020200374.70    12          374.7
1R03637 02S 020300341.10     2           341.1
FOODJAR 12S 020400374.00     12          374
1R03638 02S 020500333.90     2           333.9
FOODJAR 12S 020600374.30     12          374.3
1R03639 02S 020700351.60     2           351.6
FOODJAR 12S 020800382.60     12          382.6
1R03640 02S 020900260.40     2           260.4
```

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FOODJAR	12S	021000408.60	12	408.6
1R03641	02S	021100386.40	2	386.4
FOODJAR	12S	021200366.60	12	366.6
1R03642	02S	021300326.70	2	326.7
FOODJAR	12S	021400365.50	12	365.5
1R03643	02S	021500376.30	2	376.3
F[illegible]DJAR	12S	021600382.10	12	382.1
1[illegible]03644	02S	021700331.50	2	331.5
FOODJAR	12S	021800353.80	12	353.8
1R03645	02S	021900414.50	2	414.5
FOODJAR	12S	022000353.60	12	353.6
1R03546	03S	022100359.20	3	359.2
FOODJAR	13S	022200382.40	13	382.4
1R03547	03S	022300425.20	3	425.2
FOODJAR	13S	022400382.50	13	382.5
1R03548	03S	022500458.60	3	458.6
FOODJAR	13S	022600350.90	13	350.9
1R03549	03S	022700414.00	3	414
FOODJAR	13S	022800362.30	13	362.3
1R03550	03S	022900390.00	3	390
FOODJAR	13S	023000383.60	13	383.6
1R03551	03S	023100414.40	3	414.4
FOODJAR	13S	023200374.30	13	374.3
1R03552	03S	023300400.10	3	400.1
FOODJAR	13S	023400376.70	13	376.7
1R03553	03S	023500409.30	3	409.3
FOODJAR	13S	023600362.40	13	362.4
1R03554	03S	023700446.10	3	446.1
FOODJAR	13S	023800356.90	13	356.9
1R03555	03S	023900435.90	3	435.9
FOODJAR	13S	024000327.50	13	327.5
1R03556	03S	024100433.10	3	433.1
F[illegible]DJAR	13S	024200368.40	13	368.4
1R03557	03S	024300418.20	3	418.2
FOODJAR	13S	024400367.30	13	367.3
1R03558	03S	024500401.30	3	401.3
FOODJAR	13S	024600373.80	13	373.8
1R03559	03S	024700386.30	3	386.3
FOODJAR	13S	024800377.10	13	377.1
1R03560	03S	024900440.30	3	440.3
FOODJAR	13S	025000361.80	13	361.8
1R03561	03S	025100414.70	3	414.7
FOODJAR	13S	025200339.80	13	339.8
1R03562	03S	025300326.50	3	326.5
FOODJAR	13S	025400378.10	13	378.1
1R03563	03S	025500465.60	3	465.6
FOODJAR	13S	025600359.30	13	359.3
1R03564	03S	025700401.50	3	401.5
FOODJAR	13S	025800378.20	13	378.2
1R03565	03S	025900422.70	3	422.7
FOODJAR	13S	026000369.70	13	369.7
1R03566	03S	026100409.40	3	409.4
FOODJAR	13S	026200373.30	13	373.3
1R03567	03S	026300321.20	3	321.2
FOODJAR	13S	026400409.60	13	409.6
1R03568	03S	026500324.80	3	324.8
FOODJAR	13S	026600399.70	13	399.7
1[illegible]03569	03S	026700413.10	3	413.1
F[illegible]DJAR	13S	026800349.40	13	349.4
1R03570	03S	026900404.00	3	404
FOODJAR	13S	027000313.20	13	313.2
1R03571	03S	027100400.00	3	400
FOODJAR	13S	027200340.50	13	340.5
1R03572	03S	027300424.30	3	424.3
FOODJAR	13S	027400362.00	13	362
1R03573	03S	027500377.90	3	377.9

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FOODJAR	13S	027600373.40	13	373.4
1R03574	03S	027700414.00	3	414
FOODJAR	13S	027800370.90	13	370.9
1R03575	03S	027900441.30	3	441.3
FOODJAR	13S	028000355.50	13	355.5
1R03576	03S	028100475.80	3	475.8
F OJAR	13S	028200342.30	13	342.3
1R03577	03S	028300412.80	3	412.8
FOODJAR	13S	028400358.00	13	358
1R03578	03S	028500426.70	3	426.7
FOODJAR	13S	028600386.70	13	386.7
1R03579	03S	028700446.90	3	446.9
FOODJAR	13S	028800341.30	13	341.3
1R03580	03S	028900433.60	3	433.6
FOODJAR	13S	029000360.90	13	360.9
1R03581	03S	029100432.60	3	432.6
FOODJAR	13S	029200360.70	13	360.7
1R03582	03S	029300362.10	3	362.1
FOODJAR	13S	029400400.50	13	400.5
1R03583	03S	029500451.50	3	451.5
FOODJAR	13S	029600355.60	13	355.6
1R03584	03S	029700429.90	3	429.9
FOODJAR	13S	029800359.20	13	359.2
1R03585	03S	029900383.40	3	383.4
FOODJAR	13S	030000377.50	13	377.5
1R03586	03S	030100393.60	3	393.6
FOODJAR	13S	030200383.30	13	383.3
1R03587	03S	030300402.40	3	402.4
FOODJAR	13S	030400356.50	13	356.5
1R03588	03S	030500415.80	3	415.8
FOODJAR	13S	030600362.20	13	362.2
1R03589	03S	030700347.20	3	347.2
F OJAR	13S	030800399.20	13	399.2
1R03590	03S	030900424.40	3	424.4
FOODJAR	13S	031000347.10	13	347.1
1R03591	03S	031100383.20	3	383.2
FOODJAR	13S	031200375.30	13	375.3
1R03592	03S	031300336.60	3	336.6
FOODJAR	13S	031400391.80	13	391.8
1R03593	03S		3	481.8
FOODJAR	13S	031600343.80	13	343.8
1R03594	03S	031700438.20	3	438.2
FOODJAR	13S	031800346.70	13	346.7
1R03595	03S	031900441.40	3	441.4
FOODJAR	13S	032000362.00	13	362

BEST COPY AVAILABLE

TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 6/23/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 9

1R03516	01S	007100485.70	1	485.7
FOODJAR	11S	007200357.00	11	357
1R03517	01S	007300438.50	1	438.5
FOODJAR	11S	007400368.40	11	368.4
1R03518	01S	007500436.40	1	436.4
FOODJAR	11S	007600367.60	11	367.6
1R03519	01S	007700481.40	1	481.4
FOODJAR	11S	007800354.10	11	354.1
1R03520	01S	007900466.30	1	466.3
FOODJAR	11S	010000368.30	11	368.3
1R03521	01S	010100414.80	1	414.8
FOODJAR	11S	010200373.40	11	373.4
1R03522	01S	010300420.00	1	420
FOODJAR	11S	010400382.70	11	382.7
1R03523	01S	010500491.20	1	491.2
FOODJAR	11S	010600369.10	11	369.1
1R03524	01S	010700432.20	1	432.2
FOODJAR	11S	010800370.50	11	370.5
1R03525	01S	010900434.80	1	434.8
FOODJAR	11S	011000379.00	11	379
1R03526	01S	011100444.80	1	444.8
FOODJAR	11S	011200367.00	11	367
1R03527	01S	011300429.00	1	429
FOODJAR	11S	011400386.00	11	386
1R03528	01S	011500469.70	1	469.7
FOODJAR	11S	011600357.90	11	357.9
1R03529	01S	011700434.20	1	434.2
FOODJAR	11S	011800369.30	11	369.3
1R03530	01S	011900462.80	1	462.8
FOODJAR	11S	012000369.30	11	369.3
1R03531	01S	012100437.20	1	437.2
FOODJAR	11S	012200389.40	11	389.4
1R03532	01S	012300437.40	1	437.4
FOODJAR	11S	012400375.80	11	375.8
1R03533	01S	012500476.30	1	476.3
FOODJAR	11S	012600362.10	11	362.1
1R03534	01S	012700504.20	1	504.2
FOODJAR	11S	012800337.60	11	337.6
1R03535	01S	012900396.10	1	396.1
FOODJAR	11S	013000387.80	11	387.8
1R03536	01S	013100405.90	1	405.9
FOODJAR	11S	013200398.50	11	398.5
1R03537	01S	013300371.60	1	371.6
FOODJAR	11S	013400390.40	11	390.4
1R03538	01S	013500501.00	1	501
FOODJAR	11S	013600349.00	11	349
1R03539	01S	013700366.20	1	366.2
FOODJAR	11S	013800395.00	11	395
1R03540	01S	013900416.10	1	416.1
FOODJAR	11S	014000380.50	11	380.5

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1R03541	01S	014100476.30	1	476.3
FOODJAR	11S	014200368.00	11	368
1R03542	01S	014300454.00	1	454
FOODJAR	11S	014400361.60	11	361.6
1R03543	01S	014500497.10	1	497.1
FOODJAR	11S	014600337.60	11	337.6
1R03544	01S	014700454.20	1	454.2
[illegible]ODJAR	11S	014800353.10	11	353.1
1R03545	01S	014900484.00	1	484
FOODJAR	11S	015000347.60	11	347.6
1R03546	01S	015100479.40	1	479.4
FOODJAR	11S	015200348.80	11	348.8
1R03547	01S	015300481.60	1	481.6
FOODJAR	11S	015400316.40	11	316.4
1R03548	01S	015500499.60	1	499.6
FOODJAR	11S	015600357.00	11	357
1R03549	01S	015700414.80	1	414.8
FOODJAR	11S	015800395.10	11	395.1
1R03550	01S	015900428.50	1	428.5
FOODJAR	11S	016000383.30	11	383.3
1R03551	01S	016100336.00	1	336
FOODJAR	11S	016200412.30	11	412.3
1R03552	01S	016300461.30	1	461.3
FOODJAR	11S	016400347.90	11	347.9
1R03553	01S	016500511.70	1	511.7
FOODJAR	11S	016600376.90	11	376.9
1R03554	01S	016700363.50	1	363.5
FOODJAR	11S	016800397.40	11	397.4
1R03555	01S	016900419.80	1	419.8
FOODJAR	11S		11	371.1
1R03556	01S	017100480.20	1	480.2
FOODJAR	11S	017200370.30	11	370.3
[illegible]03557	01S	017300427.20	1	427.2
[illegible]OODJAR	11S	017400385.70	11	385.7
1R03558	01S	017500364.40	1	364.4
FOODJAR	11S	017600368.40	11	368.4
1R03559	01S	017700461.40	1	461.4
FOODJAR	11S	017800377.90	11	377.9
1R03560	01S	017900398.20	1	398.2
FOODJAR	11S	018000407.30	11	407.3
1R03561	01S	018100491.60	1	491.6
FOODJAR	11S	018200333.20	11	333.2
1R03562	01S	018300347.10	1	347.1
FOODJAR	11S	018400411.20	11	411.2
1R03563	01S	018500407.80	1	407.8
FOODJAR	11S	018600384.90	11	384.9
1R03564	01S	018700417.60	1	417.6
FOODJAR	11S	018800363.30	11	363.3
1R03565	01S	018900457.20	1	457.2
FOODJAR	11S	019000368.50	11	368.5
1R03566	01S	019100406.80	1	406.8
FOODJAR	11S	019200371.00	11	371
1R03567	01S	019300473.40	1	473.4
FOODJAR	11S	019400371.80	11	371.8
1R03568	01S	019500468.30	1	468.3
FOODJAR	11S	019600363.60	11	363.6
1R03569	01S	019700455.20	1	455.2
FOODJAR	11S	019800368.20	11	368.2
[illegible]03570	01S	019900467.90	1	467.9
FOODJAR	11S	020000346.70	11	346.7
1R03571	01S	020100492.50	1	492.5
FOODJAR	11S	020200350.00	11	350
1R03572	01S	020300436.60	1	436.6
FOODJAR	11S	020400373.80	11	373.8
1R03573	01S	020500465.00	1	465
FOODJAR	11S	020600363.50	11	363.5

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1R01574	01S	020700495.30	1	495.3
FOODJAR	11S	020800405.50	11	405.5
1R01575	01S	020900404.80	1	404.8
FOODJAR	11S	021000346.10	11	346.1
1R01576	01S	021100438.90	1	438.9
FOODJAR	11S	021200375.30	11	375.3
1R01577	01S	021300460.60	1	460.6
F OODJAR	11S	021400358.70	11	358.7
1.01578	01S	021500405.80	1	405.8
FOODJAR	11S	021600376.50	11	376.5
1R01579	01S	021700423.70	1	423.7
FOODJAR	11S	021800369.20	11	369.2
1R01580	01S	021900412.00	1	412
FOODJAR	11S	022000366.60	11	366.6
1R01581	02S	007100427.40	2	427.4
FOODJAR	12S	007200351.90	12	351.9
1R01582	02S	007300319.20	2	319.2
FOODJAR	12S	007400391.70	12	391.7
1R01583	02S	007500275.20	2	275.2
FOODJAR	12S	007600410.20	12	410.2
1R01584	02S	007700352.00	2	352
FOODJAR	12S	007800410.00	12	410
1R01585	02S	007900368.00	2	368
FOODJAR	12S	010000372.80	12	372.8
1R01586	02S	010100392.00	2	392
FOODJAR	12S	010200393.90	12	393.9
1R01587	02S	010300321.80	2	321.8
FOODJAR	12S	010400411.80	12	411.8
1R01588	02S	010500371.00	2	371
FOODJAR	12S	010600395.30	12	395.3
1R01589	02S	010700342.50	2	342.5
FOODJAR	12S	010800350.40	12	350.4
1R01590	02S	010900449.90	2	449.9
F OODJAR	12S	011000363.20	12	363.2
1R01591	02S	011100297.10	2	297.1
FOODJAR	12S	011200405.20	12	405.2
1R01592	02S	011300413.70	2	413.7
FOODJAR	12S	011400369.20	12	369.2
1R01593	02S	011500385.40	2	385.4
FOODJAR	12S	011600390.10	12	390.1
1R01594	02S	011700402.30	2	402.3
FOODJAR	12S	011800352.10	12	352.1
1R01595	02S	011900342.80	2	342.8
FOODJAR	12S	012000391.70	12	391.7
1R01596	02S	012100403.80	2	403.8
FOODJAR	12S	012200375.10	12	375.1
1R01597	02S	012300346.20	2	346.2
FOODJAR	12S	012400393.90	12	393.9
1R01598	02S	012500411.70	2	411.7
FOODJAR	12S	012600380.80	12	380.8
1R01599	02S	012700373.80	2	373.8
FOODJAR	12S	012800376.80	12	376.8
1R01600	02S	012900337.20	2	337.2
FOODJAR	12S	013000382.40	12	382.4
1R01601	02S	013100396.20	2	396.2
FOODJAR	12S	013200384.30	12	384.3
1R01602	02S	013300354.80	2	354.8
FOODJAR	12S	013400395.70	12	395.7
1 01603	02S	013500374.80	2	374.8
F JDJAR	12S	013600387.50	12	387.5
1R01604	02S	013700316.70	2	316.7
FOODJAR	12S	013800415.50	12	415.5
1R01605	02S	013900348.00	2	348
FOODJAR	12S	014000388.20	12	388.2
1R01606	02S	014100346.20	2	346.2
FOODJAR	12S	014200408.70	12	408.7

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1R03607	02S	014300390.60	2	390.6
FOODJAR	12S	014400378.10	12	378.1
1R03608	02S	014500419.20	2	419.2
FOODJAR	12S	014600323.70	12	323.7
1R03609	02S	014700360.50	2	360.5
FOODJAR	12S	014800366.40	12	366.4
1R03610	02S	014900436.70	2	436.7
[ODJAR	12S	015000371.00	12	371
1R03611	02S	015100362.70	2	362.7
FOODJAR	12S	015200381.50	12	381.5
1R03612	02S	015300379.90	2	379.9
FOODJAR	12S	015400384.00	12	384
1R03613	02S	015500452.70	2	452.7
FOODJAR	12S	015600344.60	12	344.6
1R03614	02S	015700386.10	2	386.1
FOODJAR	12S	015800360.40	12	360.4
1R03615	02S	015900355.90	2	355.9
FOODJAR	12S	016000369.20	12	369.2
1R03616	02S	016100382.80	2	382.8
FOODJAR	12S	016200362.30	12	362.3
1R03617	02S	016300373.90	2	373.9
FOODJAR	12S	016400374.00	12	374
1R03618	02S	016500423.50	2	423.5
FOODJAR	12S	016600366.60	12	366.6
1R03619	02S	016700327.90	2	327.9
FOODJAR	12S	016800410.10	12	410.1
1R03620	02S	016900373.30	2	373.3
FOODJAR	12S	017000367.30	12	367.3
1R03621	02S	017100319.90	2	319.9
FOODJAR	12S	017200409.80	12	409.8
1R03622	02S	017300324.60	2	324.6
FOODJAR	12S	017400397.20	12	397.2
[illegible]03623	02S	017500358.20	2	358.2
FOODJAR	12S	017600366.60	12	366.6
1R03624	02S	017700362.80	2	362.8
FOODJAR	12S	017800400.00	12	400
1R03625	02S	017900296.60	2	296.6
FOODJAR	12S	018000387.30	12	387.3
1R03626	02S	018100381.80	2	381.8
FOODJAR	12S	018200398.70	12	398.7
1R03627	02S	018300370.60	2	370.6
FOODJAR	12S	018400395.10	12	395.1
1R03628	02S	018500371.40	2	371.4
FOODJAR	12S	018600389.90	12	389.9
1R03629	02S	018700403.00	2	403
FOODJAR	12S	018800371.20	12	371.2
1R03630	02S	018900304.80	2	304.8
