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REPORT NO.: MSL-11771

JOB/PROJECT NO.: EHL 91200/91204, ML-91-434/ML-91-437

DATE: February 25, 1992

TITLE: Mouse Micronucleus Study of ROUNDUP® Herbicide Formulation

AUTHORS: [redacted]

ABSTRACT:
The potential for ROUNDUP herbicide formulation to induce chromosomal effects was tested in a mouse bone marrow micronucleus assay. ROUNDUP herbicide formulation was administered by intraperitoneal injection to groups of male and female CD-1 mice at target doses of 140, 280 or 555 mg/kg body weight for the low, mid and high dose groups, respectively. Negative control groups were treated with vehicle only (0.9% saline; 10 ml/kg body weight) and positive control groups were treated with cyclophosphamide (40 mg/kg body weight). Mouse bone marrow from ROUNDUP herbicide formulation and vehicle control groups was sampled at 24, 48 and 72 hours after dosing. A single sampling time of 24 hours after dosing was used for the cyclophosphamide positive control group. Slides of bone marrow cells were made from five animals/sex/time point for each group and scored for the occurrence of micronucleated polychromatic erythrocytes (micronucleated PCE) and PCE/erythrocyte ratios.

The highest ROUNDUP herbicide formulation dose level, 555 mg/kg, was observed to be toxic to treated male and female mice and was clearly an appropriate maximum dose level for the micronucleus assay. This dose level was more than 80% of the combined LD50 estimated from toxicity rangefinder experiments (643 mg/kg) and induced a low incidence of deaths in high dose level male (2/18) and female (1/22) mice in the micronucleus assay.

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NO.: MSL-11771 AUTHORS: [redacted] TITLE: Mouse Micronucleus Study of ROUNDUP® Herbicide Formulation

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Clinical signs of listlessness or unresponsiveness were observed in high dose level males and females up to 48 hours after treatment. Larger mean body weight decreases compared to control values were observed for high dose level males at 48 hours and 72 hours after dosing. In addition, a reduction in the mean PCE/erythrocyte ratio compared to control values was observed for the high dose level male group sacrificed at 48 hours after dosing. No clinical signs of toxicity were observed in the mid or low dose level groups, but a larger mean body weight decrease than control values was observed for the mid dose level male group sacrificed 72 hours after dosing.

ROUNDUP herbicide formulation did not induce increases in the frequency of micronucleated PCEs. No statistically significant increases in micronucleated PCE frequencies compared to control values were observed in any of the dose level groups at any of the time points. Significant increases in mean micronucleated PCE frequencies were observed for the cyclophosphamide treated animals demonstrating the ability of the study conditions to detect micronucleus induction.

The observations and findings of this study indicate that ROUNDUP herbicide formulation does not exhibit in vivo mammalian genotoxicity in mouse bone marrow cells under the experimental conditions of this study.

The test material, MON 12336, was tested in Ames/Salmonella plate incorporation assays using test strains TA98, TA100, TA1535 and TA1537 in the presence and absence of an Aroclor 1254-induced rat liver homogenate (S-9) activation system. The test chemical was observed to be insoluble at the maximum dose level for mutagenicity testing, 5 mg/plate. The test chemical was observed to be toxic in the absence of S9 activation for all bacterial strains and for TA100 in the presence of activation at the maximum treatment level. No significant mutagenicity was observed in either the initial assays or the subsequent confirmation assays. These results indicate that MON 12336 is not a mutagen in the Ames/Salmonella plate incorporation assay under the experimental conditions.

