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MUTAGENICITY TEST ON

T-5710

IN AN *IN VIVO* RAT MICRONUCLEUS ASSAY

DATA REQUIREMENT

U.S. EPA FIFRA Guideline 84-2

FINAL REPORT

AUTHOR

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PERFORMING LABORATORY

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LABORATORY PROJECT ID

HWA Study No.: 15516-0-454

SUBMITTED TO

3M Corporation
3M Center
St. Paul, Minnesota 55144

STUDY COMPLETION DATE

April 23, 1993

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA § 10(d)(1)(A), (B), or (C).

Company: _____

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(Typed Name)

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(Title)

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STATEMENT OF DATA CONFIDENTIALITY CLAIMS

Information claimed confidential on the basis of its falling within the scope of FIFRA § 10(d)(1)(A),(B), or (C) has been removed to a confidential appendix, and is cited by cross-reference number in the body of the study.

Company: _____

Company Agent: _____
(Typed Name)

_____
(Title)

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Signature Date

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with the EPA FIFRA Good Laboratory Practice Standards as set forth in Title 40 of the U.S. Code of Federal Regulations Part 160. Any significant deviations from the protocol and/or GLP are attached as an appendix to this report. There were no deviations from the aforementioned regulation which affected the quality or integrity of the study or the interpretation of the results in this report.

Study Director:

Hemalatha Murli — 4/23/93
Hemalatha Murli, Ph.D. — Date
Mammalian Cytogenetics
Department of Molecular and Cellular Toxicology

Study Monitor:

_____ — _____
Date

Applicant/Submitter:

_____ — _____
Date

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QUALITY ASSURANCE STATEMENT

PROJECT TITLE: *IN VIVO* RAT MICRONUCLEUS ASSAY

PROJECT NO.: 20996 ASSAY NO.: 15516

PROTOCOL NO.: 454 EDITION NO.: 5

Quality Assurance inspections of the study and/or 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
Harvest-3/4/1993	3/04/1993	B. Mullett
Draft Report review/4/14/1993	4/14/1993	B. Mullett
Final Report review/4/23/1993	4/23/1993	M. Murphy

Mary S. Murphy 4-23-93
Quality Assurance Unit Date Released

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STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Good Laboratory Practice regulations as set forth in the Code of Federal Regulations (21 CFR 58, 40 CFR 792, and 40 CFR 160); the Organization for Economic Cooperation and Development Principles of Good Laboratory Practice C(81)30 (Final) Annex 2, issued 1979-1980 (effective 1981). To the best of the signers' knowledge, 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, protocols, and a copy of the final report generated as a result of this study will be archived in the storage facilities of Hazleton Washington, 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 Hazleton Washington, Inc., for an additional period of time, or sent to a storage facility designated by the Sponsor.

SUBMITTED BY:

José Arriaga

José Arriaga, B.S.
Research Associate

4/23/93
Date

Study Director:

Hemalatha Murli

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

4/23/93
Study Completion Date

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SUMMARY

Mutagenicity Test on T-5710 in an in vivo Rat Micronucleus Assay

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-5710, to induce micronuclei in bone marrow polychromatic erythrocytes of Sprague-Dawley rats. The test article was suspended in corn oil.

At the request of the Sponsor, Trial I of the micronucleus study was conducted dosing T-5710 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 were dosed with the test article and were euthanatized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow. Due to the excessive toxicity/mortality in the animals at all dose levels, especially at the 72 hour harvest, this assay was repeated.

After consultation with the Sponsor, Trial II of the micronucleus study was conducted dosing T-5710 by oral gavage at 312.5, 625, and 1250 mg/kg. Again, 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 were dosed with the test article and were euthanatized approximately 24, 48 and 72 hours after dosing for extraction of the bone marrow.

The test material, T-5710, 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 rat bone marrow micronucleus test.

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Mutagenicity Test on T-5710 in an in vivo Micronucleus Assay

I. SPONSOR: 3M Corporation

II. MATERIAL (TEST ARTICLE):

A. Client's Identification: L-10059 (T-5710)

B. Dates Received: February 24, 1993; March 11, 1993

C. Physical Description: Cream-colored granular material

D. Genetics Assay No.: 15516

III. TYPE OF ASSAY: *In Vivo* Rat Micronucleus Assay

IV. PROTOCOL NO.: 454, Edition 5

V. STUDY DATES:

A. Initiation Date: February 24, 1993

B. Experimental Start Date: March 2, 1993

C. Experimental Termination Date: March 30, 1993

VI. SUPERVISORY PERSONNEL:

A. Study Director: Hemalatha Murli, Ph.D.

B. Laboratory Supervisor: José Arriaga, B.S.

VII. OBJECTIVE:

The objective of this *in vivo* assay was to evaluate the ability of the test article, T-5710, to induce micronuclei in bone marrow polychromatic erythrocytes of Sprague-Dawley rats. This study was conducted using modifications of the procedures suggested by Heddle et al. (1983).