FOODJAR	12S	019000432.00	12	432
1R03631	02S	019100432.50	2	432.5
FOODJAR	12S	019200366.80	12	366.8
1R03632	02S	019300389.90	2	389.9
FOODJAR	12S	019400363.50	12	363.5
1R03633	02S	019500419.60	2	419.6
FOODJAR	12S	019600367.50	12	367.5
1R03634	02S	019700282.00	2	282
FOODJAR	12S	019800399.30	12	399.3
1R03635	02S	019900303.50	2	303.5
FOODJAR	12S	020000397.80	12	397.8
[illegible]03636	02S	020100407.50	2	407.5
FOODJAR	12S	020200373.90	12	373.9
1R03637	02S	020300350.60	2	350.6
FOODJAR	12S	020400378.70	12	378.7
1R03638	02S	020500342.40	2	342.4
FOODJAR	12S	020600382.10	12	382.1
1R03639	02S	020700366.70	2	366.7
FOODJAR	12S	020800390.10	12	390.1

BEST COPY AVAILABLE

1R03640	02S	020900271.00	2	271
FOODJAR	12S	021000406.70	12	406.7
1R03641	02S	021100403.90	2	403.9
FOODJAR	12S	021200379.80	12	379.8
1R03642	02S	021300349.60	2	349.6
FOODJAR	12S	021400375.50	12	375.5
1R03643	02S	021500397.00	2	397
F[illegible]DJAR	12S	021600383.80	12	383.8
1[illegible]3644	02S	021700337.60	2	337.6
FOODJAR	12S	021800382.70	12	382.7
1R03645	02S	021900438.40	2	438.4
FOODJAR	12S	022000347.50	12	347.5
1R03646	03S	022100362.10	3	362.1
FOODJAR	13S	022200391.20	13	391.2
1R03647	03S	022300437.90	3	437.9
FOODJAR	13S	022400386.40	13	386.4
1R03648	03S	022500492.00	3	492
FOODJAR	13S	022600338.90	13	338.9
1R03649	03S	022700443.60	3	443.6
FOODJAR	13S	022800352.10	13	352.1
1R03650	03S	022900404.60	3	404.6
FOODJAR	13S	023000386.90	13	386.9
1R03651	03S	023100427.70	3	427.7
FOODJAR	13S	023200376.10	13	376.1
1R03652	03S	023300418.30	3	418.3
FOODJAR	13S	023400372.50	13	372.5
1R03653	03S	023500425.20	3	425.2
FOODJAR	13S	023600367.60	13	367.6
1R03654	03S	023700463.20	3	463.2
FOODJAR	13S	023800359.20	13	359.2
1R03655	03S	023900455.20	3	455.2
FOODJAR	13S	024000332.20	13	332.2
1R03656	03S	024100450.50	3	450.5
F[illegible]DJAR	13S	024200366.10	13	366.1
1R03657	03S	024300433.50	3	433.5
FOODJAR	13S	024400364.00	13	364
1R03658	03S	024500415.80	3	415.8
FOODJAR	13S	024600384.70	13	384.7
1R03659	03S	024700407.90	3	407.9
FOODJAR	13S	024800367.40	13	367.4
1R03660	03S	024900456.10	3	456.1
FOODJAR	13S	025000346.80	13	346.8
1R03661	03S	025100429.30	3	429.3
FOODJAR	13S	025200367.10	13	367.1
1R03662	03S	025300341.60	3	341.6
FOODJAR	13S	025400416.00	13	416
1R03663	03S	025500485.60	3	485.6
FOODJAR	13S	025600355.30	13	355.3
1R03664	03S	025700393.70	3	393.7
FOODJAR	13S	025800408.50	13	408.5
1R03665	03S	025900432.80	3	432.8
FOODJAR	13S	026000374.40	13	374.4
1R03666	03S	026100423.40	3	423.4
FOODJAR	13S	026200369.40	13	369.4
1R03667	03S	026300326.00	3	326
FOODJAR	13S	026400404.70	13	404.7
1R03668	03S	026500331.80	3	331.8
FOODJAR	13S	026600424.80	13	424.8
1[illegible]3669	03S	026700438.00	3	438
F[illegible]DJAR	13S	026800359.30	13	359.3
1R03670	03S	026900444.80	3	444.8
FOODJAR	13S	027000335.40	13	335.4
1R03671	03S	027100415.00	3	415
FOODJAR	13S	027200354.50	13	354.5
1R03672	03S	027300442.00	3	442
FOODJAR	13S	027400360.80	13	360.8

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1R03673	03S	027500388.5Q	3	388.5
FOODJAR	13S	027600398.0Q	13	398
1R03674	03S	027700435.6Q	3	435.6
FOODJAR	13S	027800359.3Q	13	359.3
1R03675	03S	027900454.3Q	3	454.3
FOODJAR	13S	028000314.4Q	13	314.4
1R03676	03S	028100492.5Q	3	492.5
F DJAR	13S	028200357.1Q	13	357.1
1R03677	03S	028300432.4Q	3	432.4
FOODJAR	13S	028400353.3Q	13	353.3
1R03678	03S	028500447.6Q	3	447.6
FOODJAR	13S	028600370.7Q	13	370.7
1R03679	03S	028700466.4Q	3	466.4
FOODJAR	13S	028800351.7Q	13	351.7
1R03680	03S	028900452.9Q	3	452.9
FOODJAR	13S	029000350.6Q	13	350.6
1R03681	03S	029100451.5Q	3	451.5
FOODJAR	13S	029200354.4Q	13	354.4
1R03682	03S	029300375.1Q	3	375.1
FOODJAR	13S	029400399.9Q	13	399.9
1R03683	03S	029500470.8Q	3	470.8
FOODJAR	13S	029600343.1Q	13	343.1
1R03684	03S	029700451.5Q	3	451.5
FOODJAR	13S	029800377.9Q	13	377.9
1R03685	03S	029900404.0Q	3	404
FOODJAR	13S	030000371.1Q	13	371.1
1R03686	03S	030100411.5Q	3	411.5
FOODJAR	13S	030200384.8Q	13	384.8
1R03687	03S	030300424.1Q	3	424.1
FOODJAR	13S	030400353.9Q	13	353.9
1R03688	03S	030500423.6Q	3	423.6
FOODJAR	13S	030600381.1Q	13	381.1
1 03689	03S	030700356.3Q	3	356.3
F JDJAR	13S	030800398.9Q	13	398.9
1R03690	03S	030900448.4Q	3	448.4
FOODJAR	13S	031000351.0Q	13	351
1R03691	03S		3	394.7
FOODJAR	13S	031200374.4Q	13	374.4
1R03692	03S	031300340.2Q	3	340.2
FOODJAR	13S	031400408.3Q	13	408.3
1R03693	03S	031500505.8Q	3	505.8
FOODJAR	13S	031600346.3Q	13	346.3
1R03694	03S	031700455.0Q	3	455
FOODJAR	13S	031800341.2Q	13	341.2
1R03695	03S	031900464.2Q	3	464.2
FOODJAR	13S	032000362.7Q	13	362.7
9999999999		99	0	

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000861

TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 6/30/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 10

1R03516	01S	007190507.00	1	507
FOODJAR	11S	007290357.40	11	357.4
1R03517	01S	007390457.80	1	457.8
FOODJAR	11S	007490370.40	11	370.4
1R03518	01S	007590444.70	1	444.7
FOODJAR	11S	007690386.00	11	386
1R03519	01S	007790491.90	1	491.9
FOODJAR	11S	007890369.20	11	369.2
1R03520	01S	007990473.40	1	473.4
FOODJAR	11S	010090387.00	11	387
1R03521	01S	010190431.30	1	431.3
FOODJAR	11S	010290371.40	11	371.4
1R03522	01S	010390430.20	1	430.2
FOODJAR	11S	010490398.50	11	398.5
1R03523	01S	010590501.60	1.	501.6
FOODJAR	11S	010690336.90	11	336.9
1R03524	01S	010790437.00	1	437
F OJAR	11S	010890392.90	11	392.9
1R03525	01S	010990448.30	1	448.3
FOODJAR	11S	011090385.40	11	385.4
1R03526	01S	011190454.80	1	454.8
FOODJAR	11S	011290379.20	11	379.2
1R03527	01S	011390427.80	1	427.8
FOODJAR	11S	011490394.80	11	394.8
1R03528	01S	011590489.50	1	489.5
FOODJAR	11S	011690364.30	11	364.3
1R03529	01S	011790443.50	1	443.5
FOODJAR	11S	011890353.70	11	353.7
1R03530	01S	011990473.20	1	473.2
FOODJAR	11S	012090383.50	11	383.5
1R03531	01S	012190450.50	1	450.5
FOODJAR	11S	012290374.30	11	374.3
1R03532	01S	012390444.00	1	444
FOODJAR	11S	012490386.60	11	386.6
1R03533	01S	012590491.50	1	491.5
FOODJAR	11S	012690350.50	11	350.5
1R03534	01S	012790517.50	1	517.5
FOODJAR	11S	012890358.60	11	358.6
1R03535	01S	012990398.40	1	398.4
FOODJAR	11S	013090403.30	11	403.3
1R03536	01S	013190416.00	1	416
FOODJAR	11S	013290411.10	11	411.1
1 3537	01S	013390388.00	1	388
FOODJAR	11S	013490398.40	11	398.4
1R03538	01S	013590520.40	1	520.4
FOODJAR	11S	013690365.60	11	365.6
1R03539	01S	013790378.70	1	378.7
FOODJAR	11S	013890410.90	11	410.9
1R03540	01S	013990423.90	1	423.9
FOODJAR	11S	014090398.80	11	398.8

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1R03541	01S	014190477.60	1	477.6
FOODJAR	11S	014290377.40	11	377.4
1R03542	01S	014390466.50	1	466.5
FOODJAR	11S	014490374.00	11	374
1R03543	01S	014590511.90	1	511.9
FOODJAR	11S	014690346.60	11	346.6
1R03544	01S	014790471.30	1	471.3
F OJAR	11S	014890360.50	11	360.5
1R03545	01S	014990499.80	1	499.8
FOODJAR	11S	015090347.70	11	347.7
1R03546	01S	015190496.40	1	496.4
FOODJAR	11S	015290387.20	11	387.2
1R03547	01S	015390498.80	1	498.8
FOODJAR	11S	015490353.50	11	353.5
1R03548	01S	015590519.10	1	519.1
FOODJAR	11S	015690366.00	11	366
1R03549	01S	015790430.00	1	430
FOODJAR	11S	015890396.60	11	396.6
1R03550	01S	015990443.80	1	443.8
FOODJAR	11S	016090378.50	11	378.5
1R03551	01S	016190341.30	1	341.3
FOODJAR	11S	016290420.10	11	420.1
1R03552	01S	016390485.40	1	485.4
FOODJAR	11S	016490361.70	11	361.7
1R03553	01S	016590526.50	1	526.5
FOODJAR	11S	016690355.40	11	355.4
1R03554	01S	016790371.70	1	371.7
FOODJAR	11S	016890406.70	11	406.7
1R03555	01S	016990429.50	1	429.5
FOODJAR	11S	017090397.70	11	397.7
1R03556	01S	017190499.90	1	499.9
FOODJAR	11S	017290384.80	11	384.8
1R03557	01S	017390442.80	1	442.8
F OJAR	11S	017490401.10	11	401.1
1R03558	01S	017590377.60	1	377.6
FOODJAR	11S	017690406.40	11	406.4
1R03559	01S	017790473.40	1	473.4
FOODJAR	11S	017890387.00	11	387
1R03560	01S	017990418.10	1	418.1
FOODJAR	11S	018090394.50	11	394.5
1R03561	01S	018190513.40	1	513.4
FOODJAR	11S	018290345.50	11	345.5
1R03562	01S	018390367.40	1	367.4
FOODJAR	11S	018490406.50	11	406.5
1R03563	01S	018590418.70	1	418.7
FOODJAR	11S	018690397.70	11	397.7
1R03564	01S	018790432.00	1	432
FOODJAR	11S	018890382.50	11	382.5
1R03565	01S	018990469.80	1	469.8
FOODJAR	11S	019090356.00	11	356
1R03566	01S	019190415.10	1	415.1
FOODJAR	11S	019290404.70	11	404.7
1R03567	01S	019390499.20	1	499.2
FOODJAR	11S	019490373.10	11	373.1
1R03568	01S	019590484.10	1	484.1
FOODJAR	11S	019690375.40	11	375.4
1R03569	01S	019790481.60	1	481.6
FOODJAR	11S	019890354.50	11	354.5
1 3570	01S	019990488.10	1	488.1
FOODJAR	11S	020090351.50	11	351.5
1R03571	01S	020190497.50	1	497.5
FOODJAR	11S	020290375.10	11	375.1
1R03572	01S	020390451.10	1	451.1
FOODJAR	11S	020490382.90	11	382.9
1R03573	01S	020590474.40	1	474.4
FOODJAR	11S	020690380.20	11	380.2

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1R03574	01S	020790518.40	1	518.4
FOODJAR	11S	020890345.10	11	345.1
1R03575	01S	020990413.80	1	413.8
FOODJAR	11S	021090363.10	11	363.1
1R03576	01S	021190444.40	1	444.4
FOODJAR	11S	021290397.90	11	397.9
1R03577	01S	021390466.00	1	466
F OJAR	11S	021490387.80	11	387.8
1R03578	01S	21590424.20	1	424.2
FOODJAR	11S	021690372.30	11	372.3
1R03579	01S	021790442.50	1	442.5
FOODJAR	11S	021890380.30	11	380.3
1R03580	01S	021990428.40	1	428.4
FOODJAR	11S	022090389.50	11	389.5
1R03581	02S	00?190441.40	2	441.4
FOODJAR	12S	00?290373.40	12	373.4
1R03582	02S	00?390329.00	2	329
FOODJAR	12S	00?490362.10	12	362.1
1R03583	02S	00?590284.80	2	284.8
FOODJAR	12S	00?690411.60	12	411.6
1R03584	02S	00?790375.70	2	375.7
FOODJAR	12S	00?890382.00	12	382
1R03585	02S	00?990375.70	2	375.7
FOODJAR	12S	010090372.00	12	372
1R03586	02S	010190399.90	2	399.9
FOODJAR	12S	010290378.90	12	378.9
1R03587	02S	010390335.90	2	335.9
FOODJAR	12S	010490413.80	12	413.8
1R03588	02S	010590315.20	2	382.5
FOODJAR	12S	010690394.40	12	394.4
1R03589	02S	010790360.70	2	360.7
FOODJAR	12S	010890362.00	12	362
1R03590	02S	010990466.00	2	466
F OJAR	12S	011090359.80	12	359.8
1R03591	02S	011190303.90	2	303.9
FOODJAR	12S	011290417.50	12	417.5
1R03592	02S	011390432.90	2	432.9
FOODJAR	12S	011490374.70	12	374.7
1R03593	02S	011590399.60	2	399.6
FOODJAR	12S	011690390.60	12	390.6
1R03594	02S	011790417.30	2	417.3
FOODJAR	12S	011890363.60	12	363.6
1R03595	02S	011990347.60	2	347.6
FOODJAR	12S	012090394.00	12	394
1R03596	02S	012190422.30	2	422.3
FOODJAR	12S	012290368.90	12	368.9
1R03597	02S	012390358.30	2	358.3
FOODJAR	12S	012490397.20	12	397.2
1R03598	02S	012590423.50	2	423.5
FOODJAR	12S	012690357.00	12	357
1R03599	02S	012790385.70	2	385.7
FOODJAR	12S	012890378.40	12	378.4
1R03600	02S	012990358.20	2	358.2
FOODJAR	12S	013090383.10	12	383.1
1R03601	02S		2	415.2
FOODJAR	12S	013290370.10	12	370.1
1R03602	02S	013390371.80	2	371.8
FOODJAR	12S	013490389.10	12	389.1
1 3603	02S	013590393.00	2	393
FOODJAR	12S	013690342.40	12	342.4
1R03604	02S	013790327.20	2	327.2
FOODJAR	12S	013890417.70	12	417.7
1R03605	02S	013990360.70	2	360.7
FOODJAR	12S	014090393.40	12	393.4
1R03606	02S	014190367.60	2	367.6
FOODJAR	12S	014290408.50	12	408.5

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1R03607	02S	014790404.10	2	404.1	
FOODJAR	12S	014490381.20	12	381.2	
1R03608	02S	14590434.50	2	434.5	
FOODJAR	12S	014690343.50	12	343.5	
1R03609	02S	014790371.80	2	371.8	
FOODJAR	12S	014890372.50	12	372.5	
1R03610	02S	014990448.60	2	448.6	
F OJAR	12S	015090372.80	12	372.8	
1R03611	02S	015190374.40	2	374.4	
FOODJAR	12S	015290377.90	12	377.9	
1R03612	02S	015390393.70	2	393.7	
FOODJAR	12S	015490385.10	12	385.1	
1R03613	02S	015590481.10	2	481.1	
FOODJAR	12S	015690348.40	12	348.4	
1R03614	02S	015790397.40	2	397.4	
FOODJAR	12S	015890362.30	12	362.3	
1R03615	02S	015990366.50	2	366.5	
FOODJAR	12S	016090369.30	12	369.3	
1R03616	02S	016190388.00	2	388	
FOODJAR	12S	016290380.70	12	380.7	
1R03617	02S	016390377.20	2	377.2	
FOODJAR	12S	016490385.10	12	385.1	
1R03618	02S	016590432.60	2	432.6	
FOODJAR	12S	016690373.70	12	373.7	
1R03619	02S	16790333.50	2	333.5	
FOODJAR	12S	016890400.10	12	400.1	
1R03620	02S	016990382.80	2	382.8	
FOODJAR	12S	017090369.60	12	369.6	
1R03621	02S	017190329.60	2	329.6	
FOODJAR	12S	017290415.80	12	415.8	
1R03622	02S	17390325.50	2	325.5	
FOODJAR	12S	017490401.30	12	401.3	
1R03623	02S	017590363.20	2	363.2	
F OJAR	12S	017690378.40	12	378.4	
1R03624	02S	017790389.10	2	389.1	
FOODJAR	12S	017890375.50	12	375.5	
1R03625	02S	017990316.40	2	316.4	