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FINAL REPORT

Mouse Micronucleus Study of ROUNDUP® Herbicide Formulation

Study Numbers: ML-91-434/ML-91-437
EHL Study Numbers: 91200/91204

Authors: [redacted]

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SUMMARY

The potential for ROUNDUP herbicide formulation to induce chromosomal effects was tested in a mouse bone marrow micronucleus assay. ROUNDUP herbicide formulation was administered by intraperitoneal injection to groups of male and female CD-1 mice at target doses of 140, 280 or 555 mg/kg body weight for the low, mid and high dose groups, respectively. Negative control groups were treated with vehicle only (0.9% saline; 10 ml/kg body weight) and positive control groups were treated with cyclophosphamide (40 mg/kg body weight). Mouse bone marrow from ROUNDUP herbicide formulation and vehicle control groups was sampled at 24, 48 and 72 hours after dosing. A single sampling time of 24 hours after dosing was used for the cyclophosphamide positive control group. Slides of bone marrow cells were made from five animals/sex/time point for each group and scored for the occurrence of micronucleated polychromatic erythrocytes (micronucleated PCE) and PCE/erythrocyte ratios.

The highest ROUNDUP herbicide formulation dose level, 555 mg/kg, was observed to be toxic to treated male and female mice and was clearly an appropriate maximum dose level for the micronucleus assay. This dose level was more than 80% of the combined LD50 estimated from toxicity rangefinder experiments (643 mg/kg) and induced a low incidence of deaths in high dose level male (2/18) and female (1/22) mice in the micronucleus assay. Clinical signs of listlessness or unresponsiveness were observed in high dose level males and females up to 48 hours after treatment. Larger mean body weight decreases compared to control values were observed for high dose level males at 48 hours and 72 hours after dosing. In addition, a reduction in the mean PCE/erythrocyte ratio compared to control values was observed for the high dose level male group sacrificed at 48 hours after dosing. No clinical signs of toxicity were observed in the mid or low dose level groups, but a larger mean body weight decrease than control values was observed for the mid dose level male group sacrificed 72 hours after dosing.

ROUNDUP herbicide formulation did not induce increases in the frequency of micronucleated PCEs. No statistically significant increases in

micronucleated PCE frequencies compared to control values were observed in any of the dose level groups at any of the time points. Significant increases in mean micronucleated PCE frequencies were observed for the cyclophosphamide treated animals demonstrating the ability of the study conditions to detect micronucleus induction.

The observations and findings of this study indicate that ROUNDUP herbicide formulation does not exhibit *in vivo* mammalian genotoxicity in mouse bone marrow cells under the experimental conditions of this study.

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INTRODUCTION

The study was designed to evaluate the potential of the test material, ROUNDUP herbicide formulation, to induce chromosome effects in an *in vivo* mammalian assay, the mouse bone marrow micronucleus assay.

The *in vivo* micronucleus assay has been found to be sensitive to a variety of chemical agents. The assay has been reviewed by the EPA Gene-Tox program (Heddle et al., 1983 and Mavournin et al., 1990). It is generally accepted that induction of micronucleus formation in the assay is indicative of either clastogenic effects or malsegregation of chromosomes. An advantage of this assay is that it evaluates effects on somatic cells of mice that are treated *in vivo* and thus is relevant to prediction of potential *in vivo* mammalian effects (MacGregor et al., 1987).

This study was conducted at the Monsanto Company Environmental Health Laboratory (645 S. Newstead, St. Louis, MO 63110). This study was sponsored by the Monsanto Agricultural Company. The protocols for studies 91200 (toxicity rangefinding study) and 91204 (micronucleus study) were signed by the study director on November 12, 1991 and November 19, 1991, respectively. Experimental work for study 91200 was initiated on November 13, 1991 and completed on November 20, 1991. Experimental work for study 91204 was initiated on November 19, 1991 and completed on December 26, 1991.

MATERIALS

Test Materials

Identification and composition of the test material samples are given below:

Name:	ROUNDUP® Herbicide Formulation
Identification:	Lot LUL-9101-2706F (initial toxicity rangefinder experiment; study 91200) Lot BS-110-388 (subsequent toxicity rangefinder experiments for study 91200 and main micronucleus experiment, study 91204)
EHL Code:	T910114 for LUL-9101-2706F T910117 for BS-110-388
Percent Active Ingredient:	31% glyphosate, acid equivalent (both lots)
Sample storage:	Samples were stored at room temperature as advised by the sponsor.
Appearance:	Samples were an amber liquid

Because of time constraints and problems with sample availability a separate lot of the test material formulated in the United States was used for the initial toxicity rangefinding experiment. Subsequent experiments were conducted using a sample formulated in Brazil. Solutions or suspensions of the test material were made using 0.9% saline as the solvent on the day of treatment. The positive control used was commercial grade cyclophosphamide (Sigma Chemical Company, lot 19F-0254).