VIII. MATERIALS:

Adult male and female rats, strain Sprague-Dawley, were purchased from Charles River Laboratories, Raleigh, NC. This healthy, random bred strain was selected to maximize genetic heterogeneity and at the same time assure access to a common source.

Animals were isolated by sex. Animals were housed two per cage during quarantine, and housed individually at randomization. The temperature was maintained at 71.8 to 80.2°F for Trial I and at 72±6°F for Trial II and humidity was maintained at 50±20%. A 12-hour light/12-hour dark cycle was maintained. A commercial diet (Purina® Certified Laboratory Chow® #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. Sanitary, stainless steel, hanging wire cages were used. 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.

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.

IX. SOLUBILITY AND STABILITY:

A. Solubility and Stability

The test article, T-5710, was supplied as a cream-colored granular material. The solubility of the test article was evaluated in corn oil and 0.5% high viscosity carboxymethylcellulose (CMC). Unsuitable suspensions were obtained in CMC. An opaque, viscous suspension was obtained when 0.66 ml of corn oil was added to 589.2 mg of T-5710, resulting in a final volume of about 2.3 ml, and a final concentration of about 256.2 mg/ml that passed easily through an 18G gavage needle. The vehicle used to suspend the test article for the bone marrow micronucleus assay was corn oil. The stability of the test article under the preparation and dosing conditions of the assay is the responsibility of the sponsor.

B. Dose Selection

The dose levels used in Trial I of this assay were selected by the Sponsor. The doses selected for this assay were 1250, 2500, and 5000 mg/kg body weight, and were administered by oral gavage.

C. Micronucleus Assay Dosing Information

TRIAL I

The animals used in Trial I of the micronucleus assay were dosed on Tuesday, March 2, 1993. Cyclophosphamide (CP, Sigma, Lot #70H0948), the positive control, was solubilized in sterile deionized water (Lot#13, prepared at HWA) and was administered by oral gavage at 60 mg/kg. The vehicle control consisted of corn oil (Duke's corn oil, Lot 2B 25 17:59) and was administered concurrently with the test article at a volume of 20 ml/kg. The weight range of the animals used in the micronucleus assay was 251.1 - 302.7 grams and 169.7 - 210.4 grams for the males and females, respectively. The dosing solutions for the assay were prepared by making a 250 mg/ml stock for the high dose (5000 mg/kg). An opaque, cream-colored, slightly viscous suspension was obtained when 112.5 ml of corn oil was added 87.5001 grams of T-5710, resulting in a final volume of 350.0 ml and a final concentration of 250 mg/ml. This suspension was homogenized in a Tissuemizer® for about 5 minutes to ensure an uniform suspension. Dilutions of this stock were prepared for the 2500 and 1250 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.

The test article dosed animals were euthanatized approximately 24, 48 and 72 hours after administration of the test article. The positive and vehicle control animals were euthanatized approximately 24 hours after the administration of the control articles. An outline of the dosing scheme is found in the following table:

Dosing Scheme for Trial I of the Micronucleus Assay

A total of 126 animals was used in this assay.

Number of Animals Assigned

Treatment	Primary Dose Groups						Secondary Dose Groups[a]	
	24 Hr		48 Hr		72 Hr			
	M	F	M	F	M	F	Male	Female
T-5710								
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	8	8
Vehicle Control, Corn oil								
20 ml/kg	5	5	-	-	-	-	-	-
Positive Control, Cyclophosphamide								
60 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 euthanatized at the completion of the trial.

The age of the animals at the time of dosing was ≈8 weeks.

Volumes dosed were 20 ml/kg (except for the positive controls) and were based upon individual animal weights. The positive control animals were dosed at 10 ml/kg.

Animal Observations

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 and approximately 4 hours after dosing.

Approximately 23 hours after dosing, all animals from the 1250, 2500, and 5000 mg/kg dose groups appeared ataxic with diarrhea. One male (#6216, 2500 mg/kg dose and 72 hour harvest group) and 1 female (#6273, 5000 mg/kg and 48 hour harvest group) were also experiencing lacrimination of the eyes.