FOODJAR	12S	018090387.90	12	387.9	
1R03626	02S	018190401.50	2	401.5	
FOODJAR	12S	018290387.50	12	387.5	
1R03627	02S	018390380.60	2	380.6	
FOODJAR	12S	018490399.30	12	399.3	
1R03628	02S	018590380.70	2	380.7	
FOODJAR	12S	018690399.50	12	399.5	
1R03629	02S	018790418.10	2	418.1	
FOODJAR	12S	018890340.70	12	340.7	
1R03630	02S	018990323.30	2	323.3	
FOODJAR	12S	019090410.10	12	410.1	
1R03631	02S	019190439.20	2	439.2	
FOODJAR	12S	019290373.10	12	373.1	
1R03632	02S	019390405.90	2	405.9	
FOODJAR	12S	019490369.10	12	369.1	
1R03633	02S	019590437.90	2	437.9	
FOODJAR	12S	019690373.10	12	373.1	
1R03634	02S	019790279.20	2	279.2	
FOODJAR	12S	019890407.40	12	407.4	
1R03635	02S	019990317.40	2	317.4	
FOODJAR	12S	020090409.60	12	409.6	
J 3636	02S	020190414.90	2	414.9	
FOODJAR	12S	020290389.50	12	389.5	
1R03637	02S	020390364.30	2	364.3	
FOODJAR	12S	020490387.00	12	387	
1R03638	02S	020590349.80	2	349.8	
FOODJAR	12S	020690389.30	12	389.3	
1R03639	02S	020790376.20	2	376.2	
FOODJAR	12S	020890394.60	12	394.6	

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1R03640	03S	020990284.20	2	284.2	
FOODJAR	13S	021090416.60	12	416.6	
1R03641	03S	021190417.70	2	417.7	
FOODJAR	13S	021290384.80	12	384.8	
1R03642	03S	021390345.70	2	345.7	
FOODJAR	13S	021490389.40	12	389.4	
1R03643	03S	021590408.60	2	408.6	
F OJAR	13S	021690382.20	12	382.2	
1R03644	03S	021790359.30	2	359.3	
FOODJAR	13S	021890364.50	12	364.5	
1R03645	03S	021990458.10	2	458.1	
FOODJAR	13S	022090342.40	12	342.4	
1R03646	03S	022190374.00	3	374	
FOODJAR	13S	022290396.70	13	396.7	
1R03647	03S	022390453.90	3	453.9	
FOODJAR	13S	022490375.10	13	375.1	
1R03648	03S	022590519.00	3	519	
FOODJAR	13S	022690340.30	13	340.3	
1R03649	03S	022790456.60	3	456.6	
FOODJAR	13S	022890350.80	13	350.8	
1R03650	03S	022990407.10	3	407.1	
FOODJAR	13S	023090397.30	13	397.3	
1R03651	03S	023190445.60	3	445.6	
FOODJAR	13S	023290373.00	13	373	
1R03652	03S	023390431.80	3	431.8	
FOODJAR	13S	023490355.10	13	355.1	
1R03653	03S	023590432.80	3	432.8	
FOODJAR	13S	023690381.30	13	381.3	
1R03654	03S	023790484.40	3	484.4	
FOODJAR	13S	023890358.90	13	358.9	
1R03655	03S	023990471.60	3	471.6	
FOODJAR	13S	024090354.30	13	354.3	
1R03656	03S	024190473.50	3	473.5	
F OJAR	13S	024290368.20	13	368.2	
1R03657	03S	024390449.80	3	449.8	
FOODJAR	13S	024490371.10	13	371.1	
1R03658	03S	024590432.10	3	432.1	
FOODJAR	13S	024690396.10	13	396.1	
1R03659	03S	024790428.80	3	428.8	
FOODJAR	13S	024890374.00	13	374	
1R03660	03S	024990468.40	3	468.4	
FOODJAR	13S	025090366.30	13	366.3	
1R03661	03S	025190447.00	3	447	
FOODJAR	13S	025290362.60	13	362.6	
1R03662	03S	025390351.10	3	351.1	
FOODJAR	13S	025490415.90	13	415.9	
1R03663	03S	025590501.70	3	501.7	
FOODJAR	13S	025690359.90	13	359.9	
1R03664	03S	025790410.10	3	410.1	
FOODJAR	13S	025890393.60	13	393.6	
1R03665	03S	025990435.20	3	435.2	
FOODJAR	13S	026090387.20	13	387.2	
1R03666	03S	026190440.40	3	440.4	
FOODJAR	13S	026290369.10	13	369.1	
1R03667	03S	026390335.00	3	335	
FOODJAR	13S	026490412.30	13	412.3	
1R03668	03S	026590341.70	3	341.7	
FOODJAR	13S	026690412.50	13	412.5	
1 3669	03S	026790443.60	3	443.6	
FOODJAR	13S	026890384.00	13	384	
1R03670	03S	026990463.00	3	463	
FOODJAR	13S	027090359.10	13	359.1	
1R03671	03S	027190423.90	3	423.9	
FOODJAR	13S	027290365.70	13	365.7	
1R03672	03S	027390457.50	3	457.5	
FOODJAR	13S	027490369.70	13	369.7	

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1R03673	03S	027590400.50	3	400.5
FOODJAR	13S	027690390.90	13	390.9
1R03674	03S	027790449.90	3	449.9
FOODJAR	13S	027890374.80	13	374.8
1R03675	03S	027990469.60	3	469.6
FOODJAR	13S	028090366.20	13	366.2
1R03676	03S	028190510.00	3	510
F OJAR	13S	028290348.80	13	348.8
1R03677	03S	028390448.90	3	448.9
FOODJAR	13S	028490359.50	13	359.5
1R03678	03S	028590453.10	3	453.1
FOODJAR	13S	028690392.80	13	392.8
1R03679	03S	028790485.90	3	485.9
FOODJAR	13S	028890351.30	13	351.3
1R03680	03S	028990469.90	3	469.9
FOODJAR	13S	029090362.40	13	362.4
1R03681	03S	029190469.50	3	469.5
FOODJAR	13S	029290354.60	13	354.6
1R03682	03S	029390382.30	3	382.3
FOODJAR	13S	029490404.90	13	404.9
1R03683	03S	029590482.80	3	482.8
FOODJAR	13S	029690350.40	13	350.4
1R03684	03S	029790470.70	3	470.7
FOODJAR	13S	029890352.60	13	352.6
1R03685	03S	29990416.30	3	416.3
FOODJAR	13S	030090385.60	13	385.6
1R03686	03S	030190430.40	3	430.4
FOODJAR	13S	030290370.00	13	370
1R03687	03S	030390442.00	3	442
FOODJAR	13S	030490364.30	13	364.3
1R03688	03S	030590442.90	3	442.9
FOODJAR	13S	030690364.80	13	364.8
1R03689	03S	030790367.90	3	367.9
F DJAR	13S	030890394.20	13	394.2
1R03690	03S	030990463.80	3	463.8
FOODJAR	13S	031090346.10	13	346.1
1R03691	03S	031190408.10	3	408.1
FOODJAR	13S	031290382.60	13	382.6
1R03692	03S	031390348.40	3	348.4
FOODJAR	13S	031490414.10	13	414.1
1R03693	03S	031590527.50	3	527.5
FOODJAR	13S	031690338.70	13	338.7
1R03694	03S	031790477.20	3	477.2
FOODJAR	13S	031890340.40	13	340.4
1R03695	03S	031990477.50	3	477.5
FOODJAR	13S	032090367.30	13	367.3
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 7/7/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 11

1R03516	01S	007100516.40	1	516.4
FOODJAR	11S	007200360.30	11	360.3
1R03517	01S	007300461.90	1	461.9
FOODJAR	11S	007400374.20	11	374.2
1R03518	01S	007500456.80	1	456.8
FOODJAR	11S	007600381.00	11	381
1R03519	01S	007700505.30	1	505.3
FOODJAR	11S	007800371.70	11	371.7
1R03520	01S	007900483.70	1	483.7
FOODJAR	11S	010000377.50	11	377.5
1R03521	01S	010100436.40	1	436.4
FOODJAR	11S	010200379.20	11	379.2
1R03522	01S	010300445.10	1	445.1
FOODJAR	11S	010400385.90	11	385.9
1R03523	01S	010500522.30	1	522.3
FOODJAR	11S	010600368.50	11	368.5
1R03524	01S		1	447.5
F OJAR	11S	010800384.80	11	384.8
1R03525	01S	010900458.90	1	458.9
FOODJAR	11S	011000387.70	11	387.7
1R03526	01S	011100465.10	1	465.1
FOODJAR	11S	011200377.20	11	377.2
1R03527	01S	011300450.30	1	450.3
FOODJAR	11S	011400383.50	11	383.5
1R03528	01S	011500498.30	1	498.3
FOODJAR	11S	011600373.70	11	373.7
1R03529	01S	011700462.70	1	462.7
FOODJAR	11S	011800372.70	11	372.7
1R03530	01S	011900491.20	1	491.2
FOODJAR	11S	012000372.00	11	372
1R03531	01S	012100463.20	1	463.2
FOODJAR	11S	012200383.00	11	383
1R03532	01S	012300460.70	1	460.7
FOODJAR	11S	012400376.40	11	376.4
1R03533	01S	012500505.90	1	505.9
FOODJAR	11S	012600367.20	11	367.2
1R03534	01S	012700531.40	1	531.4
FOODJAR	11S	012800355.40	11	355.4
1R03535	01S	012900404.50	1	404.5
FOODJAR	11S	013000405.50	11	405.5
1R03536	01S	013100417.60	1	417.6
FOODJAR	11S	013200414.60	11	414.6
1R03537	01S	013300391.00	1	391
FOODJAR	11S	013400398.00	11	398
1R03538	01S	013500534.20	1	534.2
FOODJAR	11S	013600359.10	11	359.1
1R03539	01S	013700385.80	1	385.8
FOODJAR	11S	013800402.50	11	402.5
1R03540	01S	013900441.70	1	441.7
FOODJAR	11S	014000388.40	11	388.4

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1R03541	01S	014100498.30	1		498.3
FOODJAR	11S	014200365.30	11		365.3
1R03542	01S	014100471.00	1		471
FOODJAR	11S	014400373.60	11		373.6
1R03543	01S	014500532.50	1		532.5
FOODJAR	11S	014600339.70	11		339.7
1R03544	01S	014700484.70	1		484.7
F JAR	11S	014800362.50	11		362.5
1R03545	01S	014900508.60	1		508.6
FOODJAR	11S	015000364.80	11		364.8
1R03546	01S	015100515.50	1		515.5
FOODJAR	11S	015200376.30	11		376.3
1R03547	01S	015300515.90	1		515.9
FOODJAR	11S	015400359.80	11		359.8
1R03548	01S	015500535.40	1		535.4
FOODJAR	11S	015600359.80	11		359.8
1R03549	01S	015700438.20	1		438.2
FOODJAR	11S	015800393.20	11		393.2
1R03550	01S	015900457.10	1		457.1
FOODJAR	11S	016000378.80	11		378.8
1R03551	01S	016100348.90	1		348.9
FOODJAR	11S	016200419.40	11		419.4
1R03552	01S	016300503.00	1		503
FOODJAR	11S	016400354.30	11		354.3
1R03553	01S	016500556.00	1		556
FOODJAR	11S	016600346.50	11		346.5
1R03554	01S	016700383.50	1		383.5
FOODJAR	11S	016800400.60	11		400.6
1R03555	01S	016900447.60	1		447.6
FOODJAR	11S	017000387.30	11		387.3
1R03556	01S	017100511.20	1		511.2
FOODJAR	11S	017200377.10	11		377.1
1R03557	01S	017300451.00	1		451
FOODJAR	11S	017400392.90	11		392.9
1R03558	01S	017500385.00	1		385
FOODJAR	11S	017600396.80	11		396.8
1R03559	01S	017700485.50	1		485.5
FOODJAR	11S	017800384.10	11		384.1
1R03560	01S	017900430.50	1		430.5
FOODJAR	11S	018000390.50	11		390.5
1R03561	01S	018100530.90	1		530.9
FOODJAR	11S	018200335.80	11		335.8
1R03562	01S	018300388.90	1		388.9
FOODJAR	11S	018400383.40	11		383.4
1R03563	01S	018500428.70	1		428.7
FOODJAR	11S	018600390.30	11		390.3
1R03564	01S	018700447.80	1		447.8
FOODJAR	11S	018800347.10	11		347.1
1R03565	01S	018900490.50	1		490.5
FOODJAR	11S	019000368.20	11		368.2
1R03566	01S	019100430.70	1		430.7
FOODJAR	11S	019200397.00	11		397
1R03567	01S	019300503.30	1		503.3
FOODJAR	11S	019400375.70	11		375.7
1R03568	01S	019500491.60	1		491.6
FOODJAR	11S	019600375.50	11		375.5
1R03569	01S	019700485.30	1		485.3
FOODJAR	11S	019800366.40	11		366.4
1R03570	01S	019900509.70	1		509.7
FOODJAR	11S	020000345.60	11		345.6
1R03571	01S	020100508.80	1		508.8
FOODJAR	11S	020200363.70	11		363.7
1R03572	01S	020300464.20	1		464.2
FOODJAR	11S	020400370.70	11		370.7
1R03573	01S	020500464.00	1		464
FOODJAR	11S	020600384.30	11		384.3

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1R03574	01S	020700517.50	1	517.5
FOODJAR	11S	020800338.60	11	338.6
1R03575	01S	020900427.10	1	427.1
FOODJAR	11S	021000350.60	11	350.6
1R03576	01S	021100457.00	1	457
FOODJAR	11S	021200391.00	11	391
1R03577	01S	021300488.00	1	488
FOODJAR	11S	021400371.50	11	371.5
1R03578	01S	021500442.60	1	442.6
FOODJAR	11S	021600364.40	11	364.4
1R03579	01S	021700450.70	1	450.7
FOODJAR	11S	021800381.50	11	381.5
1R03580	01S	021900442.00	1	442
FOODJAR	11S	022000379.70	11	379.7
1R03581	02S	022100450.80	2	450.8
FOODJAR	12S	022200372.90	12	372.9
1R03582	02S	022300331.20	2	331.2
FOODJAR	12S	022400403.70	12	403.7
1R03583	02S	022500302.30	2	302.3
FOODJAR	12S	022600406.40	12	406.4
1R03584	02S	022700383.20	2	383.2
FOODJAR	12S	022800378.90	12	378.9
1R03585	02S	022900390.10	2	390.1
FOODJAR	12S	023000372.70	12	372.7
1R03586	02S	023100412.50	2	412.5
FOODJAR	12S	023200377.90	12	377.9
1R03587	02S	023300349.10	2	349.1
FOODJAR	12S	023400406.50	12	406.5
1R03588	02S	023500397.80	2	397.8
FOODJAR	12S	023600385.40	12	385.4
1R03589	02S	023700380.10	2	380.1
FOODJAR	12S	023800360.70	12	360.7
1R03590	02S	023900478.50	2	478.5
FOODJAR	12S	024000359.10	12	359.1
1R03591	02S	024100318.00	2	318
FOODJAR	12S	024200387.60	12	387.6
1R03592	02S	024300450.60	2	450.6
FOODJAR	12S	024400367.40	12	367.4
1R03593	02S	024500406.70	2	406.7
FOODJAR	12S	024600347.20	12	347.2
1R03594	02S	024700437.20	2	437.2
FOODJAR	12S	024800364.90	12	364.9
1R03595	02S	024900358.70	2	358.7
FOODJAR	12S	025000397.90	12	397.9
1R03596	02S	025100443.90	2	443.9
FOODJAR	12S	025200373.90	12	373.9
1R03597	02S	025300372.90	2	372.9
FOODJAR	12S	025400391.00	12	391
1R03598	02S	025500438.30	2	438.3
FOODJAR	12S	025600374.80	12	374.8
1R03599	02S	025700400.30	2	400.3
FOODJAR	12S	025800374.30	12	374.3
1R03600	02S	025900374.30	2	374.3
FOODJAR	12S	026000385.20	12	385.2
1R03601	02S	026100423.60	2	423.6
FOODJAR	12S	026200371.50	12	371.5
1R03602	02S	026300386.10	2	386.1
FOODJAR	12S	026400388.70	12	388.7
1R03603	02S	026500412.20	2	412.2
FOODJAR	12S	026600373.60	12	373.6
1R03604	02S	026700337.80	2	337.8
FOODJAR	12S	026800413.80	12	413.8
1R03605	02S	026900384.10	2	384.1
FOODJAR	12S	027000379.60	12	379.6
1R03606	02S	027100372.80	2	372.8
FOODJAR	12S	027200412.30	12	412.3

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1R03607	02S	027100414.80	2	414.8
FOODJAR	12S	027000379.10	12	379.1
1R03608	02S	027500451.10	2	451.1
FOODJAR	12S	027600341.20	12	341.2
1R03609	02S	027700378.60	2	378.6
FOODJAR	12S	027800373.60	12	373.6
1R03610	02S	027900465.20	2	465.2
F JJAR	12S	028000364.90	12	364.9
1R03611	02S	028100377.80	2	377.8
FOODJAR	12S	028200380.80	12	380.8
1R03612	02S	028300402.50	2	402.5
FOODJAR	12S	028400383.10	12	383.1
1R03613	02S	028500500.50	2	500.5
FOODJAR	12S	028600354.00	12	354
1R03614	02S	028700411.20	2	411.2
FOODJAR	12S	028800330.10	12	330.1
1R03615	02S	028900372.70	2	372.7
FOODJAR	12S	029000370.60	12	370.6
1R03616	02S	029100408.50	2	408.5
FOODJAR	12S	029200371.60	12	371.6
1R03617	02S	029300386.70	2	386.7
FOODJAR	12S	029400387.30	12	387.3
1R03618	02S	029500449.60	2	449.6
FOODJAR	12S	029600365.80	12	365.8
1R03619	02S	029700351.00	2	351
FOODJAR	12S	029800385.60	12	385.6