Animals

The animals used were eight to twelve week old male and female CD-1 mice (Source: Charles River Laboratories Inc., Portage, MI.). Upon receipt, the animals were quarantined for a minimum of seven days. Only animals considered to be normal were released from quarantine and used for testing. Prior to testing, the mice were

uniquely identified using ear tags and corresponding cage cards. The animals were housed two per cage prior to dosing and subsequently one per cage after dosing. The animals were housed in stainless steel cages with stainless steel mesh bottoms.

Animals were selected for the different test (or control) groups by a computer-generated randomization scheme. Water (supplied by the public water system of St.Louis, MO) was provided *ad libitum* via an automatic watering system. Purina Certified Laboratory Rodent Chow No. 5002 (Trademark of Purina Mills Inc., St. Louis, Mo.) was used as the diet and was provided ad libitum. This diet has been determined to be nutritionally acceptable for the maintenance of laboratory rodents and has been certified by the manufacturer not to contain contaminants likely to interfere with the study. The animals were housed in rooms designed to routinely maintain a 12-hour light cycle, a temperature between 64 and 79 °F, and relative humidity between 40 and 70%. There were no excursions in animal room environmental conditions which had any obvious impact on the results of the study.

METHODS AND EXPERIMENTAL DESIGN

Administration of Test Chemical

Animals were treated by a single intraperitoneal injection of 0.9% saline (vehicle control, 10 ml/kg body weight), ROUNDUP herbicide formulation in 0.9% saline (10 ml of solution/kg body weight) or cyclophosphamide in 0.9% saline (positive control, 10 ml of solution/kg body weight).

Animal Observations

During the study, all animals were observed for visible toxic effects and mortality immediately after dose administration, 3-5 hours after dosing, and daily thereafter for up to 72 hours after treatment. Animals were weighed at the time of treatment (all experiments)

and at the time of sacrifice for bone marrow extraction (main experiment).

Preliminary Experiments for Dose Selection

In the initial rangefinding experiment, two mice of each sex were treated by intraperitoneal injection with the test material at doses of 1000 and 5000 mg/kg body weight. Vehicle control animals were dosed with an appropriate volume of 0.9% saline. Based on the results of the first experiment doses of 250, 500, 750 and 1000 mg/kg body weight were tested in a subsequent rangefinding experiment. A third experiment was conducted with doses of 600, 700 and 800 mg/kg body weight. An additional animal per sex was added to the second rangefinding experiment to evaluate the effect of the test doses on the ability to score for PCE/total erythrocyte ratio. Animals added for evaluating treatment effects on slide quality were sacrificed approximately 24 hours after treatment.

Mouse Micronucleus Experiment:

Dose levels for the main study were selected based on toxicity rangefinding study data. The maximum dose selected for testing in the micronucleus experiment was 555 mg/kg body weight (more than 80% of the combined calculated LD50 of 643 mg/kg). Other doses selected were approximately 1/2 (280 mg/kg body weight) and 1/4 (140 mg/kg body weight) of the maximum dose. Doses were administered once. Groups of at least fifteen males and fifteen females were used for each dose level. Animals were sacrificed for micronucleus evaluation (five animals/sex/group) at 24, 48 and 72 hours after dosing. Vehicle control groups of fifteen males and females were treated with 0.9% saline only. Concurrent positive control groups of five males and five females were treated with 40 mg/kg cyclophosphamide and sacrificed 24 hours after treatment. Design of the mouse micronucleus experiment is summarized in Table 1.