Approximately 47 hours after dosing, 2 males (#'s 6250, 6238,, 72 hour harvest group) and 2 females (#6273, 48 hour harvest group; #6241, secondary dose group) from the 5000 mg/kg dose group, and 2 males (#6234, 48 hour harvest group; #6216, 72 hour harvest group) from the 2500 mg/kg dose group, and 1 female (#6198) from the 1250 mg/kg dose and 48 hour harvest group were found dead. All remaining animals from the 5000, 2500, and 1250 mg/kg dose groups appeared ataxic with diarrhea.

Approximately 49 hours after dosing, 2 males (#'s 6235, 6287, secondary dose group) and 1 female (#6246, secondary dose group) were found dead. All remaining animals from the 5000, 2500, and 1250 mg/kg dose groups appeared ataxic with diarrhea.

Approximately 70 hours after dosing, 3 males (# 6217, 72 hour harvest group; #'s 6205,6240, secondary dose group) and 3 females (#'s6191, 6259, 72 hour harvest group; #6299, secondary dose group) from the 5000 mg/kg dose group, 3 males (#'s6210, 6310, 6281, 72 hour harvest group) and 2 females (#'s6309, 6204, 72 hour harvest group) from the 2500 mg/kg dose group, and 1 male (#6303, 72 hour harvest group) and 1 female (#6242, 72 hour harvest group) from the 1250 mg/kg dose group were found dead. All remaining animals from the 5000, 2500, and 1250 mg/kg dose groups appeared ataxic with diarrhea, and red crusts around the nose.

Approximately 71 hours after dosing, 1 female (# 6290, 72 hour harvest group) from the 5000 mg/kg dose group and 1 female (#6257, 72 hour harvest group) from the 2500 mg/kg dose group were found dead. All remaining animals from the 5000, 2500, and 1250 mg/kg dose groups remained unchanged from the earlier set of observations.

There were too few animals surviving in this Trial for a valid analysis. Thus, after consultation with the Sponsor, a Trial II was conducted testing dose levels of 312.5, 625, and 1250 mg/kg body weight.

TRIAL II

The animals used in the micronucleus assay were dosed on Tuesday, March 23, 1993. Cyclophosphamide (CP, Sigma, Lot #70H0948), the positive control, was solubilized in sterile deionized water (Lot#13, prepared at HWA) and was administered by oral gavage at 60 mg/kg. The vehicle control consisted of corn oil (Duke's corn oil, Lot 2B 25 17:59) and 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 224.4 - 275.0 grams and 165.0 - 213.0 grams for the males and females, respectively. The dosing solutions for the assay were prepared by making a 125 mg/ml stock for the high dose (1250 mg/kg). An opaque, pale yellow suspension was obtained when 179.2 ml of corn oil was added 23.7500 grams of T-5710, resulting in a final volume of 190.0 ml and a final concentration of 125 mg/ml. This suspension was homogenized in a Tissuemizer® for about 5 minutes to ensure an uniform suspension. Dilutions of this stock were prepared for the 625.0 and 312.5 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.

The test article dosed animals were euthanatized approximately 24, 48 and 72 hours after administration of the test article. The positive and vehicle control animals were euthanatized approximately 24 hours after the administration of the control articles. An outline of the dosing scheme is found in the following table:

Dosing Scheme for Trial II of the Micronucleus Assay

A total of 130 animals was used in this assay.

Number of Animals Assigned

Treatment	Primary Dose Groups						Secondary Dose Groups[a]	
	24 Hr		48 Hr		72 Hr			
	M	F	M	F	M	F	Male	Female
T-5710								
312.5 mg/kg	5	5	5	5	5	5	-	-
625.0 mg/kg	5	5	5	5	5	5	-	-
1250 mg/kg	5	5	5	5	5	5	10	10
Vehicle Control, Corn oil 10 ml/kg	5	5	-	-	-	-	-	-
Positive Control, Cyclophosphamide 60 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 euthanatized at the completion of the trial.

The age of the animals at the time of dosing was ≈8 weeks.

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

Animal Observations

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 5 hours after dosing, all animals from the 312.5, 625.0, and 1250 mg/kg dose groups including the secondary dose group were ataxic.

Approximately 23 hours after dosing, 1 male (#6557) from the 1250 mg/kg dose and 24 hour harvest group appeared languid. All remaining animals from the 1250 mg/kg dose group including the secondary dose group appeared ataxic. All animals from the 312.5 and 625.0 mg/kg dose groups appeared normal at this time.

Approximately 47 hours after dosing, all animals from the 1250 mg/kg dose group including the secondary dose group appeared ataxic. All animals from the 312.5 and 625.0 mg/kg dose groups appeared normal at this time.