1R03620	02S	029900387.50	2	387.5
FOODJAR	12S	030000369.50	12	369.5
1R03621	02S	030100338.50	2	338.5
FOODJAR	12S	030200414.00	12	414
1R03622	02S	030300334.20	2	334.2
FOODJAR	12S	030400398.70	12	398.7
1 3623	02S	030500366.90	2	366.9
F JDJAR	12S	030600385.20	12	385.2
1R03624	02S	030700418.00	2	418
FOODJAR	12S	030800362.50	12	362.5
1R03625	02S	030900329.30	2	329.3
FOODJAR	12S	031000385.30	12	385.3
1R03626	02S	031100418.30	2	418.3
FOODJAR	12S	031200378.10	12	378.1
1R03627	02S	031300389.60	2	389.6
FOODJAR	12S	031400392.30	12	392.3
1R03628	02S	031500391.90	2	391.9
FOODJAR	12S	031600397.20	12	397.2
1R03629	02S	031700430.90	2	430.9
FOODJAR	12S	031800370.10	12	370.1
1R03630	02S	031900332.40	2	332.4
FOODJAR	12S	032000402.40	12	402.4
1R03631	02S	032100454.30	2	454.3
FOODJAR	12S	032200375.70	12	375.7
1R03632	02S	032300413.80	2	413.8
FOODJAR	12S	032400363.70	12	363.7
1R03633	02S	032500449.60	2	449.6
FOODJAR	12S	032600372.70	12	372.7
1R03634	02S	032700295.70	2	295.7
FOODJAR	12S	032800395.50	12	395.5
1R03635	02S	032900325.00	2	325
FOODJAR	12S	033000404.20	12	404.2
1 3636	02S	033100435.00	2	435
FOODJAR	12S	033200381.10	12	381.1
1R03637	02S	033300383.60	2	383.6
FOODJAR	12S	033400375.70	12	375.7
1R03638	02S	033500367.20	2	367.2
FOODJAR	12S	033600378.90	12	378.9
1R03639	02S	033700393.90	2	393.9
FOODJAR	12S	033800381.90	12	381.9

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1R03640	02S	024900291.40	2	291.4
FOODJAR	12S	024000411.30	12	411.3
1R03641	02S	024100426.20	2	426.2
FOODJAR	12S	024200383.70	12	383.7
1R03642	02S	024300337.00	2	337
FOODJAR	12S	024400427.20	12	427.2
1R03643	02S	024500413.90	2	413.9
FOODJAR	12S	024600382.20	12	382.2
1R03644	02S	024700373.80	2	373.8
FOODJAR	12S	024800363.80	12	363.8
1R03645	02S	024900464.20	2	464.2
FOODJAR	12S	025000342.90	12	342.9
1R03646	03S	035100378.40	3	378.4
FOODJAR	13S	035200401.90	13	401.9
1R03647	03S	035300470.40	3	470.4
FOODJAR	13S	035400379.50	13	379.5
1R03648	03S	035500527.00	3	527
FOODJAR	13S	035600352.70	13	352.7
1R03649	03S	035700470.80	3	470.8
FOODJAR	13S	035800332.20	13	332.2
1R03650	03S	035900410.30	3	410.3
FOODJAR	13S	036000401.50	13	401.5
1R03651	03S	036100464.10	3	464.1
FOODJAR	13S	036200373.00	13	373
1R03652	03S	036300446.40	3	446.4
FOODJAR	13S	036400382.50	13	382.5
1R03653	03S	036500447.10	3	447.1
FOODJAR	13S	036600371.80	13	371.8
1R03654	03S	036700495.10	3	495.1
FOODJAR	13S	036800366.20	13	366.2
1R03655	03S	036900481.70	3	481.7
FOODJAR	13S	037000354.90	13	354.9
1R03656	03S	037100489.90	3	489.9
FOODJAR	13S	037200366.40	13	366.4
1R03657	03S	037300470.10	3	470.1
FOODJAR	13S	037400369.10	13	369.1
1R03658	03S	037500440.70	3	440.7
FOODJAR	13S	037600402.20	13	402.2
1R03659	03S	037700441.90	3	441.9
FOODJAR	13S	037800372.70	13	372.7
1R03660	03S	037900480.20	3	480.2
FOODJAR	13S	038000380.20	13	380.2
1R03661	03S	038100459.70	3	459.7
FOODJAR	13S	038200369.70	13	369.7
1R03662	03S	038300359.80	3	359.8
FOODJAR	13S	038400418.00	13	418
1R03663	03S	038500515.50	3	515.5
FOODJAR	13S	038600366.40	13	366.4
1R03664	03S	038700419.90	3	419.9
FOODJAR	13S	038800399.20	13	399.2
1R03665	03S	038900443.70	3	443.7
FOODJAR	13S	039000387.10	13	387.1
1R03666	03S	039100446.00	3	446
FOODJAR	13S	039200371.80	13	371.8
1R03667	03S	039300330.10	3	330.1
FOODJAR	13S	039400413.20	13	413.2
1R03668	03S	039500351.70	3	351.7
FOODJAR	13S	039600413.70	13	413.7
1R03669	03S	039700468.10	3	468.1
FOODJAR	13S	039800367.50	13	367.5
1R03670	03S	039900475.10	3	475.1
FOODJAR	13S	040000359.90	13	359.9
1R03671	03S	040100432.80	3	432.8
FOODJAR	13S	040200364.20	13	364.2
1R03672	03S	040300462.00	3	462
FOODJAR	13S	040400383.30	13	383.3

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1R03673	03S	040500410.90	3	410.9
FOODJAR	13S	040600386.60	13	386.6
1R03674	03S	040700467.30	3	467.3
FOODJAR	13S	040800378.20	13	378.2
1R03675	03S	040900489.30	3	489.3
FOODJAR	13S	041000362.10	13	362.1
1R03676	03S	041100518.60	3	518.6
F DJAR	13S	041200368.70	13	368.7
1R03677	03S	041300461.20	3	461.2
FOODJAR	13S	041400363.90	13	363.9
1R03678	03S	041500471.60	3	471.6
FOODJAR	13S	041600378.60	13	378.6
1R03679	03S	041700500.60	3	500.6
FOODJAR	13S	041800357.50	13	357.5
1R03680	03S	041900484.20	3	484.2
FOODJAR	13S	042000353.70	13	353.7
1R03681	03S	042100482.10	3	482.1
FOODJAR	13S	042200362.10	13	362.1
1R03682	03S	042300389.20	3	389.2
FOODJAR	13S	042400410.00	13	410
1R03683	03S	042500498.50	3	498.5
FOODJAR	13S	042600356.60	13	356.6
1R03684	03S	042700487.60	3	487.6
FOODJAR	13S	042800348.30	13	348.3
1R03685	03S	042900424.10	3	424.1
FOODJAR	13S	043000379.30	13	379.3
1R03686	03S	043100441.80	3	441.8
FOODJAR	13S	043200382.10	13	382.1
1R03687	03S	043300461.50	3	461.5
FOODJAR	13S	043400367.70	13	367.7
1R03688	03S	043500458.00	3	458
FOODJAR	13S	043600362.30	13	362.3
1 3689	03S	043700377.10	3	377.1
FOODJAR	13S	043800397.50	13	397.5
1R03690	03S	043900470.90	3	470.9
FOODJAR	13S	044000367.60	13	367.6
1R03691	03S	044100413.50	3	413.5
FOODJAR	13S	044200376.80	13	376.8
1R03692	03S	044300357.50	3	357.5
FOODJAR	13S	044400411.80	13	411.8
1R03693	03S	044500546.70	3	546.7
FOODJAR	13S	044600344.50	13	344.5
1R03694	03S	044700497.60	3	497.6
FOODJAR	13S	044800346.70	13	346.7
1R03695	03S	044900493.70	3	493.7
FOODJAR	13S	045000362.70	13	362.7
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 7/14/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 12

1R03516	01S	007100508.80	1	508.8
FOODJAR	11S	007200381.20	11	381.2
1R03517	01S	007300462.90	1	462.9
FOODJAR	11S	007400376.30	11	376.3
1R03518	01S	007500465.40	1	465.4
FOODJAR	11S	007600404.00	11	404
1R03519	01S	007700514.80	1	514.8
FOODJAR	11S	007800366.20	11	366.2
1R03520	01S	007900488.40	1	488.4
FOODJAR	11S	010000375.80	11	375.8
1R03521	01S	010100450.70	1	450.7
FOODJAR	11S	010200373.20	11	373.2
1R03522	01S	010300450.90	1	450.9
FOODJAR	11S	010400393.10	11	393.1
1R03523	01S	010500520.10	1	520.1
FOODJAR	11S	010600377.80	11	377.8
1R03524	01S	010700456.80	1	456.8
F OJAR	11S	010800386.00	11	386
1R03525	01S	010900461.80	1	461.8
FOODJAR	11S	011000387.00	11	387
1R03526	01S	011100476.20	1	476.2
FOODJAR	11S	011200382.50	11	382.5
1R03527	01S	011300459.10	1	459.1
FOODJAR	11S	011400409.40	11	409.4
1R03528	01S	011500503.30	1	503.3
FOODJAR	11S	011600368.80	11	368.8
1R03529	01S	011700467.00	1	467
FOODJAR	11S	011800381.60	11	381.6
1R03530	01S	011900492.60	1	492.6
FOODJAR	11S	012000387.50	11	387.5
1R03531	01S	012100471.60	1	471.6
FOODJAR	11S	012200383.10	11	383.1
1R03532	01S	012300472.30	1	472.3
FOODJAR	11S	012400397.80	11	397.8
1R03533	01S	012500508.20	1	508.2
FOODJAR	11S	012600369.70	11	369.7
1R03534	01S	012700540.70	1	540.7
FOODJAR	11S	012800371.70	11	371.7
1R03535	01S	012900406.20	1	406.2
FOODJAR	11S	013000407.30	11	407.3
1R03536	01S	013100438.80	1	438.8
FOODJAR	11S	013200398.40	11	398.4
J 3537	01S	013300404.70	1	404.7
FOODJAR	11S	013400415.50	11	415.5
1R03538	01S	013500546.60	1	546.6
FOODJAR	11S	013600354.30	11	354.3
1R03539	01S	013700390.30	1	390.3
FOODJAR	11S	013800400.80	11	400.8
1R03540	01S	013900444.70	1	444.7
FOODJAR	11S	014000410.00	11	410

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1R03541	01S	014100501.70	1	501.7
FOODJAR	11S	014200383.30	11	383.3
1R03542	01S	014300464.60	1	464.6
FOODJAR	11S	014400408.40	11	408.4
1R03543	01S	014500539.00	1	539
FOODJAR	11S	014600336.20	11	336.2
1R03544	01S	014700493.50	1	493.5
F OJAR	11S	014800364.30	11	364.3
1R03545	01S	014900518.90	1	518.9
FOODJAR	11S	015000364.20	11	364.2
1R03546	01S	015100520.00	1	520
FOODJAR	11S	015200381.40	11	381.4
1R03547	01S	015300522.80	1	522.8
FOODJAR	11S	015400356.50	11	356.5
1R03548	01S	015500535.50	1	535.5
FOODJAR	11S	015600385.50	11	385.5
1R03549	01S	015700445.70	1	445.7
FOODJAR	11S	015800391.20	11	391.2
1R03550	01S	.15900459.30	1	459.3
FOODJAR	11S	016000387.50	11	387.5
1R03551	01S	0	1	354.1
FOODJAR	11S	016200416.60	11	416.6
1R03552	01S	016300510.80	1	510.8
FOODJAR	11S	016400367.50	11	367.5
1R03553	01S	016500551.30	1	551.3
FOODJAR	11S	016600353.80	11	353.8
1R03554	01S	016700389.70	1	389.7
FOODJAR	11S	016800386.80	11	386.8
1R03555	01S	016900459.10	1	459.1
FOODJAR	11S	017000384.90	11	384.9
1R03556	01S	017100518.40	1	518.4
FOODJAR	11S	017200381.40	11	381.4
1R03557	01S	017300457.20	1	457.2
F OJAR	11S	017400390.10	11	390.1
1R03558	01S	017500396.00	1	396
FOODJAR	11S	017600394.70	11	394.7
1R03559	01S	017700499.70	1	499.7
FOODJAR	11S	017800409.20	11	409.2
1R03560	01S	017900438.50	1	438.5
FOODJAR	11S	018000386.50	11	386.5
1R03561	01S	018100537.00	1	537
FOODJAR	11S	018200346.90	11	346.9
1R03562	01S	018300349.60	1	354.2
FOODJAR	11S	018400421.00	11	421
1R03563	01S	018500432.10	1	432.1
FOODJAR	11S	018600394.80	11	394.8
1R03564	01S	018700455.30	1	455.3
FOODJAR	11S	018800409.50	11	409.5
1R03565	01S	018900494.30	1	494.3
FOODJAR	11S	019000397.00	11	397
1R03566	01S	019100435.30	1	435.3
FOODJAR	11S	019200373.20	11	373.2
1R03567	01S	019300514.80	1	514.8
FOODJAR	11S	019400388.60	11	388.6
1R03568	01S	019500514.80	1	514.8
FOODJAR	11S	019600365.80	11	365.8
1R03569	01S	019700504.70	1	504.7
FOODJAR	11S	019800342.90	11	342.9
1 3570	01S	019900492.10	1	492.1
FOODJAR	11S	020000364.50	11	364.5
1R03571	01S	020100517.40	1	517.4
FOODJAR	11S	020200362.00	11	362
1R03572	01S	020300482.80	1	482.8
FOODJAR	11S	020400355.00	11	355
1R03573	01S	020500501.00	1	501
FOODJAR	11S	020600370.10	11	370.1

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1R02574	01S	020.00510.40	1	510.4
FOODJAR	11S	020800396.60	11	396.6
1R02575	01S	020900431.20	1	431.2
FOODJAR	11S	021000255.40	11	355.4
1R02576	01S	021100462.50	1	462.5
FOODJAR	11S	021200391.20	11	391.2
1R02577	01S	021300492.40	1	492.4
F OJAR	11S	021400377.10	11	377.1
1R03578	01S	021500446.70	1	446.7
FOODJAR	11S	021600350.90	11	350.9
1R02579	01S	021700464.60	1	464.6
FOODJAR	11S	021800347.40	11	347.4
1R03580	01S	021900445.30	1	445.3
FOODJAR	11S	022000388.80	11	388.8
1R03581	02S	000?000000.00	2	461.2
FOODJAR	12S	00?000371.20	12	371.2
1R03582	02S	00?100335.10	2	335.1
FOODJAR	12S	00?200396.10	12	396.1
1R03583	02S	00?300317.50	2	317.5
FOODJAR	12S	00?400399.30	12	399.3
1R03584	02S	00?500396.00	2	396
FOODJAR	12S	00?600375.20	12	375.2
1R03585	02S	00?700405.90	2	405.9
FOODJAR	12S	00?800386.80	12	386.8
1R03586	02S	00?900422.30	2	422.3
FOODJAR	12S	010000376.50	12	376.5
1R03587	02S	010100355.80	2	355.8
FOODJAR	12S	010200349.80	12	349.8
1R03588	02S	010300394.10	2	394.1
FOODJAR	12S	010400395.50	12	395.5
1R03589	02S	010500384.70	2	384.7
FOODJAR	12S	010600387.70	12	387.7
1 3590	02S	010700492.40	2	492.4
FOODJAR	12S	010800367.40	12	367.4
1R03591	02S	010900322.30	2	322.3
FOODJAR	12S	011000409.30	12	409.3
1R03592	02S	011100461.30	2	461.3
FOODJAR	12S	011200370.60	12	370.6
1R03593	02S	011300413.00	2	413
FOODJAR	12S	011400387.00	12	387
1R03594	02S	011500448.80	2	448.8
FOODJAR	12S	011600362.00	12	362
1R03595	02S	011700359.40	2	359.4
FOODJAR	12S	011800415.30	12	415.3
1R03596	02S	011900455.10	2	455.1
FOODJAR	12S	012000375.10	12	375.1
1R03597	02S	012100381.40	2	381.4
FOODJAR	12S	012200393.30	12	393.3
1R03598	02S	012300444.20	2	444.2
FOODJAR	12S	012400381.30	12	381.3
1R03599	02S	012500409.80	2	409.8
FOODJAR	12S	012600380.30	12	380.3
1R03600	02S	012700383.30	2	383.3
FOODJAR	12S	012800389.40	12	389.4
1R03601	02S	012900424.70	2	424.7
FOODJAR	12S	013000376.10	12	376.1
1R03602	02S	013100394.10	2	394.1
F OJAR	12S	013200380.00	12	380
1R03603	02S	013300416.20	2	416.2
FOODJAR	12S	013400385.00	12	385
1R03604	02S	013500357.50	2	357.5
FOODJAR	12S	013600432.20	12	432.2
1R03605	02S	013700389.50	2	389.5
FOODJAR	12S	013800374.60	12	374.6
1R03606	02S	013900382.30	2	382.3

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FOODJAR	12S	0140000409.20	12	409.2	
1R01607	02S	014100418.20	2	418.2	
FOODJAR	12S	014200385.80	12	385.8	
1R01608	02S	014300460.10	2	460.1	
FOODJAR	12S	014400337.30	12	337.3	
1R01609	02S	014500389.60	2	389.6	
FOODJAR	12S	014600373.00	12	373	
1 3610	02S	014700473.20	2	473.2	
FOODJAR	12S	014800397.60	12	397.6	
1R01611	02S	014900384.10	2	384.1	
FOODJAR	12S	015000406.40	12	406.4	
1R01612	02S	015100417.20	2	417.2	
FOODJAR	12S	015200387.90	12	387.9	
1R01613	02S	015300496.20	2	496.2	
FOODJAR	12S	015400378.20	12	378.2	
1R03614	02S	015500413.40	2	413.4	
FOODJAR	12S	015600377.40	12	377.4	
1R03615	02S	015700364.10	2	364.1	
FOODJAR	12S	015800392.80	12	392.8	
1R03616	02S	015900409.50	2	409.5	