Table 1
Design of the Mouse Micronucleus Assay

Treatment Group	Number of Mice Treated		Number of Mice to be Sacrificed at the Specified Time Following Treatment					
			24 hours		48 hours		72 hours	
	Male	Female	Male	Female	Male	Female	Male	Female
High Dose *	18	22	5	5	5	5	5	5
Mid Dose	15	15	5	5	5	5	5	5
Low Dose	15	15	5	5	5	5	5	5
Vehicle Control	15	15	5	5	5	5	5	5
Positive Control	5	5	5	5	-	-	-	-

* Additional animals added to the high dose to assure adequate survivors at time of sacrifice for bone marrow extraction.

Extraction of Bone Marrow Cells and Slide Preparation

All animals were sacrificed by cervical dislocation and their femora were removed. Each bone was opened at the end and the bone marrow was flushed with approximately 2 ml of fetal bovine serum into a centrifuge tube. Bone marrow from both femora of each animal were pooled for slide preparation. The suspension was centrifuged to remove the serum. Portions of the remaining cells were placed on clean glass microscope slides and smears were prepared. Two slides were initially prepared for each sample and the remaining cell suspension was stored refrigerated to prepare additional slides if needed. Following preparation of the smears the slides were allowed to air dry overnight. The slides were stained using a HemaTek II slide staining machine and a Wright-Giemsa Stain Pak which includes stain, buffer and rinse solutions.

Scoring of Slides

Slides of bone marrow cells were coded prior to distribution and slides were scored without knowledge of the treatment or control

group to which the slides belonged. For each animal, two scorers evaluated: a) 500 total erythrocytes for polychromatic erythrocytes (PCEs) and normochromatic erythrocytes (NCEs) and b) 500 PCEs for micronucleated polychromatic erythrocytes (MN PCEs). PCEs and NCEs were distinguished by different staining properties. Micronuclei were identified as uniform, darkly stained, round or oval shaped bodies found in the cytoplasm of PCEs. Bodies in PCEs which were refractile, improperly shaped or stained, or which were not in the focal plane of the cell, were not scored as micronuclei. PCEs containing more than one micronucleus were scored as a single micronucleated PCE. In a few cases significant discordance in MN PCE frequency were initially observed between two slide scorers (e.g. a difference of 4 or more MN PCE per 500 PCEs scored where one or both MN PCE frequencies were less than 10/500). In these cases slides were rescored to determine if the discordance was reproducible and the rescored values were used for reporting and analysis. The slides to be rescored were evaluated without knowledge of the treatment group to which the slides belonged. Scoring data were used to calculate, for each animal, the ratio of PCEs to total erythrocytes (PCEs plus NCEs) per 1000 erythrocytes and the number of MN PCEs per 1000 PCEs.

Statistical Analysis

LD50 estimates were calculated using the Probit method on toxicity rangefinder data. The individual test animal was used as the individual unit for analysis of micronucleated PCE frequency and PCE/erythrocyte ratio and body weight change. Micronucleated PCE frequencies observed for each animal were transformed as the square root prior to analysis (Snedecor and Cochran, 1967; MacGregor et al., 1987). PCE/total erythrocyte ratios were not transformed. Dunnett's test (one sided) was used for comparison of treatment group and positive control values with vehicle control values (Dunnett, 1955). A critical value of $p \leq 0.05$ was used for statistical significance.

Data Evaluation

To determine whether a statistically significant response is treatment related the following criteria are considered: (a) whether there are dose and time-dependent effects that are consistent with a treatment-induced response and (b) the degree of the response in relation to both concurrent and historical negative and positive control data.

RESULTS

Results of the rangefinding experiments are summarized in Appendix I, Table 1. In the rangefinding experiments ROUNDUP herbicide formulation was found to be toxic to male CD-1 mice at 600 mg/kg body weight and greater as indicated by clinical signs of toxicity and death and to be toxic to female mice at 500 mg/kg body weight and greater as indicated by clinical signs of toxicity. The test material caused deaths to the females at 700 mg/kg body weight and greater. The combined LD50 was determined to be 643 mg/kg body weight (Probit).

Based on these results, 555 mg/kg (approximately 86% of the combined LD50 value) was selected as a maximum dose that would insure a reasonable probability of observing signs of toxicity but allow survival of the treated animals through the 72 hour time point. Two additional lower doses (140 and 280 mg/kg body weight) were also selected for testing.