Approximately 71 hours after dosing, 2 males (#6481, 1250 mg/kg dose and 72 hour harvest group; #6454 from the secondary dose group) were found dead. All remaining animals from the 1250 mg/kg dose group including the secondary dose group appeared ataxic. All animals from the 312.5 and 625.0 mg/kg dose groups appeared normal at this time.

X. BONE MARROW HARVEST, SLIDE PREPARATION AND ANALYSIS:

At the appropriate harvest time, the animals were euthanatized with CO_2 and the adhering soft tissue and epiphyses of both tibiae were removed. The marrow was aspirated from the bone and mixed in a syringe with ~0.1 ml fetal calf serum to form a suspension. The cells were then placed on slides and air-dried, 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 coded slides were then scored for micronuclei and the polychromatic (PCE) to normochromatic (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 rat 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.

XI. EVALUATION CRITERIA:

A. General:

The criteria for the identification of micronuclei were those of Schmid (1976). Micronuclei were darkly stained and generally round, although almond and ring-shaped micronuclei occasionally occur. 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).

B. 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 the data was performed using an Analysis of Variance on the square root arcsine transformation which was performed on the proportion of cells with micronuclei per animal (square root arcsine proportion). Once the Analysis of Variance had been performed, Tukey's Studentized range test (HSD) with adjustment for multiple comparisons (Sokal and Rohlf, 1981) was used at each harvest time to determine which dose groups, if any, were significantly different ($p<0.05$) from the vehicle control. Analyses were performed separately for each harvest time and sex combination, and also at each harvest time for the sexes combined.

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.

XII. RESULTS AND INTERPRETATION:

The test article, T-5710, 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, CP, induced significant increases in micronucleated PCEs in both sexes, with means and standard errors of 4.64% ± 0.64% and 3.12% ± 0.70% 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 4.

XIII. CONCLUSION:

The test material, T-5710, 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 rat bone marrow micronucleus test.

XIV. REFERENCES:

Heddle, J.A., Hite, M., Kirkhart, B., Larsen, K., MacGregor, J.T., Newell, G.W., and Salamone, M.F.: The induction of micronuclei as a measure of genotoxicity. Mutation Res., 123:61-118, 1983.

Schmid, W.: The micronucleus test. Mutation Res., 31:9-15, 1975.

Schmid, W.: The micronucleus test for cytogenetic analysis. In, Chemical Mutagens: Principles and Methods for Their Detection, Vol. 4 (A. Hollaender, ed.). Plenum, pp. 31-53, 1976.

Sokal, R.R. and Rohlf, J.J.: Biometry, Freeman, 1981.

XV. DEVIATION FROM THE SIGNED PROTOCOL:

The following deviation was made from the protocol.

The temperature was maintained at 71.8 to 80.2°F for Trial I of the micronucleus assay and not maintained at 72±6°F. This was due to technical difficulties at the animal facility. This slight deviation did not affect the animals in any way.

XVI. EXPERIMENT DATA TABLES

TABLE 1

MICRONUCLEUS DATA SUMMARY TABLE

SPONSOR: 3M Corporation

TEST ARTICLE: T-5710

ASSAY: 15516

TREATMENT	DOSE	HARVEST TIME (HR)	% MICRONUCLEATED PCEs MEAN OF 1000 PER ANIMAL ± S.E.			RATIO PCE:NCE MEAN ± S.E.	
			MALES	FEMALES	TOTAL	MALES	FEMALES
VEHICLE CONTROL CORN OIL	10 ml/kg	24	0.12 ± 0.05	0.12 ± 0.04	0.12 ± 0.03	0.82 ± 0.09	0.39 ± 0.05
POSITIVE CONTROL CYCLOPHOSPHAMIDE	60 mg/kg	24	4.64 ± 0.64*	3.12 ± 0.70*	3.88 ± 0.51*	0.70 ± 0.08	0.42 ± 0.08
TEST ARTICLE T-5710	312.5 mg/kg	24	0.12 ± 0.04	0.12 ± 0.04	0.12 ± 0.02	0.71 ± 0.07	0.53 ± 0.06
		48	0.06 ± 0.02	0.10 ± 0.04	0.08 ± 0.02	0.63 ± 0.11	0.60 ± 0.07
		72	0.14 ± 0.04	0.12 ± 0.04	0.13 ± 0.03	0.74 ± 0.08	0.49 ± 0.09
	625.0 mg/kg	24	0.08 ± 0.05	0.14 ± 0.07	0.11 ± 0.04	0.66 ± 0.06	0.50 ± 0.14
		48	0.16 ± 0.09	0.08 ± 0.06	0.12 ± 0.05	0.54 ± 0.10	0.51 ± 0.09
		72	0.16 ± 0.07	0.12 ± 0.05	0.14 ± 0.04	0.74 ± 0.09	0.41 ± 0.11
	1250 mg/kg	24	0.14 ± 0.05	0.12 ± 0.04	0.13 ± 0.03	0.58 ± 0.05	0.54 ± 0.14
		48	0.04 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	0.56 ± 0.18	0.47 ± 0.16
		72	0.22 ± 0.02	0.04 ± 0.02	0.13 ± 0.03	0.53 ± 0.04	0.52 ± 0.13

* Significantly different from the corresponding vehicle control, $p<0.05$.