FOODJAR	12S	016000382.50	12	382.5	
1R03617	02S	016100388.80	2	388.8	
FOODJAR	12S	016200410.60	12	410.6	
1R03618	02S	016300454.30	2	454.3	
FOODJAR	12S	016400374.50	12	374.5	
1R03619	02S	016500355.30	2	355.3	
FOODJAR	12S	016600392.10	12	392.1	
1R03620	02S	016700390.00	2	390	
FOODJAR	12S	016800379.10	12	379.1	
1R03621	02S	016900344.50	2	344.5	
FOODJAR	12S	017000419.80	12	419.8	
1R03622	02S	017100339.10	2	339.1	
FOODJAR	12S	017200399.10	12	399.1	
1. 3623	02S	017300364.00	2	364	
FOODJAR	12S	017400422.80	12	422.8	
1R03624	02S	017500419.10	2	419.1	
FOODJAR	12S	017600368.70	12	368.7	
1R03625	02S	017700329.20	2	329.2	
FOODJAR	12S	017800398.00	12	398	
1R03626	02S	017900432.20	2	432.2	
FOODJAR	12S	018000379.40	12	379.4	
1R03627	02S	018100394.20	2	394.2	
FOODJAR	12S	018200395.80	12	395.8	
1R03628	02S	018300398.70	2	398.7	
FOODJAR	12S	018400402.20	12	402.2	
1R03629	02S	018500441.40	2	441.4	
FOODJAR	12S	018600371.90	12	371.9	
1R03630	02S	018700339.70	2	339.7	
FOODJAR	12S	018800406.20	12	406.2	
1R03631	02S		2	460.2	
FOODJAR	12S	019000383.70	12	383.7	
1R03632	02S	019100414.70	2	414.7	
FOODJAR	12S	0192 0375.40	12	375.4	
1R03633	02S	019300453.60	2	453.6	
FOODJAR	12S	019400370.60	12	370.6	
1R03634	02S	019500294.60	2	294.6	
FOODJAR	12S	019600423.70	12	423.7	
1R03635	02S	019700331.30	2	331.3	
F OJAR	12S	019800410.30	12	410.3	
1R03636	02S	019900432.80	2	432.8	
FOODJAR	12S	020000389.40	12	389.4	
1R03637	02S	020100385.80	2	385.8	
FOODJAR	12S	020200378.80	12	378.8	
1R03638	02S	020300370.30	2	370.3	
FOODJAR	12S	020400390.90	12	390.9	
1R03639	02S	020500387.90	2	387.9	

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FOODJAR	12S	020600395.00	12	395
1R03640	02S	020700390.70	2	390.7
FOODJAR	12S	020800430.10	12	430.1
1R03641	02S	020900419.90	2	419.9
FOODJAR	12S	021000362.00	12	362
1R03642	02S	021100334.20	2	334.2
FOODJAR	12S	021200418.30	12	418.3
1R03643	02S	021300414.50	2	414.5
FOODJAR	12S	021400381.00	12	381
1R03644	02S	021500379.20	2	379.2
FOODJAR	12S	021600373.50	12	373.5
1R03645	02S	021700469.60	2	469.6
FOODJAR	12S	021800371.50	12	371.5
1R03646	02S	021900392.00	2	392
FOODJAR	13S	022000397.30	13	397.3
1R03647	03S	022100483.00	3	483
FOODJAR	13S	022200375.20	13	375.2
1R03648	03S	022300535.80	3	535.8
FOODJAR	13S	022400357.60	13	357.6
1R03649	03S	022500471.90	3	471.9
FOODJAR	13S	022600364.00	13	364
1R03650	03S	022700413.00	3	413
FOODJAR	13S	022800398.00	13	398
1R03651	03S	022900462.90	3	462.9
FOODJAR	13S	023000377.50	13	377.5
1R03652	03S	023100459.20	3	459.2
FOODJAR	13S	023200330.80	13	330.8
1R03653	03S	023300455.90	3	455.9
FOODJAR	13S	023400377.50	13	377.5
1R03654	03S	023500503.40	3	503.4
FOODJAR	13S	023600393.20	13	393.2
1R03655	03S	023700472.30	3	472.3
FOODJAR	13S	023800394.50	13	394.5
1R03656	03S	023900488.60	3	488.6
FOODJAR	13S	024000375.70	13	375.7
1R03657	03S	024100469.80	3	469.8
FOODJAR	13S	024200379.60	13	379.6
1R03658	03S	024300436.30	3	436.3
FOODJAR	13S	024400412.50	13	412.5
1R03659	03S	024500452.30	3	452.3
FOODJAR	13S	024600375.10	13	375.1
1R03660	03S	024700479.90	3	479.9
FOODJAR	13S	024800376.50	13	376.5
1R03661	03S		3	466.5
FOODJAR	13S	025000370.60	13	370.6
1R03662	03S	025100359.20	3	359.2
FOODJAR	13S	025200417.90	13	417.9
1R03663	03S	025300520.10	3	520.1
FOODJAR	13S	025400364.10	13	364.1
1R03664	03S	025500417.90	3	417.9
FOODJAR	13S	025600404.90	13	404.9
1R03665	03S	025700446.00	3	446
FOODJAR	13S	025800414.40	13	414.4
1R03666	03S	025900452.70	3	452.7
FOODJAR	13S	026000375.00	13	375
1R03667	03S	026100338.30	3	338.3
FOODJAR	13S	026200434.30	13	434.3
1R03668	03S	026300359.00	3	359
FOODJAR	13S	026400430.60	13	430.6
1R03669	03S	026500472.20	3	472.2
FOODJAR	13S	026600383.00	13	383
1R03670	03S	026700496.20	3	487.2
FOODJAR	13S	026800359.20	13	359.2
1R03671	03S	026900433.10	3	433.1
FOODJAR	13S	027000374.60	13	374.6
1R03672	03S	027100462.50	3	462.5

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000878

FOODJAR	13S	027200396.4Q	13	396.4
1R03673	03S	027300414.8Q	3	414.8
FOODJAR	13S	027400411.2Q	13	411.2
1R03674	03S	027500475.5Q	3	475.5
FOODJAR	13S	027600379.1Q	13	379.1
1R03675	03S	027700494.9Q	3	494.9
FOODJAR	13S	027800385.8Q	13	385.8
1 3676	03S	027900524.5Q	3	524.5
FOODJAR	13S	028000369.3Q	13	369.3
1R03677	03S	028100461.1Q	3	461.1
FOODJAR	13S	028200400.6Q	13	400.6
1R03678	03S	028300469.0Q	3	469
FOODJAR	13S	028400400.3Q	13	400.3
1R03679	03S	028500509.9Q	3	509.9
FOODJAR	13S	028600388.8Q	13	388.8
1R03680	03S	028700487.7Q	3	487.7
FOODJAR	13S	028800363.0Q	13	363
1R03681	03S	028900487.4Q	3	487.4
FOODJAR	13S	029000373.2Q	13	373.2
1R03682	03S	029100394.8Q	3	394.8
FOODJAR	13S	029200411.6Q	13	411.6
1R03683	03S	029300500.8Q	3	500.8
FOODJAR	13S	029400390.3Q	13	390.3
1R03684	03S	029500506.8Q	3	506.8
FOODJAR	13S	029600348.9Q	13	348.9
1R03685	03S	029700432.2Q	3	432.2
FOODJAR	13S	029800376.3Q	13	376.3
1R03686	03S	029900454.0Q	3	454
FOODJAR	13S	030000383.7Q	13	383.7
1R03687	03S	030100465.8Q	3	465.8
FOODJAR	13S	030200396.7Q	13	396.7
1R03688	03S	030300459.2Q	3	459.2
FOODJAR	13S	030400370.6Q	13	370.6
1. 3689	03S	030500378.3Q	3	378.3
FOODJAR	13S	030600397.8Q	13	397.8
1R03690	03S	030700473.1Q	3	473.1
FOODJAR	13S	030800389.5Q	13	389.5
1R03691	03S	030900413.4Q	3	413.4
FOODJAR	13S	031000411.4Q	13	411.4
1R03692	03S	031100361.5Q	3	361.5
FOODJAR	13S	031200428.4Q	13	428.4
1R03693	03S	031300553.6Q	3	553.6
FOODJAR	13S	031400337.5Q	13	337.5
1R03694	03S	031500499.6Q	3	499.6
FOODJAR	13S	031600360.6Q	13	360.6
1R03695	03S	031700497.6Q	3	497.6
FOODJAR	13S	031800386.3Q	13	386.3
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 7/21/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 13

1R03516	01S	00?100523.4Q	1	523.4
FOODJAR	11S	00?200376.4Q	11	376.4
1R03517	01S	00?300477.4Q	1	477.4
FOODJAR	11S	00?400357.8Q	11	357.8
1R03518	01S	00?500464.5Q	1	464.5
FOODJAR	11S	00?600387.3Q	11	387.3
1R03519	01S	00?700524.2Q	1	524.2
FOODJAR	11S	00?800363.1Q	11	363.1
1R03520	01S	00?900499.3Q	1	499.3
FOODJAR	11S	010000378.9Q	11	378.9
1R03521	01S	010100458.0Q	1	458
FOODJAR	11S	010200371.1Q	11	371.1
1R03522	01S	010300458.8Q	1	458.8
FOODJAR	11S	010400390.8Q	11	390.8
1R03523	01S	010500534.2Q	1	534.2
FOODJAR	11S		11	377.7
1R03524	01S	010700452.1Q	1	473.7
FOODJAR	11S	010800379.6Q	11	379.6
1R03525	01S	010900480.3Q	1	480.3
FOODJAR	11S	011000379.1Q	11	379.1
1R03526	01S	011100489.8Q	1	489.8
FOODJAR	11S	011200379.1Q	11	379.1
1R03527	01S	011300464.5Q	1	464.5
FOODJAR	11S	011400387.9Q	11	387.9
1R03528	01S	011500524.7Q	1	524.7
FOODJAR	11S	011600362.0Q	11	362
1R03529	01S	011700485.9Q	1	485.9
FOODJAR	11S	011800376.6Q	11	376.6
1R03530	01S	011900507.0Q	1	507
FOODJAR	11S	012000384.5Q	11	384.5
1R03531	01S	012100493.8Q	1	493.8
FOODJAR	11S	012200340.5Q	11	340.5
1R03532	01S	012300480.6Q	1	480.6
FOODJAR	11S	012400383.4Q	11	383.4
1R03533	01S	012500528.2Q	1	528.2
FOODJAR	11S	012600364.7Q	11	364.7
1R03534	01S	012700546.9Q	1	546.9
FOODJAR	11S	012800352.4Q	11	352.4
1R03535	01S	012900428.8Q	1	428.8
FOODJAR	11S	013000398.2Q	11	398.2
1R03536	01S	013100440.6Q	1	440.6
FOODJAR	11S	013200408.0Q	11	408
1R03537	01S	013300408.4Q	1	408.4
FOODJAR	11S	013400390.6Q	11	390.6
1R03538	01S	013500561.7Q	1	561.7
FOODJAR	11S	013600337.3Q	11	337.3
1R03539	01S	013700409.0Q	1	409
FOODJAR	11S	013800387.3Q	11	387.3
1R03540	01S	013900450.3Q	1	450.3

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000880

FOODJAR	11S	014000397.80	11	397.8
1R03541	01S	014100515.30	1	515.3
FOODJAR	11S	014200376.20	11	376.2
1R03542	01S	014300480.00	1	480
FOODJAR	11S	014400388.00	11	388
1R03543	01S	014500556.00	1	556
FOODJAR	11S	014600339.40	11	339.4
1R03544	01S	014700507.60	1	507.6
FOODJAR	11S	014800363.20	11	363.2
1R03545	01S	014900529.60	1	529.6
FOODJAR	11S	015000361.60	11	361.6
1R03546	01S	015100529.70	1	529.7
FOODJAR	11S	015200384.90	11	384.9
1R03547	01S	015300541.50	1	541.5
FOODJAR	11S	015400350.90	11	350.9
1R03548	01S	015500535.60	1	535.6
FOODJAR	11S	015600383.80	11	383.8
1R03549	01S	015700448.70	1	448.7
FOODJAR	11S	015800394.60	11	394.6
1R03550	01S	015900468.90	1	468.9
FOODJAR	11S	016000390.00	11	390
1R03551	01S	016100360.90	1	360.9
FOODJAR	11S	016200419.50	11	419.5
1R03552	01S		1	499.1
FOODJAR	11S	016400361.60	11	361.6
1R03553	01S	016500564.90	1	564.9
FOODJAR	11S	016600355.60	11	355.6
1R03554	01S	016700393.70	1	393.7
FOODJAR	11S	016800405.90	11	405.9
1R03555	01S	016900467.70	1	467.7
FOODJAR	11S	017000390.40	11	390.4
1R03556	01S	017100538.80	1	538.8
FOODJAR	11S	017200380.90	11	380.9
1R03557	01S	017300463.90	1	463.9
FOODJAR	11S	017400391.00	11	391
1R03558	01S	017500403.30	1	403.3
FOODJAR	11S	017600392.90	11	392.9
1R03559	01S	017700493.00	1	493
FOODJAR	11S	017800386.90	11	386.9
1R03560	01S	017900442.10	1	442.1
FOODJAR	11S	018000392.90	11	392.9
1R03561	01S	018100559.70	1	559.7
FOODJAR	11S	018200342.30	11	342.3
1R03562	01S	018300406.80	1	406.8
FOODJAR	11S	018400337.90	11	337.9
1R03563	01S	018500437.40	1	437.4
FOODJAR	11S	018600396.80	11	396.8
1R03564	01S	018700453.80	1	453.8
FOODJAR	11S	018800389.30	11	389.3
1R03565	01S	018900498.50	1	498.5
FOODJAR	11S	019000375.00	11	375
1R03566	01S	019100438.30	1	438.3
FOODJAR	11S	019200388.60	11	388.6
1R03567	01S	019300525.30	1	525.3
FOODJAR	11S	019400375.60	11	375.6
1R03568	01S	019500521.40	1	521.4
FOODJAR	11S	019600377.80	11	377.8
1R03569	01S	019700502.30	1	502.3
FOODJAR	11S	019800375.90	11	375.9
1R03570	01S	019900462.80	1	462.8
FOODJAR	11S	020000428.20	11	428.2
1R03571	01S	020100528.80	1	528.8
FOODJAR	11S	020200370.50	11	370.5
1R03572	01S	020300494.10	1	494.1
FOODJAR	11S	020400357.60	11	357.6
1R03573	01S	020500511.50	1	511.5

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FOODJAR	11S	020600372.5Q	11	372.5
1R03574	01S	020700528.6Q	1	528.6
FOODJAR	11S	020800382.3Q	11	382.3
1R03575	01S	020900438.2Q	1	438.2
FOODJAR	11S	021000353.9Q	11	353.9
1R03576	01S	021100370.5Q	1	370.5
FOODJAR	11S	021200471.8Q	11	471.8
1R03577	01S	021300421.6Q	1	421.6
FOODJAR	11S	021400455.4Q	11	455.4
1R03578	01S	021500372.0Q	1	372
FOODJAR	11S	021600469.4Q	11	469.4
1R03579	01S	021700414.4Q	1	414.4
FOODJAR	11S	021800435.7Q	11	435.7
1R03580	01S	021900393.7Q	1	393.7
FOODJAR	11S	022000437.2Q	11	437.2
1R03581	02S	00?100468.8Q	2	468.8
FOODJAR	12S	00?200373.9Q	12	373.9
1R03582	02S	00?300344.7Q	2	344.7
FOODJAR	12S	00?400395.2Q	12	395.2
1R03583	02S	00?500333.6Q	2	333.6
FOODJAR	12S	00?600395.0Q	12	395
1R03584	02S	00?700408.0Q	2	408
FOODJAR	12S	00?800379.0Q	12	379
1R03585	02S	00?900402.2Q	2	402.2
FOODJAR	12S	010000374.4Q	12	374.4
1R03586	02S	010100430.5Q	2	430.5
FOODJAR	12S	010200373.7Q	12	373.7
1R03587	02S	010300346.5Q	2	346.5
FOODJAR	12S	010400408.6Q	12	408.6
1R03588	02S	010500403.1Q	2	403.1
FOODJAR	12S	010600393.9Q	12	393.9
1R03589	02S	010700386.3Q	2	386.3
FOODJAR	12S	010800368.6Q	12	368.6
1R03590	02S	010900501.8Q	2	501.8
FOODJAR	12S	011000369.2Q	12	369.2
1R03591	02S	011100334.9Q	2	334.9
FOODJAR	12S	011200394.6Q	12	394.6
1R03592	02S	011300457.9Q	2	457.9
FOODJAR	12S	011400382.9Q	12	382.9
1R03593	02S	011500408.7Q	2	408.7
FOODJAR	12S	011600406.1Q	12	406.1
1R03594	02S	011700462.9Q	2	462.9
FOODJAR	12S	011800364.5Q	12	364.5
1R03595	02S	011900365.6Q	2	365.6
FOODJAR	12S	012000394.4Q	12	394.4
1R03596	02S	012100465.4Q	2	465.4
FOODJAR	12S	012200364.3Q	12	364.3
1R03597	02S	012300388.2Q	2	388.2
FOODJAR	12S	012400396.9Q	12	396.9
1R03598	02S	012500447.9Q	2	447.9
FOODJAR	12S	012600386.8Q	12	386.8
1R03599	02S	012700420.0Q	2	420
FOODJAR	12S	012800372.2Q	12	372.2
1R03600	02S	012900398.8Q	2	398.8
FOODJAR	12S	013000386.4Q	12	386.4
1R03601	02S	013100443.1Q	2	443.1
FOODJAR	12S	013200356.8Q	12	356.8
1R03602	02S	013300410.2Q	2	410.2
FOODJAR	12S	013400375.0Q	12	375
1R03603	02S	013500425.8Q	2	425.8
FOODJAR	12S	013600383.1Q	12	383.1
1R03604	02S	013700352.9Q	2	352.9
FOODJAR	12S	013800418.4Q	12	418.4
1R03605	02S	013900396.0Q	2	396
FOODJAR	12S	014000386.7Q	12	386.7
1R03606	02S	014100386.2Q	2	386.2

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FOODJAR	12S	014200409.4Q	12	409.4
1R03607	02S	014300430.1Q	2	430.1
FOODJAR	12S	014400374.6Q	12	374.6
1R03608	02S	014500470.9Q	2	470.9
FOODJAR	12S	014600350.0Q	12	350
1R03609	02S	014700395.8Q	2	395.8
FOODJAR	12S	014800373.5Q	12	373.5
1 3610	02S	014900480.9Q	2	480.9
FOODJAR	12S	015000366.4Q	12	366.4
1R03611	02S	015100387.9Q	2	387.9
FOODJAR	12S	015200381.9Q	12	381.9
1R03612	02S	015300420.2Q	2	420.2
FOODJAR	12S	015400381.8Q	12	381.8