Results of the micronucleus experiment are summarized in Appendix I, Tables 2 - 5 with individual animal data in Appendix II, Tables 1-3. In the main micronucleus experiment, ROUNDUP herbicide formulation was toxic to the male and female mice dosed at the 555 mg/kg treatment level as evidenced by clinical signs and death. Three deaths were observed in the high dose level group (2/18 males and 1/22 females). No deaths were observed in other treatment or control groups. Clinical signs of toxicity (listlessness and/or

unresponsiveness) were observed in high dose males and females up to 48 hours after dosing. At the 72 hour time point all remaining high dose level male and female mice appeared normal. All animals in the mid and low dose groups appeared normal throughout the experiment. All positive and vehicle control animals also appeared normal throughout the experiment.

Statistically significant decreases in mean body weight were observed for the high dose male group animals sacrificed at the 48, and 72 hour time points. A statistically significant decrease in mean body weight was observed for the male mid dose group sacrificed at the 72 hour time point. No statistically significant decreases in mean body weight were observed for any of the other dose groups.

A statistically significant decrease in the PCE/total erythrocyte ratio was observed for the high dose male group sacrificed at the 48 hour time point. No statistically significant decreases in mean PCE/total erythrocyte ratios were observed for any of the other treatment groups.

No statistically significant increases in the mean micronucleated PCE frequencies were observed in any ROUNDUP herbicide formulation treated groups when compared to corresponding vehicle control groups. The positive control (cyclophosphamide) yielded expected positive responses in micronucleated PCE frequency indicating the adequacy of the experimental conditions.

DISCUSSION

ROUNDUP herbicide formulation was tested in a micronucleus assay in male and female CD-1 mice at dose levels of 140, 280 and 555 mg/kg with sacrifice times of 24, 48 and 72 hours. The high dose level was an appropriate maximum level as judged by several criteria. The high dose level was more than 80% of the estimated LD50 and induced a low level of lethality. Clinical signs of toxicity were observed in the treated high dose level male and female groups

and there were statistically significant decreases in mean body weight in high dose level male groups sacrificed at 48 and 72 hours after dosing. Additionally, a statistically significant decrease in the PCE/total erythrocyte ratio observed for the high dose male group sacrificed at the 48 hour time point suggests effects on the bone marrow.

At the dose levels tested, which included an appropriate maximum dose level, no statistically significant increases in the number of micronucleated PCEs were observed in the male or female groups sacrificed at the 24, 48 or 72 hour time points. The positive control, cyclophosphamide, yielded the expected positive responses in micronucleus induction indicating the adequacy of the experimental conditions.

CONCLUSION

Based on the observations and findings of this study, it is concluded that ROUNDUP herbicide formulation is not genotoxic *in vivo* in mouse bone marrow cells under the experimental conditions of the study.

GENERAL INFORMATION

The protocol, raw data, and final report for this study are located in the archives of the Environmental Health Laboratory.

For testing efficiency, the positive and saline vehicle control animals used in this study were also used for separate studies that were performed concurrently. This procedure in no way adversely affected the results of this assay.

SUPERVISORY PERSONNEL:

, Ph.D., Manager
Analytical, Biochemical and Genetic Toxicology

D.V.M., Dipl. A.C.V.P.
Pathology and Research Studies Director

, Ph.D.
Director, Environmental Health Laboratory

TRADEMARKS

The following registered trademarks are used in this report:

ITEM	*REGISTERED TRADEMARK OF:*
ROUNDUP	Monsanto Agricultural Company, St. Louis, MO
RODENT CHOW	Purina Mills, Inc., St. Louis, MO
CD-1 Mice	Charles River Laboratories Inc., Portage, MI.

REFERENCES

Dunnett, C.W (1955). A multiple comparison procedure for comparing

several treatments with a control. Jour. Am. Stat. Assoc. 50, 1096-1121.