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TABLE 2

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation TEST ARTICLE: T-5710

ASSAY NO.: 15516

	MALES			FEMALES		
TREATMENT	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE
Vehicle Control	6477	1	0.78	6476	1	0.58
(24 hour harvest)	6482	1	0.66	6487	2	0.32
	6508	3	0.99	6497	0	0.42
	6509	0	1.04	6522	1	0.31
	6523	1	0.62	6539	2	0.31
Positive Control	6502	36	0.69	6467	20	0.38
(24 hour harvest)	6517	47	0.72	6472	15	0.49
	6524	29	0.48	6479	51	0.24
	6554	65	0.68	6527	26	0.33
	6582	55	0.95	6578	44	0.68
Test Article	6526	0	0.94	6488	2	0.42
(24 hour harvest)	6528	2	0.69	6512	2	0.65
312.5 mg/kg	6541	1	0.48	6536	1	0.40
	6561	2	0.71	6572	1	0.51
	6569	1	0.73	6584	0	0.67
625.0 mg/kg	6462	0	0.78	6500	3	0.12
	6464	0	0.64	6531	0	0.41
	6473	2	0.79	6567	0	0.62
	6491	0	0.45	6568	3	0.39
	6571	2	0.64	6583	1	0.94
1250 mg/kg	6460	1	0.69	6458	1	0.98
	6556	3	0.58	6558	2	0.25
	6557	1	0.39	6575	0	0.69
	6570	0	0.62	6577	2	0.57
	6579	2	0.62	6580	1	0.21

MN = Micronucleus
PCE = Polychromatic erythrocyte
No. MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

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TABLE 3

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation TEST ARTICLE: T-5710

ASSAY NO.: 15516

TREATMENT	MALES			FEMALES		
	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE
Test Article	6461	1	0.60	6493	0	0.47
(48 hour harvest)	6484	0	0.23	6511	2	0.40
312.5 mg/kg	6486	0	0.70	6546	0	0.67
	6559	1	0.92	6550	2	0.66
	6573	1	0.69	6551	1	0.80
625.0 mg/kg	6457	1	0.40	6449	0	0.36
	6470	0	0.33	6483	0	0.24
	6480	5	0.80	6532	3	0.67
	6499	0	0.76	6544	1	0.68
	6566	2	0.39	6552	0	0.58
1250 mg/kg	6451	1	0.68	6459	0	0.22
	6469	0	0.10	6505	1	0.18
	6496	0	0.20	6540	0	0.31
	6518	0	1.02	6542	0	0.99
	6543	1	0.81	6562	1	0.68

MN = Micronucleus
PCE = Polychromatic erythrocyte
No. MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte

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TABLE 4

MICRONUCLEUS TEST - INDIVIDUAL ANIMAL DATA

SPONSOR: 3M Corporation TEST ARTICLE: T-5710

ASSAY NO.: 15516

	MALES			FEMALES		
TREATMENT	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE	ANIMAL NUMBER	NO. MN PCEs (1000)	RATIO PCE:NCE
Test Article	6456	2	0.71	6463	1	0.67
(72 hour harvest)	6503	1	0.66	6489	2	0.31
312.5 mg/kg	6534	2	0.50	6490	2	0.35
	6563	2	0.88	6507	1	0.37
	6581	0	0.94	6565	0	0.73
625.0 mg/kg	6465	2	0.58	6455	1	0.83
	6468	4	1.00	6485	3	0.29
	6513	1	0.58	6498	1	0.43
	6545	1	0.65	6514	0	0.22
	6574	0	0.89	6533	1	0.27
1250 mg/kg	6448	2	0.46	6495	0	1.00
	6452	2	0.44	6519	0	0.40
	6492	2	0.54	6548	0	0.20
	6529	3	0.53	6555	1	0.55
	6564	2	0.68	6585	1	0.43

MN = Micronucleus
PCE = Polychromatic erythrocyte
No. MN PCEs = Micronucleated PCEs
NCE = Normochromatic erythrocyte