1R03613	02S	015500503.3Q	2	503.3
FOODJAR	12S	015600371.4Q	12	371.4
1R03614	02S	015700415.9Q	2	415.9
FOODJAR	12S	015800361.4Q	12	361.4
1R03615	02S	015900369.4Q	2	369.4
FOODJAR	12S	016000359.2Q	12	359.2
1R03616	02S	016100418.9Q	2	418.9
FOODJAR	12S	016200375.4Q	12	375.4
1R03617	02S	016300399.3Q	2	399.3
FOODJAR	12S	016400386.8Q	12	386.8
1R03618	02S	016500458.7Q	2	458.7
FOODJAR	12S	016600373.4Q	12	373.4
1R03619	02S	016700364.4Q	2	364.4
FOODJAR	12S	016800386.6Q	12	386.6
1R03620	02S	016900413.3Q	2	413.3
FOODJAR	12S	017000359.0Q	12	359
1R03621	02S	017100351.6Q	2	351.6
FOODJAR	12S	017200413.2Q	12	413.2
1R03622	02S	017300351.4Q	2	351.4
FOODJAR	12S	017400389.3Q	12	389.3
1 3623	02S	017500365.4Q	2	365.4
FOODJAR	12S	017600402.4Q	12	402.4
1R03624	02S	017700437.3Q	2	437.3
FOODJAR	12S	017800371.2Q	12	371.2
1R03625	02S	017900330.3Q	2	330.3
FOODJAR	12S	018000395.0Q	12	395
1R03626	02S	018100430.7Q	2	430.7
FOODJAR	12S	018200312.9Q	12	312.9
1R03627	02S	018300409.2Q	2	409.2
FOODJAR	12S	018400397.9Q	12	397.9
1R03628	02S	018500408.1Q	2	408.1
FOODJAR	12S	018600396.9Q	12	396.9
1R03629	02S	018700455.3Q	2	455.3
FOODJAR	12S	018800366.8Q	12	366.8
1R03630	02S	018900352.8Q	2	352.8
FOODJAR	12S	019000396.4Q	12	396.4
1R03631	02S	019100472.7Q	2	472.7
FOODJAR	12S	019200380.7Q	12	380.7
1R03632	02S	019300416.4Q	2	416.4
FOODJAR	12S	019400360.4Q	12	360.4
1R03633	02S	019500471.2Q	2	471.2
FOODJAR	12S	019600368.9Q	12	368.9
1R03634	02S	019700306.1Q	2	306.1
FOODJAR	12S	019800395.8Q	12	395.8
1R03635	02S	019900346.0Q	2	346
F DJAR	12S	020000402.1Q	12	402.1
1..03636	02S	020100449.0Q	2	449
FOODJAR	12S	020200384.9Q	12	384.9
1R03637	02S	020300402.2Q	2	402.2
FOODJAR	12S	020400366.7Q	12	366.7
1R03638	02S	020500382.4Q	2	382.4
FOODJAR	12S	020600388.4Q	12	388.4
1R03639	02S	020700406.6Q	2	406.6

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FOODJAR	12S	020800383.50	12	383.5
1R03640	02S	020900306.40	2	306.4
FOODJAR	12S	021000419.10	12	419.1
1R03641	02S	021100437.10	2	437.1
FOODJAR	12S	021200389.10	12	389.1
1R03642	02S	021300348.00	2	348
FOODJAR	12S	021400401.10	12	401.1
1 3643	02S	021500411.40	2	411.4
FOODJAR	12S	021600394.60	12	394.6
1R03644	02S	021700391.30	2	391.3
FOODJAR	12S	021800373.20	12	373.2
1R03645	02S	021900480.20	2	480.2
FOODJAR	12S	022000367.90	12	367.9
1R03646	03S	022100402.90	3	402.9
FOODJAR	13S	022200387.30	13	387.3
1R03647	03S	022300492.40	3	492.4
FOODJAR	13S	022400379.70	13	379.7
1R03648	03S	022500554.20	3	554.2
FOODJAR	13S	022600350.90	13	350.9
1R03649	03S	022700485.80	3	485.8
FOODJAR	13S	022800364.10	13	364.1
1R03650	03S	022900431.00	3	431
FOODJAR	13S	023000390.30	13	390.3
1R03651	03S		3	475.9
FOODJAR	13S	023200360.20	13	360.2
1R03652	03S	023300470.10	3	470.1
FOODJAR	13S	023400378.30	13	378.3
1R03653	03S	023500468.90	3	468.9
FOODJAR	13S	023600375.60	13	375.6
1R03654	03S	023700506.80	3	506.8
FOODJAR	13S	023800373.40	13	373.4
1R03655	03S	023900478.70	3	478.7
F[illegible]ODJAR	13S	024000362.40	13	362.4
1[illegible]03656	03S	024100504.60	3	504.6
FOODJAR	13S	024200370.80	13	370.8
1R03657	03S	024300483.80	3	483.8
FOODJAR	13S	024400378.80	13	378.8
1R03658	03S	024500446.70	3	446.7
FOODJAR	13S	024600405.80	13	405.8
1R03659	03S	024700458.70	3	458.7
FOODJAR	13S	024800368.20	13	368.2
1R03660	03S	024900496.60	3	496.6
FOODJAR	13S	025000377.50	13	377.5
1R03661	03S	025100480.10	3	480.1
FOODJAR	13S	025200363.20	13	363.2
1R03662	03S	025300367.40	3	367.4
FOODJAR	13S	025400410.30	13	410.3
1R03663	03S	025500537.60	3	537.6
FOODJAR	13S	025600366.80	13	366.8
1R03664	03S	025700424.40	3	424.4
FOODJAR	13S	025800407.00	13	407
1R03665	03S	025900447.30	3	447.3
FOODJAR	13S	026000395.70	13	395.7
1R03666	03S	026100463.90	3	463.9
FOODJAR	13S	026200361.50	13	361.5
1R03667	03S	026300352.40	3	352.4
FOODJAR	13S	026400399.60	13	399.6
1R03668	03S	026500369.00	3	369
F[illegible]DJAR	13S	026600414.70	13	414.7
1R03669	03S	026700485.90	3	485.9
FOODJAR	13S	026800376.30	13	376.3
1R03670	03S	026900503.90	3	503.9
FOODJAR	13S	027000355.40	13	355.4
1R03671	03S	027100451.70	3	451.7
FOODJAR	13S	027200361.90	13	361.9
1R03672	03S	027300484.30	3	484.3

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FOODJAR 13S 027400369.40     13          369.4
1R03673 03S 027500430.00     3           430
FOODJAR 13S 027600376.20     13          376.2
1R03674 03S 027700485.80     3           485.8
FOODJAR 13S 027800375.30     13          375.3
1R03675 03S 027900505.60     3           505.6
FOODJAR 13S 028000353.70     13          353.7
1R03676 03S 028100544.70     3           544.7
FOODJAR 13S 028200360.50     13          360.5
1R03677 03S 028300476.40     3           476.4
FOODJAR 13S 028400372.00     13          372
1R03678 03S 028500475.60     3           475.6
FOODJAR 13S 028600394.40     13          394.4
1R03679 03S 028700522.40     3           522.4
FOODJAR 13S 028800363.50     13          363.5
1R03680 03S 028900504.80     3           504.8
FOODJAR 13S 029000349.70     13          349.7
1R03681 03S 029100498.70     3           498.7
FOODJAR 13S 029200367.30     13          367.3
1R03682 03S 029300403.20     3           403.2
FOODJAR 13S 029400409.10     13          409.1
1R03683 03S 029500512.90     3           512.9
FOODJAR 13S 029600356.20     13          356.2
1R03684 03S 029700523.70     3           523.7
FOODJAR 13S 029800342.50     13          342.5
1R03685 03S 029900444.50     3           444.5
FOODJAR 13S 030000375.10     13          375.1
1R03686 03S 030100475.80     3           475.8
FOODJAR 13S 030200375.50     13          375.5
1R03687 03S 030300477.20     3           477.2
FOODJAR 13S 030400364.90     13          364.9
1R03688 03S 030500471.30     3           471.3
FOODJAR 13S 030600361.40     13          361.4
1R03689 03S 030700384.60     3           384.6
FOODJAR 13S 030800392.60     13          392.6
1R03690 03S 030900482.00     3           482
FOODJAR 13S 031000353.80     13          353.8
1R03691 03S 031100430.50     3           430.5
FOODJAR 13S 031200383.60     13          383.6
1R03692 03S 031300367.20     3           367.2
FOODJAR 13S 031400406.90     13          406.9
1R03693 03S 031500562.40     3           562.4
FOODJAR 13S 031600354.00     13          354
1R03694 03S 031700509.20     3           509.2
FOODJAR 13S 031800356.10     13          356.1
1R03695 03S 031900512.60     3           512.6
FOODJAR 13S 032000356.40     13          356.4
9999999999     99            0
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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 7/28/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 14

1R03516	01S	007100542.5Q	1	542.5
FOODJAR	11S	007200362.8Q	11	362.8
1R03517	01S	007300483.2Q	1	483.2
FOODJAR	11S	007400363.5Q	11	363.5
1R03518	01S	007500483.7Q	1	483.7
FOODJAR	11S	007600380.5Q	11	380.5
1R03519	01S	007700540.6Q	1	540.6
FOODJAR	11S	007800358.1Q	11	358.1
1R03520	01S	007900507.2Q	1	507.2
FOODJAR	11S	010000379.2Q	11	379.2
1R03521	01S	010100456.7Q	1	456.7
FOODJAR	11S	010200381.6Q	11	381.6
1R03522	01S	010300465.8Q	1	465.8
FOODJAR	11S	010400385.5Q	11	385.5
1R03523	01S	010500541.2Q	1	541.2
FOODJAR	11S	010600375.1Q	11	375.1
1 3524	01S	010700484.8Q	1	484.8
FOODJAR	11S	010800381.4Q	11	381.4
1R03525	01S	010900490.5Q	1	490.5
FOODJAR	11S	011000379.7Q	11	379.7
1R03526	01S	011100494.1Q	1	494.1
FOODJAR	11S	011200317.7Q	11	317.7
1R03527	01S	011300471.7Q	1	471.7
FOODJAR	11S	011400387.6Q	11	387.6
1R03528	01S	011500531.9Q	1	531.9
FOODJAR	11S	011600357.9Q	11	357.9
1R03529	01S	011700489.4Q	1	489.4
FOODJAR	11S	011800377.7Q	11	377.7
1R03530	01S	011900511.5Q	1	511.5
FOODJAR	11S	012000377.9Q	11	377.9
1R03531	01S	012100502.4Q	1	502.4
FOODJAR	11S	012200371.7Q	11	371.7
1R03532	01S	012300482.5Q	1	482.5
FOODJAR	11S	012400381.4Q	11	381.4
1R03533	01S	012500528.7Q	1	528.7
FOODJAR	11S	012600367.1Q	11	367.1
1R03534	01S	012700566.4Q	1	566.4
FOODJAR	11S	012800359.5Q	11	359.5
1R03535	01S	012900436.8Q	1	436.8
FOODJAR	11S	013000396.4Q	11	396.4
1R03536	01S	013100448.1Q	1	448.1
FOODJAR	11S	013200401.1Q	11	401.1
1 3537	01S	013300421.4Q	1	421.4
FOODJAR	11S	013400380.9Q	11	380.9
1R03538	01S	013500570.0Q	1	570
FOODJAR	11S	013600344.7Q	11	344.7
1R03539	01S	013700420.0Q	1	420
FOODJAR	11S	013800389.9Q	11	389.9
1P03540	01S	013900459.6Q	1	459.6

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FOODJAR	11S	014000397.30	11	397.3
1R03541	01S	014100525.00	1	525
FOODJAR	11S	014200367.40	11	367.4
1R03542	01S	014300489.90	1	489.9
FOODJAR	11S	014400381.80	11	381.8
1R03543	01S	014500578.60	1	578.6
FOODJAR	11S	014600328.50	11	328.5
1 3544	01S	014700520.50	1	520.5
FOODJAR	11S	014800357.80	11	357.8
1R03545	01S	014900540.20	1	540.2
FOODJAR	11S	015000358.20	11	358.2
1R03546	01S	015100535.90	1	535.9
FOODJAR	11S	015200377.40	11	377.4
1R03547	01S	015300553.70	1	553.7
FOODJAR	11S	015400346.60	11	346.6
1R03548	01S	015500547.50	1	547.5
FOODJAR	11S	015600375.90	11	375.9
1R03549	01S	015700454.50	1	454.5
FOODJAR	11S	015800389.40	11	389.4
1R03550	01S	015900478.00	1	478
FOODJAR	11S	016000383.10	11	383.1
1R03551	01S	016100362.80	1	362.8
FOODJAR	11S	016200423.10	11	423.1
1R03552	01S	016300529.00	1	529
FOODJAR	11S	016400350.60	11	350.6
1R03553	01S	016500574.40	1	574.4
FOODJAR	11S	016600355.70	11	355.7
1R03554	01S	016700401.00	1	401
FOODJAR	11S	016800402.30	11	402.3
1R03555	01S	016900481.00	1	481
FOODJAR	11S	017000341.30	11	341.3
1R03556	01S	017100541.90	1	541.9
F DJAR	11S	017200382.20	11	382.2
1R03557	01S	017300478.20	1	478.2
FOODJAR	11S	017400389.00	11	389
1R03558	01S	017500412.60	1	412.6
FOODJAR	11S	017600389.40	11	389.4
1R03559	01S	017700511.10	1	511.1
FOODJAR	11S	017800376.40	11	376.4
1R03560	01S	017900453.60	1	453.6
FOODJAR	11S	018000386.60	11	386.6
1R03561	01S	018100559.30	1	559.3
FOODJAR	11S	018200335.80	11	335.8
1R03562	01S	018300412.50	1	412.5
FOODJAR	11S	018400390.70	11	390.7
1R03563	01S	018500447.90	1	447.9
FOODJAR	11S	018600391.30	11	391.3
1R03564	01S	018700463.10	1	463.1
FOODJAR	11S	018800386.70	11	386.7
1R03565	01S	018900507.00	1	507
FOODJAR	11S	019000382.50	11	382.5
1R03566	01S	019100445.00	1	445
FOODJAR	11S	019200388.10	11	388.1
1R03567	01S	019300543.60	1	543.6
FOODJAR	11S	019400367.20	11	367.2
1R03568	01S	019500533.90	1	533.9
FOODJAR	11S	019600371.80	11	371.8
1R03569	01S	019700524.20	1	524.2
F DJAR	11S	019800362.70	11	362.7
1R03570	01S	019900439.60	1	439.6
FOODJAR	11S	020000429.40	11	429.4
1R03571	01S	020100539.10	1	539.1
FOODJAR	11S	020200364.60	11	364.6
1R03572	01S	020300510.40	1	510.4
FOODJAR	11S	020400353.20	11	353.2
1R03573	01S	020500521.60	1	521.6

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FOODJAR 11S 020600370.50    11    370.5
1R03574 01S 020700539.70    1     539.7
FOODJAR 11S 020800348.90    11    348.9
1R03575 01S 020900448.60    1     448.6
FOODJAR 11S 021000340.60    11    340.6
1R03576 01S 021100452.10    1     452.1
FOODJAR 11S 021200362.60    11    362.6
1R03577 01S 021300498.00    1     498
FOODJAR 11S 021400334.10    11    334.1
1R03578 01S 021500444.20    1     444.2
FOODJAR 11S 021600331.00    11    331
1R03579 01S 021700479.80    1     479.8
FOODJAR 11S 021800348.30    11    348.3
1R03580 01S 021900447.60    1     447.6
FOODJAR 11S 022000360.40    11    360.4
1R03581 02S 00?300477.60    2     477.6
FOODJAR 12S 00?400369.40    12    369.4
1R03582 02S 00?500344.20    2     344.2
FOODJAR 12S 00?600353.60    12    353.6
1R03583 02S 00?700336.60    2     336.6
FOODJAR 12S 00?800401.50    12    401.5
1R03584 02S 00?900407.90    2     407.9
FOODJAR 12S 010000390.10    12    390.1
1R03585 02S 010100411.60    2     411.6
FOODJAR 12S 010200321.50    12    321.5
1R03586 02S 010300444.00    2     444
FOODJAR 12S 010400366.20    12    366.2
1R03587 02S 010500362.20    2     362.2
FOODJAR 12S 010600411.20    12    411.2
1R03588 02S 010700399.70    2     399.7
FOODJAR 12S 010800400.60    12    400.6
1R03589 02S 010900406.90    2     406.9
FOODJAR 12S 011000359.90    12    359.9
1  3590 02S 011100504.50    2     504.5
FOODJAR 12S 011200393.50    12    393.5
1R03591 02S 011300337.50    2     337.5
FOODJAR 12S 011400401.30    12    401.3
1R03592 02S 011500455.30    2     455.3
FOODJAR 12S 011600387.60    12    387.6
1R03593 02S 011700419.10    2     419.1
FOODJAR 12S 011800391.00    12    391
1R03594 02S 011900472.80    2     472.8
FOODJAR 12S 012000361.90    12    361.9