Heddle, J. A., Hite, M., Kirkhart, B., Mavournin, K., MacGregor, J.T., Newell, G.W. and Salamone, M.F. (1983). The induction of micronuclei as a measure of genotoxicity. A report of the U.S. Environmental Protection Agency Gene-Tox Program. Mutation Res. 123, 61-118.

MacGregor, J.T., Heddle, J.A., Hite, M., Margolin, B. H., Ramel C., Salamone, M.F., Tice, R.R. and Wild, D. (1987). Guidelines for the conduct of micronucleus assays in mammalian bone marrow erythrocytes. Mutation Res. 189, 103-112.

Mavournin K.H., Blakey D.H., Cimino M.C., Salamone M.F., and Heddle J.A. (1990). The in vivo micronucleus assay in mammalian bone marrow and peripheral blood. A report of the U.S. Environmental Protection Agency Gene-Tox Program. Mutation Res. 239, 29-80.

Snedecor, G.W. and Cochran, W.G. (1967). Statistical Methods, 6th edition, 223-226 and 325-327, Iowa State Press, Ames, IO.

S&EH QUALITY ASSURANCE AUDIT STATEMENT

Study Number: 91200/91204
ML-91-434/ML-91-437

Protocol Amendments: None

Study Title: Mouse Micronucleus Study of Roundup® Herbicide Formulation

Dates of Inspections and Communication of Findings:

91200	91204
November 15, 1991	November 19, 1991
January 09, 28, 29, 1992	December 06, 12, 1991
February 18, 21, 1992	January 28, 29, 1992
	February 18, 21, 1992

Quality Assurance Review Conducted by:

91200

[redacted]er

91204

[redacted]

Results: The Quality Assurance review indicates the final report accurately presents the raw data as developed during the study. There appears to be no significant deviation from applicable GLP regulations that adversely affected study quality or integrity.

[redacted]

Quality Assurance Director

FEBRUARY 25, 1992
Date

Statement of Compliance

To the best of our knowledge, these studies were conducted in general accordance with the U.S. Environmental Protection Agency Good Laboratory Practice (GLP) Standards; the Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) GLP Standards; and the OECD GLP Principles, with the following exceptions:

1. Characterization of test and control substances was not conducted according to the standards as part of these studies.

2. Test and control substance concentrations and homogeneity in carrier were not confirmed.

3. The stability of test and control substances, neat and after mixing with carrier were not determined. Mixtures of test substances with carrier were prepared on each day of use.

[redacted] 2/25/92

Study Director Date

[redacted] 2/25/92

Laboratory Management Date

APPENDIX I
Data Summary

APPENDIX I - TABLE 1
SUMMARY OF TOXICITY RANGEFINDER RESULTS FOR ROUNDUP HERBICIDE FORMULATION

Dose mg/kg	Number Treated		Number of Deaths												
			0-5 Hours		Day 1		Day 2		Day 3		Day 4		Total		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Combined [a]
250	3	3	_	_	_	_	_	_	_	_	_	_	0	0	0/6
500	3	3	_	_	_	_	_	_	_	_	_	_	0	0	0/5 b
600	2	2	_	_	_	_	_	_	1	_	1	_	2	0	2/4
700	2	2	_	_	_	1	1	_	_	_	1	_	2	1	3/4
750	3	3	_	_	2	1	_	_	1	_	1	_	3	2	5/5 b
800	2	2	_	_	1	1	_	1	_	_	_	_	1	2	3/4
1000	5	5	2	2	2	2	_	_	_	_	_	_	4	4	8/10
5000	2	2	2	2	_	_	_	_	_	_	_	_	2	2	4/4

a Number of deaths / total number of animals treated.
b One animal sacrificed for erythrocyte evaluation at 24 hours after dosing

APPENDIX I - TABLE 1 (continued)