1R03595 02S 012100379.60    2     379.6
FOODJAR 12S 012200387.90    12    387.9
1R03596 02S 012300468.70    2     468.7
FOODJAR 12S 012400371.20    12    371.2
1R03597 02S 012500389.60    2     389.6
FOODJAR 12S 012600403.10    12    403.1
1R03598 02S 012700454.30    2     454.3
FOODJAR 12S 012800377.90    12    377.9
1R03599 02S 012900419.60    2     419.6
FOODJAR 12S 013000382.00    12    382
1R03600 02S 013100408.20    2     408.2
FOODJAR 12S 013200377.70    12    377.7
1R03601 02S 013300449.30    2     449.3
FOODJAR 12S 013400366.90    12    366.9
1R03602 02S 013500410.90    2     410.9
FOODJAR 12S 013600387.80    12    387.8
1R03603 02S 013700439.00    2     439
FOODJAR 12S 013800373.80    12    373.8
1R03604 02S 013900367.00    2     367
FOODJAR 12S 014000400.00    12    400
1R03605 02S 014100404.40    2     404.4
FOODJAR 12S 014200351.30    12    351.3
1R03606 02S 014300384.70    2     384.7
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FOODJAR	12S	014400414.10	12	414.1
1R03607	02S	014500438.80	2	438.8
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1R03608	02S	014700474.30	2	474.3
FOODJAR	12S	014800355.80	12	355.8
1R03609	02S	014900396.70	2	396.7
FOODJAR	12S	015000376.40	12	376.4
1 3610	02S	015100489.40	2	489.4
FOODJAR	12S	015200373.30	12	373.3
1R03611	02S	015300397.20	2	397.2
FOODJAR	12S	015400379.50	12	379.5
1R03612	02S	015500429.60	2	429.6
FOODJAR	12S	015600375.60	12	375.6
1R03613	02S	015700507.70	2	507.7
FOODJAR	12S	015800367.70	12	367.7
1R03614	02S	015900407.00	2	407
FOODJAR	12S	016000362.80	12	362.8
1R03615	02S	016100371.10	2	371.1
FOODJAR	12S	016200380.00	12	380
1R03616	02S	016300426.00	2	426
FOODJAR	12S	016400375.60	12	375.6
1R03617	02S	016500414.10	2	414.1
FOODJAR	12S	016600369.60	12	369.6
1R03618	02S	016700466.10	2	466.1
FOODJAR	12S	016800358.40	12	358.4
1R03619	02S	016900350.00	2	350
FOODJAR	12S	017000390.70	12	390.7
1R03620	02S	017100427.20	2	427.2
FOODJAR	12S	017200353.60	12	353.6
1R03621	02S	017300358.50	2	358.5
FOODJAR	12S	017400411.20	12	411.2
1R03622	02S	017500360.70	2	360.7
F DJAR	12S	017600381.40	12	381.4
1R03623	02S	017700371.90	2	371.9
FOODJAR	12S	017800394.70	12	394.7
1R03624	02S	017900444.40	2	444.4
FOODJAR	12S	018000352.80	12	352.8
1R03625	02S	018100335.60	2	335.6
FOODJAR	12S	018200388.00	12	388
1R03626	02S	018300455.60	2	455.6
FOODJAR	12S	018400361.80	12	361.8
1R03627	02S	018500403.20	2	403.2
FOODJAR	12S	018600391.10	12	391.1
1R03628	02S	018700409.40	2	409.4
FOODJAR	12S	018800360.70	12	360.7
1R03629	02S	018900465.20	2	465.2
FOODJAR	12S	019000362.90	12	362.9
1R03630	02S	019100359.50	2	359.5
FOODJAR	12S	019200397.10	12	397.1
1R03631	02S	019300485.80	2	485.8
FOODJAR	12S	019400370.10	12	370.1
1R03632	02S	019500415.40	2	415.4
FOODJAR	12S	019600359.20	12	359.2
1R03633	02S	019700478.80	2	478.8
FOODJAR	12S	019800371.80	12	371.8
1R03634	02S	019900318.10	2	318.1
FOODJAR	12S	020000388.50	12	388.5
1P03635	02S	020100345.20	2	345.2
F DJAR	12S	020200401.80	12	401.8
1R03636	02S	020300454.00	2	454
FOODJAR	12S	020400376.40	12	376.4
1R03637	02S	020500412.10	2	412.1
FOODJAR	12S	020600361.00	12	361
1R03638	02S	020700393.60	2	393.6
FOODJAR	12S	020800383.10	12	383.1
1R03639	02S	020900407.90	2	407.9

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FOODJAR	12S	021000378.40	12	378.4
1R03640	02S	021100317.80	2	317.8
FOODJAR	12S	021200414.50	12	414.5
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FOODJAR	12S	021400381.80	12	381.8
1R03642	02S	021500351.90	2	351.9
FOODJAR	12S	021600347.30	12	347.3
1R03643	02S	021700421.30	2	421.3
FOODJAR	12S	021800388.60	12	388.6
1R03644	02S	021900396.90	2	396.9
FOODJAR	12S	022000375.70	12	375.7
1R03645	02S	022100477.20	2	477.2
FOODJAR	12S	022200369.80	12	369.8
1R03646	03S	022300409.40	3	409.4
FOODJAR	13S	022400382.90	13	382.9
1R03647	03S	022500487.00	3	487
FOODJAR	13S	022600392.60	13	392.6
1R03648	03S	022700562.90	3	562.9
FOODJAR	13S	022800326.30	13	326.3
1R03649	03S	022900496.00	3	496
FOODJAR	13S	023000360.90	13	360.9
1R03650	03S	023100438.90	3	438.9
FOODJAR	13S	023200384.80	13	384.8
1R03651	03S	023300482.20	3	482.2
FOODJAR	13S	023400378.80	13	378.8
1R03652	03S	023500485.40	3	485.4
FOODJAR	13S	023600369.80	13	369.8
1R03653	03S	023700479.40	3	479.4
FOODJAR	13S	023800376.10	13	376.1
1R03654	03S	023900514.70	3	514.7
FOODJAR	13S	024000374.40	13	374.4
1R03655	03S	024100486.20	3	486.2
FOODJAR	13S	024200365.60	13	365.6
1R03656	03S	024300506.90	3	506.9
FOODJAR	13S	024400369.80	13	369.8
1R03657	03S	024500488.60	3	488.6
FOODJAR	13S	024600375.70	13	375.7
1R03658	03S	024700451.50	3	451.5
FOODJAR	13S	024800406.30	13	406.3
1R03659	03S		3	475.9
FOODJAR	13S	025000358.10	13	358.1
1R03660	03S	025100505.60	3	505.6
FOODJAR	13S	025200365.20	13	365.2
1R03661	03S	025300481.70	3	481.7
FOODJAR	13S	025400368.00	13	368
1R03662	03S	025500363.70	3	363.7
FOODJAR	13S	025600404.40	13	404.4
1R03663	03S	025700540.70	3	540.7
FOODJAR	13S	025800367.50	13	367.5
1R03664	03S	025900430.10	3	430.1
FOODJAR	13S	026000405.20	13	405.2
1R03665	03S	026100456.80	3	456.8
FOODJAR	13S	026200399.40	13	399.4
1R03666	03S	026300473.90	3	473.9
FOODJAR	13S	026400360.90	13	360.9
1R03667	03S	026500363.20	3	363.2
FOODJAR	13S	026600401.10	13	401.1
1R03668	03S	026700371.40	3	371.4
FOODJAR	13S	026800408.30	13	408.3
1R03669	03S	026900496.80	3	496.8
FOODJAR	13S	027000374.30	13	374.3
1R03670	03S	027100509.70	3	509.7
FOODJAR	13S	027200358.10	13	358.1
1R03671	03S	027300454.90	3	454.9
FOODJAR	13S	027400368.00	13	368
1R03672	03S	027500487.60	3	487.6

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FOODJAR	13S	027600357.70	13	357.7
1R03673	03S	027700431.70	3	431.7
FOODJAR	13S	027800386.20	13	386.2
1R03674	03S	027900500.20	3	500.2
FOODJAR	13S	028000371.20	13	371.2
1R03675	03S	028100506.20	3	506.2
FOODJAR	13S	028200376.90	13	376.9
1 3676	03S	028300544.40	3	544.4
FOODJAR	13S	028400362.10	13	362.1
1R03677	03S	028500480.40	3	480.4
FOODJAR	13S	028600379.20	13	379.2
1R03678	03S	028700482.10	3	482.1
FOODJAR	13S	028800376.50	13	376.5
1R03679	03S	028900528.20	3	528.2
FOODJAR	13S	029000362.60	13	362.6
1R03680	03S	029100508.10	3	508.1
FOODJAR	13S	029200357.40	13	357.4
1R03681	03S	029300501.60	3	501.6
FOODJAR	13S	029400365.30	13	365.3
1R03682	03S	029500406.10	3	406.1
FOODJAR	13S	029600409.80	13	409.8
1R03683	03S	029700515.40	3	515.4
FOODJAR	13S	029800318.50	13	318.5
1R03684	03S	029900517.90	3	517.9
FOODJAR	13S	030000350.90	13	350.9
1R03685	03S	030100452.60	3	452.6
FOODJAR	13S	030200375.60	13	375.6
1R03686	03S	030300475.90	3	475.9
FOODJAR	13S	030400369.20	13	369.2
1R03687	03S	030500484.50	3	484.5
FOODJAR	13S	030600353.90	13	353.9
1R03688	03S	030700485.40	3	485.4
F DJAR	13S	030800343.70	13	343.7
1R03689	03S	030900382.50	3	382.5
FOODJAR	13S	031000400.60	13	400.6
1R03690	03S	031100486.90	3	486.9
FOODJAR	13S	031200364.50	13	364.5
1R03691	03S	031300423.40	3	423.4
FOODJAR	13S	031400388.80	13	388.8
1R03692	03S	031500371.70	3	371.7
FOODJAR	13S	031600401.30	13	401.3
1R03693	03S		3	543.0
FOODJAR	13S	031800312.20	13	312.2
1R03694	03S	031900513.50	3	513.5
FOODJAR	13S	032000352.10	13	352.1
1R03695	03S	032100524.80	3	524.8
FOODJAR	13S	032200355.50	13	355.5
9999999999		99	0	

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000891

1 YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS

EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 8/4/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340, D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 15

1R03516	01S 00?200551.80	1	551.8
FOODJAR	11S 00?300355.20	11	355.2
1R03517	01S 00?400491.00	1	491
FOODJAR	11S 00?500347.90	11	347.9
1R03518	01S 00?600483.00	1	483
FOODJAR	11S 00?700391.30	11	391.3
1R03519	01S 00?800531.70	1	531.7
FOODJAR	11S 00?900380.30	11	380.3
1R03520	01S 010000517.20	1	517.2
FOODJAR	11S 010100389.50	11	389.5
1R03521	01S 010200446.30	1	446.3
FOODJAR	11S 010300374.50	11	374.5
1R03522	01S 010400465.80	1	465.8
FOODJAR	11S 010500393.20	11	393.2
1R03523	01S 010600542.50	1	542.5
FOODJAR	11S 010700370.90	11	370.9
1R03524	01S 010800481.90	1	481.9
FOODJAR	11S 010900389.60	11	389.6
1R03525	01S 011000481.50	1	481.5
FOODJAR	11S 011100379.60	11	379.6
1R03526	01S 011200494.40	1	494.4
FOODJAR	11S 011300391.90	11	391.9

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1R03527	01S	011400468.50	1	468.5
FOODJAR	11S	011500179.50	11	379.5
1R03528	01S	011600531.40	1	531.4
FOODJAR	11S	011700320.30	11	320.3
1R03529	01S	011800493.00	1	493
FOODJAR	11S	011900349.20	11	349.2
1R03530	01S	012000511.10	1	511.1
F DJAR	11S	012100389.70	11	389.7
1R03531	01S	012200500.80	1	500.8
FOODJAR	11S	012300390.80	11	390.8
1R03532	01S	012400490.50	1	490.5
FOODJAR	11S	012500377.00	11	377
1R03533	01S	012600526.10	1	526.1
FOODJAR	11S	012700358.40	11	358.4
1R03534	01S	012800562.10	1	562.1
FOODJAR	11S	012900376.00	11	376
1R03535	01S	013000437.80	1	437.8
FOODJAR	11S	013100408.50	11	408.5
1R03536	01S	013200444.30	1	444.3
FOODJAR	11S	013300410.30	11	410.3
1R03537	01S	013400426.70	1	426.7
FOODJAR	11S	013500378.70	11	378.7
1R03538	01S	013600572.40	1	572.4
FOODJAR	11S	013700351.80	11	351.8
1R03539	01S	013800415.40	1	415.4
FOODJAR	11S	013900386.80	11	386.8
1R03540	01S	014000461.60	1	461.6
FOODJAR	11S	014100396.60	11	396.6
1R03541	01S	014200526.20	1	526.2
FOODJAR	11S	014300377.50	11	377.5
1R03542	01S	014400487.60	1	487.6
FOODJAR	11S	014500384.60	11	384.6
1R03543	01S	014600574.00	1	574
F DJAR	11S	014700345.80	11	345.8
1R03544	01S	014800513.60	1	513.6
FOODJAR	11S	014900320.00	11	320
1R03545	01S	015000537.40	1	537.4
FOODJAR	11S	015100371.00	11	371
1R03546	01S	015200536.80	1	536.8
FOODJAR	11S	015300384.90	11	384.9
1R03547	01S	015400551.90	1	551.9
FOODJAR	11S	015500379.30	11	379.3
1R03548	01S	015600552.80	1	552.8
FOODJAR	11S	015700380.90	11	380.9
1R03549	01S	015800459.10	1	459.1
FOODJAR	11S	015900394.20	11	394.2
1R03550	01S	016000482.40	1	482.4
FOODJAR	11S	016100384.80	11	384.8
1R03551	01S	016200359.80	1	359.8
FOODJAR	11S	016300421.30	11	421.3
1R03552	01S	016400536.70	1	536.7
FOODJAR	11S	016500334.70	11	334.7
1R03553	01S	016600562.00	1	562
FOODJAR	11S	016700315.50	11	315.5
1R03554	01S	016800399.50	1	399.5
FOODJAR	11S	016900407.30	11	407.3
1R03555	01S	017000480.30	1	480.3
FOODJAR	11S	017100385.00	11	385
1 03556	01S	017200548.90	1	548.9
FOODJAR	11S	017300380.70	11	380.7
1R03557	01S	017400475.20	1	475.2
FOODJAR	11S	017500389.70	11	389.7
1R03558	01S	017600411.40	1	411.4
FOODJAR	11S	017700396.30	11	396.3
1R03559	01S	017800509.00	1	509
FOODJAR	11S	017900382.20	11	382.2

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1R02560	01S	018000446.90	1	446.9
FOODJAR	11S	018100396.70	11	396.7
1R02561	01S	018200574.70	1	574.7
FOODJAR	11S	018300335.30	11	335.3
1R02562	01S	018400419.30	1	419.3
FOODJAR	11S	018500384.00	11	384
1R02563	01S	018600454.90	1	454.9
F OODJAR	11S	018700386.70	11	386.7
1 02564	01S	018800465.50	1	465.5
FOODJAR	11S	018900386.60	11	386.6
1R02565	01S	019000513.10	1	513.1
FOODJAR	11S	019100372.50	11	372.5
1R03566	01S	019200449.00	1	449
FOODJAR	11S	019300389.00	11	389
1R03567	01S	019400540.10	1	540.1
FOODJAR	11S	019500377.20	11	377.2
1R03568	01S	019600532.20	1	532.2
FOODJAR	11S	019700375.60	11	375.6
1R03569	01S	019800495.80	1	495.8
FOODJAR	11S	019900383.30	11	383.3
1R03570	01S	020000387.00	1	387
FOODJAR	11S	020100466.00	11	466
1R03571	01S	020200536.10	1	536.1
FOODJAR	11S	020300367.00	11	367
1R03572	01S	020400512.10	1	512.1
FOODJAR	11S	020500360.00	11	360
1R03573	01S	020600522.10	1	522.1
FOODJAR	11S	020700374.20	11	374.2
1R03574	01S	020800538.10	1	538.1
FOODJAR	11S	020900336.80	11	336.8
1R03575	01S	021000447.80	1	447.8
FOODJAR	11S	021100347.90	11	347.9
1R03576	01S	021200469.90	1	469.9
F OODJAR	11S	021300348.20	11	348.2
1R03577	01S	021400507.80	1	507.8
FOODJAR	11S	021500323.10	11	323.1
1R03578	01S	021600460.70	1	460.7
FOODJAR	11S	021700342.10	11	342.1
1R03579	01S	021800480.70	1	480.7
FOODJAR	11S	021900371.50	11	371.5
1R03580	01S	022000456.40	1	456.4
FOODJAR	11S	022100368.40	11	368.4
1R02581	02S	007100499.00	2	499
FOODJAR	12S	007200360.80	12	360.8
1R02582	02S	007300352.50	2	352.5
FOODJAR	12S	007400370.30	12	370.3
1R03583	02S	007500339.90	2	339.9
FOODJAR	12S	007600402.50	12	402.5
1R03584	02S	007700410.30	2	410.3
FOODJAR	12S	007800383.30	12	383.3
1R03585	02S	007900422.20	2	422.2
FOODJAR	12S	010000364.40	12	364.4
1R03586	02S	010100449.70	2	449.7
FOODJAR	12S	010200370.30	12	370.3
1R03587	02S	010300372.60	2	372.6
FOODJAR	12S	010400402.50	12	402.5
1R03588	02S	010500406.50	2	406.5
FOODJAR	12S	010600391.40	12	391.4
1R02589	02S	010700416.90	2	416.9
F OJAR	12S	010800358.40	12	358.4
1R02590	02S	010900489.90	2	489.9
FOODJAR	12S	011000424.00	12	424
1R03591	02S	011100330.80	2	330.8
FOODJAR	12S	011200416.30	12	416.3
1R03592	02S	011300471.80	2	471.8
FOODJAR	12S	011400376.40	12	376.4

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1R02593	02S	011500424.80	2		424.8
FOODJAR	12S	011600365.20	12		365.3
1R02594	02S	011700475.20	2		475.2
FOODJAR	12S	011800356.40	12		356.4
1R02595	02S	011900389.10	2		389.1
FOODJAR	12S	012000345.80	12		345.8
1R02596	02S	012100476.20	2		476.2
F OJAR	12S	012200365.80	12		365.8
1R02597	02S	012300399.60	2		399.6
FOODJAR	12S	012400396.10	12		396.1
1R02598	02S	012500455.10	2		455.1
FOODJAR	12S	012600382.80	12		382.8
1R02599	02S	012700425.80	2		425.8
FOODJAR	12S	012800381.40	12		381.4
1R02600	02S	012900413.60	2		413.6
FOODJAR	12S	013000380.30	12		380.3
1R02601	02S	013100452.90	2		452.9
FOODJAR	12S	013200362.30	12		362.3
1R03602	02S	013300418.90	2		418.9
FOODJAR	12S	013400379.10	12		379.1
1R03603	02S	013500444.00	2		444
FOODJAR	12S	013600383.50	12		383.5
1R02604	02S	013700376.70	2		376.7
FOODJAR	12S	013800395.10	12		395.1
1R03605	02S	013900411.50	2		411.5
FOODJAR	12S	014000376.60	12		376.6
lR03606			2		390.8
FOODJAR	12S	014200407.40	12		407.4
1R03607	02S	014400442.40	2		442.4
FOODJAR	12S	014500373.00	12		373
1R03608	02S	014600478.40	2		478.4
FOODJAR	12S	014700356.40	12		356.4
1 .3609	02S	014800406.00	2		406
FOODJAR	12S	014900373.60	12		373.6
1R02610	02S	015000498.20	2		498.2
FOODJAR	12S	015100363.10	12		363.1
1R02611	02S	015200400.00	2		400
FOODJAR	12S	015300376.70	12		376.7
1R03612	02S	015400432.80	2		432.8
FOODJAR	12S	015500385.70	12		385.7
1R03613	02S	015600509.00	2		509
FOODJAR	12S	015700368.60	12		368.6
1R03614	02S	015800404.70	2		404.7
FOODJAR	12S	015900361.20	12		361.2
1R03615	02S	016000374.90	2		374.9
FOODJAR	12S	016100384.10	12		384.1
1R03616	02S	016200426.50	2		426.5
FOODJAR	12S	016300383.20	12		383.2
1R03617	02S	016400419.20	2		419.2
FOODJAR	12S	016500374.40	12		374.4
1R03618	02S	016600473.00	2		473
FOODJAR	12S	016700362.00	12		362
1R03619	02S	016800354.40	2		354.4
FOODJAR	12S	016900375.90	12		375.9
1R03620	02S	017000419.60	2		419.6
FOODJAR	12S	017100368.30	12		368.3
1R03621	02S	017200355.60	2		355.6
F OJAR	12S	017300416.20	12		416.2
1..03622	02S	017400355.40	2		355.4
FOODJAR	12S	017500393.90	12		393.9
1R03623	02S	017600369.70	2		369.7
FOODJAR	12S	017700388.00	12		388
1R03624	02S	017800455.20	2		455.2
FOODJAR	12S	017900357.90	12		357.9
1R03625	02S	018000342.20	2		342.2

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[illegible]	12S	016100[illegible]	40	12	388.4
1R01[illegible]	02S	016200460	90	2	460.9
FOODJAR	12S	016300382	20	12	382.2
1R01[illegible]	02S	016400403	50	2	403.5
FOODJAR	12S	016500396	20	12	396.2
1R01[illegible]	02S	016600415	50	2	415.5
FOODJAR	12S	016700402	90	12	402.9
1R01[illegible]	02S	016800469	90	2	469.9
F[illegible]ODJAR	12S	016900373	10	12	373.1
1R01[illegible]	02S	017000360	90	2	360.9
FOODJAR	12S	017100406	40	12	406.4
1R01[illegible]	02S	017200483	90	2	483.9
FOODJAR	12S	017300381	00	12	381
1R01[illegible]	02S	017400415	40	2	415.4
FOODJAR	12S	017500369	60	12	369.6
1R01[illegible]	02S	017600487	70	2	487.7
FOODJAR	12S	017700368	90	12	368.9
[illegible]	02S	017800322	10	2	322.1
[illegible]	12S	[illegible]	90	12	389.9
[illegible]	02S	[illegible]	60	2	344.6
[illegible]	12S	[illegible]	00	12	404
1R01[illegible]	02S	018200457	90	2	457.9
[illegible]	12S	018300378	40	12	378.4
1R01[illegible]	02S	018400416	90	2	416.9
FOODJAR	12S	018500367	50	12	367.5
1R01[illegible]	02S	018600395	00	2	395
FOODJAR	12S	018700387	00	12	387
1R01[illegible]	02S	018800416	90	2	416.9
FOODJAR	12S	018900372	20	12	372.2
1R01640	02S	019000318	30	2	318.3
FOODJAR	12S	019100419	70	12	419.7
1R01641	02S	019200442	60	2	442.6
FOODJAR	12S	019300366	90	12	366.9
1R01642	02S	019400356	30	2	356.3
FOODJAR	12S	019500391	10	12	391.1
1R01643	02S	019600423	00	2	423
FOODJAR	12S	019700381	60	12	381.6
1R01644	02S	019800395	90	2	395.9
FOODJAR	12S	019900374	80	12	374.8
1R01645	02S	020000476	20	2	476.2
FOODJAR	12S	020100376	00	12	376
1R01646	02S	020200413	70	3	413.7
FOODJAR	12S	020300388	40	13	388.4
1R01647	03S	020400491	50	3	491.5
FOODJAR	12S	020500377	70	13	377.7
1R01648	03S	020600572	30	3	572.3
FOODJAR	12S	020700329	90	13	329.9
1R01649	03S	020800508	80	3	508.8
FOODJAR	12S	020900342	40	13	342.4
1R01650	03S	021000441	00	3	441
FOODJAR	12S	021100387	80	13	387.8
1R01651	03S	021200488	80	3	488.8
FOODJAR	12S	021300378	60	13	378.6
1R01652	03S	021400488	40	3	488.4
FOODJAR	12S	021500376	30	13	376.3
1R01653	03S	021600476	70	3	476.7
FOODJAR	12S	021700380	50	13	380.5
1R01654	03S	021800521	00	3	521
FOODJAR	12S	021900373	90	13	373.9
1R01655	03S	022000483	30	3	483.3
FOODJAR	12S	022100372	90	13	372.9
1R01656	03S	022200518	10	3	518.1
FOODJAR	12S	022300370	90	13	370.9
1R01657	03S	022400492	20	3	495.9
FOODJAR	12S	022500382	10	13	382.1
1R01658	03S	022600447	40	3	447.4

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FOODJAR	13S	0247000406.50	13	406.5	
1R03659	03S		3	484.4	
FOODJAR	13S		13	366.6	
1R03660	03S		3	508.0	
FOODJAR	13S		13	371.1	
1R03661	03S	0252000484.80	3	484.8	
FOODJAR	13S	0253000372.40	13	372.4	
1R03662	03S	0254000364.30	3	364.3	
FOODJAR	13S	0255000417.10	13	417.1	
1R03663	03S	0256000554.00	3	554	
FOODJAR	13S	0257000359.90	13	359.9	
1R03664	03S	0258000420.00	3	420	
FOODJAR	13S	0259000413.20	13	413.2	
1R03665	03S	0260000459.60	3	459.6	
FOODJAR	13S	0261000392.50	13	392.5	
1R03666	03S	0262000479.40	3	479.4	
FOODJAR	13S	0263000366.40	13	366.4	
1R03667	03S	0264000371.50	3	371.5	
FOODJAR	13S	0265000401.90	13	401.9	
1R03668	03S	0266000374.90	3	374.9	
FOODJAR	13S	0267000364.70	13	364.7	
1R03669	03S	0268000499.50	3	499.5	
FOODJAR	13S	0269000375.60	13	375.6	
1R03670	03S	0270000523.70	3	523.7	
FOODJAR	13S	0271000335.70	13	335.7	
1R03671	03S	0272000460.20	3	460.2	
FOODJAR	13S	0273000365.90	13	365.9	
1R03672	03S	0274000489.70	3	489.7	
FOODJAR	13S	0275000372.20	13	372.2	
1R03673	03S	0276000436.80	3	436.8	
FOODJAR	13S	0277000383.50	13	383.5	
1R03674	03S	0278000506.80	3	506.8	
FOODJAR	13S	0279000372.40	13	372.4	
1R03675	03S	0280000518.20	3	518.2	
FOODJAR	13S	0281000383.90	13	383.9	
1R03676	03S	0282000550.50	3	550.5	
FOODJAR	13S	0283000364.30	13	364.3	
1R03677	03S	0284000490.60	3	490.6	
FOODJAR	13S	0285000369.80	13	369.8	
1R03678	03S	0286000497.70	3	497.7	
FOODJAR	13S	0287000380.30	13	380.3	
1R03679	03S	0288000539.10	3	539.1	
FOODJAR	13S	0289000350.30	13	350.3	
1R03680	03S	0290000514.80	3	514.8	
FOODJAR	13S	0291000362.70	13	362.7	
1R03681	03S	0292000514.10	3	514.1	
FOODJAR	13S	0293000365.70	13	365.7	
1R03682	03S	0294000408.60	3	408.6	
FOODJAR	13S	0295000410.90	13	410.9	
1R03683	03S	0296000526.30	3	526.3	
FOODJAR	13S	0297000350.00	13	350	
1R03684	03S	0298000531.70	3	531.7	
FOODJAR	13S	0299000351.70	13	351.7	
1R03685	03S	0300000464.20	3	464.2	
FOODJAR	13S	0301000361.40	13	361.4	
1R03686	03S	0302000490.10	3	490.1	
FOODJAR	13S	0303000363.90	13	363.9	
1R03687	03S	0304000495.40	3	495.4	
FOODJAR	13S	0305000367.10	13	367.1	
1R03688	03S	0306000490.00	3	490	
FOODJAR	13S	0307000355.70	13	355.7	
1R03689	03S	0308000387.10	3	387.1	
FOODJAR	13S	0309000384.40	13	384.4	
1R03690	03S	0310000495.10	3	495.1	
FOODJAR	13S	0311000362.30	13	362.3	
1R03691	03S	0312000432.60	3	432.6	

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FOODJAR	13S	031300384.30	13	384.3
1R03692	03S	031400382.10	3	382.1
FOODJAR	13S	031500400.10	13	400.1
1R03693	03S	031600569.20	3	569.2
FOODJAR	13S	031700342.30	13	342.3
1R03694	03S	031800522.00	3	522
FOODJAR	13S	03190035e.20	13	356.2
1[illegible]3695	03S	032000532.70	3	532.7
[illegible]JDJAR	13S	032100354.70	13	354.7
9999999999		99	0	

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TWO YEAR ORAL(DIET) TOX-ONC STUDY OF FM-3924 & FC-143 IN RATS
EXP. # 0281CR0012

TECHNICIAN INITIALS:S MH
TODAY'S DATE:S 8/11/81
SEX OF RATS:S MALE
ROOM NUMBER:S D-340,D-338
WEIGHT OF FULL FOOD JAR:S 550GRAMS

WEEK 16

1R03516 01S 007000556.80	1	556.8
FOODJAR 11S 007100361.90	11	361.9
1R03517 01S 007200498.00	1	498
FOODJAR 11S 007300368.70	11	368.7
1R03518 01S 007400481.50	1	481.5
FOODJAR 11S 007500395.20	11	395.2
1R03519 01S 007600542.00	1	542
FOODJAR 11S 007700379.80	11	379.8
1R03520 01S 007800525.20	1	525.2
FOODJAR 11S 007900388.60	11	388.6
1R03521 01S 010000452.80	1	452.8
FOODJAR 11S 010100392.60	11	392.6
1R03522 01S 010200476.70	1	476.7
FOODJAR 11S 010300392.60	11	392.6
1R03523 01S 010400541.20	1	541.2
FOODJAR 11S 010500393.50	11	393.5
1R03524 01S 010600489.10	1	489.1
FOODJAR 11S 010700387.50	11	387.5
1R03525 01S	1	488.9

FOODJAR 11S 010900390.70	11	390.7
1R03527 01S 011000498.20	1	498.2
FOODJAR 11S 011100373.30	11	373.3
1R03528 01S 011200477.30	1	477.3
FOODJAR 11S 011300398.50	11	398.5
1R03529 01S 011400548.30	1	548.3
FOODJAR 11S 011500357.60	11	357.6
1R03530 01S 011600508.30	1	508.3
FOODJAR 11S 011700392.80	11	392.8
1R03531 01S 011800509.90	1	509.9
FOODJAR 11S 011900403.20	11	403.2
1R03532 01S 012000503.80	1	503.8
FOODJAR 11S 012100390.80	11	390.8
1R03533 01S 012200494.40	1	494.4
FOODJAR 11S 012300384.70	11	384.7
1R03534 01S 012400547.80	1	547.8
FOODJAR 11S 012500368.70	11	368.7
1R03535 01S 012600555.90	1	555.9
FOODJAR 11S 012700388.60	11	388.6
1R03536 01S 012800448.50	1	448.5
FOODJAR 11S 012900399.50	11	399.5
1R03537 01S 013000450.70	1	450.7
FOODJAR 11S 013100415.20	11	415.2
1R03538 01S 013200430.70	1	430.7
FOODJAR 11S 013300400.30	11	400.3
1R03539 01S 013400583.30	1	583.3
FOODJAR 11S 013500359.50	11	359.5
1R03539 01S 013600417.80	1	417.8
FOODJAR 11S 013700403.60	11	403.6
1R03540 01S 013800467.30	1	467.3
FOODJAR 11S 013900398.20	11	398.2
1R03541 01S 014000528.40	1	528.4
FOODJAR 11S 014100382.30	11	382.3

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1R0[illegible]	01S	014200492.40	1	492.4
F[illegible]JAR	11S	014300389.70	11	389.7
1R03543	01S	014400589.50	1	589.5
FOODJAR	11S	014500342.30	11	342.3
1R03544	01S	014600530.00	1	530
FOODJAR	11S	014700367.30	11	367.3
1R03545	01S	014800541.20	1	541.2
F[illegible]JAR	11S	014900372.80	11	372.8
1R03[illegible]	01S	015000544.10	1	544.1
FOODJAR	11S	015100400.90	11	400.9
1R03547	01S	015200564.20	1	564.2
FOODJAR	11S	015300373.80	11	373.8
1R03548	01S	015400566.60	1	566.6
FOODJAR	11S	015500376.20	11	376.2
1R03549	01S	015600461.30	1	461.3
FOODJAR	11S	015700408.80	11	408.8
1R03550	01S	015800501.10	1	501.1
FOODJAR	11S	015900381.40	11	381.4
1R03551	01S	016000366.60	1	366.6
FOODJAR	11S	016100423.80	11	423.8
1R03552	01S	016200542.00	1	542
FOODJAR	11S	016300352.40	11	352.4
1R03553	01S	016400576.50	1	576.5
FOODJAR	11S	016500364.70	11	364.7
1R03554	01S	016600404.10	1	404.1
FOODJAR	11S	016700414.00	11	414
1R03555	01S	016800487.90	1	487.9
FOODJAR	11S	016900394.80	11	394.8
1R03556	01S	017000557.30	1	557.3
FOODJAR	11S	017100391.00	11	391
1R03557	01S	017200481.80	1	481.8
FOODJAR	11S	017300399.90	11	399.9
1R03558	01S	017400420.30	1	420.3
FOODJAR	11S	017500400.10	11	400.1
1R03559	01S	017600522.60	1	522.6
FOODJAR	11S	017700376.10	11	376.1
1R03560	01S	017800455.40	1	455.4
FOODJAR	11S	017900397.90	11	397.9
1R03561	01S	018000586.70	1	586.7
FOODJAR	11S	018100347.80	11	347.8
1R03562	01S	018200431.60	1	431.6
FOODJAR	11S	018300388.90	11	388.9
1R03563	01S	018400460.40	1	460.4
FOODJAR	11S	018500400.60	11	400.6
1R03564	01S	018600476.60	1	476.6
FOODJAR	11S	018700356.70	11	356.7
1R03565	01S	018800519.00	1	519
FOODJAR	11S	018900373.00	11	373
1R03566	01S	019000449.80	1	449.8
FOODJAR	11S	019100366.40	11	366.4
1R03567	01S	019200554.60	1	554.6
FOODJAR	11S	019300384.60	11	384.6
1R03568	01S	019400548.60	1	548.6
FOODJAR	11S	019500373.10	11	373.1
1R03569	01S	019600552.60	1	552.6
FOODJAR	11S	019700350.00	11	350
1R03570	01S	019800434.70	1	434.7
FOODJAR	11S	019900414.30	11	414.3
1R03571	01S	020000550.40	1	550.4
FOODJAR	11S	020100370.30	11	370.3
1R03572	01S	020200514.50	1	514.5
FOODJAR	11S	020300383.20	11	383.2
1R03573	01S	020400536.40	1	536.4
FOODJAR	11S	020500337.20	11	337.2
1R03574	01S	020600538.70	1	538.7
FOODJAR	11S	020700333.40	11	333.4

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