SUMMARY OF TOXICITY RANGEFINDER RESULTS FOR ROUNDUP HERBICIDE FORMULATION

Dose (mg/kg)	Observations - Males
250	All animals appeared normal through day four.
500	All males appeared normal through day four.
600	One male appeared normal immediately after dosing, appeared listless at the 3-5 hour observation and through day 2. This animal appeared unresponsive on day 3 and was found dead on day 4. The second male appeared normal immediately after dosing, appeared listless at the 3-5 hour observation and through day 1. This animal appeared unresponsive on day 2 and was found dead on day 3
700	One male appeared listless immediately after dosing and through day 1. This animal was found dead on day 2. One male appeared listless immediately after dosing, appeared listless at the 3-5 hour observation and through day 2. This animal appeared unresponsive on day 3 and was found dead on day 4
750	One male appeared unresponsive through day 1 and was found dead on day 2. One male appeared listless immediately after dosing, was unresponsive at the 3-5 hour observation and was found dead on day 1. The third treated male was listless through the 3-5 hour observation and was found dead on day 1.
800	One treated male appeared listless immediately after dosing, was unresponsive at 3-5 hours after dosing and was found dead on day 1. The remaining male appeared listless immediately after dosing and through day 2, then appeared normal through day 4.
1000	In the initial rangefinding experiment, the treated males died immediately after dosing. In the second rangefinding experiment one treated male was listless through the 3-5 hour observation and was found dead on day 1. One male appeared listless immediately after dosing, was unresponsive at the 3-5 hour observation and was found dead on day 1. The third treated male appeared normal through day 4.
5000	In the initial rangefinding experiment, the treated males died immediately after dosing.

APPENDIX I - TABLE 1 (continued)
SUMMARY OF TOXICITY RANGEFINDER RESULTS FOR ROUNDUP HERBICIDE FORMULATION

Dose (mg/kg)	Observations - Females
250	All animals appeared normal through day four.
500	One treated female appeared listless through 24 hours, then appeared normal through day four. The other two treated females appeared normal through day four.
600	The two treated females appeared listless immediately after dosing, then appeared normal at 3-5 hours through day four.
700	One female appeared listless immediately after dosing and at 3-5 hours. This animals was found dead on day 1. The second treated female appeared listless immediately after dosing and through day 3, then appeared normal on day four.
750	One female appeared listless through 24 hours and then was sacrificed for erythrocyte ratio evaluation. One animal appeared normal through day 1, appeared unresponsive on day 2 and was found dead on day 3. The third treated female appeared normal through day 3 and was found dead on day 4.
800	One female appeared listless immediately after dosing and at 3-5 hours. This animal was found dead on day 1. The second treated female appeared listless immediately after dosing and through day 1. This animal was found dead on day 2.
1000	In the initial rangefinding experiment, the treated females died immediately after dosing. In the second rangefinding experiment, one female appeared normal immediately after dosing, was unresponsive at the 3-5 hour observation and was found dead on day 1. One female appeared listless immediately after dosing, was unresponsive at the 3-5 hour observation and was found dead on day 1. The third treated female appeared normal immediately after dosing, appeared listless at 3-5 hours and on day 1, the appeared normal through day 4.
5000	In the initial rangefinding experiment, the treated females died immediately after dosing.

APPENDIX I - TABLE 2

SUMMARY OF MICRONUCLEUS ASSAY RESULTS FOR ROUNDUP HERBICIDE FORMULATION
MEAN BODY WEIGHT CHANGE AND ANIMAL OBSERVATIONS

Dose	Sex	Number Treated	Mean Body Weight Change (g) ± Standard Deviation			Deaths
			24 Hours	48 Hours	72 Hours	
Saline Vehicle Control	Male	15	- 0.5 ± 0.6	- 0.4 ± 0.7	- 0.8 ± 2.0	0
	Female	15	- 1.2 ± 0.3	- 0.8 ± 0.3	- 0.4 ± 0.4	0
Roundup 140 mg/kg	Male	15	- 0.8 ± 0.5	- 0.9 ± 0.7	- 0.8 ± 0.2	0
	Female	15	- 1.5 ± 0.8	- 0.3 ± 1.1	- 0.4 ± 0.5	0
Roundup 280 mg/kg	Male	15	- 0.8 ± 0.3	- 0.8 ± 0.7	- 1.6 ± 0.8 **	0
	Female	15	- 0.9 ± 0.6	- 0.4 ± 0.3	- 0.1 ± 0.7	0
Roundup 555 mg/kg	Male	18	- 2.7 ± 4.4	- 2.4 ± 1.1 **	- 1.2 ± 1.3 *	2
	Female	22	- 0.9 ± 0.8	- 0.8 ± 1.2	- 0.2 ± 2.0	1
Cyclo-phosphamide (40 mg/kg)	Male	5	- 1.3 ± 0.6			0
	Female	5	- 0.6 ± 0.4			0

*p ≤ 0.05; ** p ≤ 0.01 by one-sided t-test.

APPENDIX I - TABLE 2 (continued)
SUMMARY OF MICRONUCLEUS ASSAY RESULTS FOR ROUNDUP HERBICIDE FORMULATION
ANIMAL OBSERVATIONS

Dosing Observations:	One high dose (555 mg/kg) male and nine high dose females appeared listless immediately after dosing.
3-5 hour observations:	One high dose female was found dead, one high dose male appeared unresponsive, eleven high dose males and five high dose females appeared listless.
24 hour observations:	One high dose male was found dead, twelve high dose males and five high dose females appeared listless.
48 hour observations:	One high dose male was found dead, two high dose males appeared unresponsive and four high dose males appeared listless.
72 hour observations:	All remaining high dose male and female mice appeared normal.

All animals in the mid (280 mg/kg) and low (140 mg/kg) dose groups appeared normal throughout the experiment. All positive and vehicle control animals also appeared normal throughout the experiments.

APPENDIX I - TABLE 3
SUMMARY OF MICRONUCLEUS ASSAY RESULTS FOR ROUNDUP HERBICIDE FORMULATION
PCE RATIO AND MICRONUCLEUS DATA FOR LOW DOSE ANIMALS

Harvest Time (Hours)	Sex	Number	Mean PCE / Total Erythrocyte Ratio ± Standard Deviation			Mean Micronucleated PCE / 1000 PCE ± Standard Deviation		
			Vehicle Control	Test Material	Positive Control	Vehicle Control	Test Material	Positive Control
24	Male	5	0.43 ± 0.04	0.49 ± 0.03	0.49 ± 0.06	1.4 ± 0.5	0.8 ± 0.8	29.2 ± 8.4**
	Female	5	0.48 ± 0.05	0.52 ± 0.08	0.51 ± 0.04	0.8 ± 1.1	1.0 ± 1.4	25.6 ± 7.8**
48	Male	5	0.49 ± 0.04	0.50 ± 0.05		1.2 ± 2.2	1.6 ± 2.5	
	Female	5	0.53 ± 0.07	0.49 ± 0.03		0.8 ± 0.8	1.0 ± 1.2	
72	Male	5	0.54 ± 0.09	0.61 ± 0.11		2.4 ± 1.1	0.8 ± 0.4	
	Female	5	0.52 ± 0.10	0.59 ± 0.07		1.8 ± 1.3	1.6 ± 0.5	

* $p \leq 0.05$; ** $p \leq 0.01$ by one-sided t-test. Square root transformed data used for statistical analysis of micronucleated PCE.

APPENDIX I - TABLE 4
SUMMARY OF MICRONUCLEUS ASSAY RESULTS FOR ROUNDUP HERBICIDE FORMULATION
PCE RATIO AND MICRONUCLEUS DATA FOR MIDDLE DOSE ANIMALS

Harvest Time (Hours)	Sex	Number	Mean PCE / Total Erythrocyte Ratio ± Standard Deviation			Mean Micronucleated PCE / 1000 PCE ± Standard Deviation		
			Vehicle Control	Test Material	Positive Control	Vehicle Control	Test Material	Positive Control
24	Male	5	0.43 ± 0.04	0.50 ± 0.04	0.49 ± 0.06	1.4 ± 0.5	2.2 ± 0.8	29.2 ± 8.4**
	Female	5	0.48 ± 0.05	0.52 ± 0.06	0.51 ± 0.04	0.8 ± 1.1	0.2 ± 0.4	25.6 ± 7.8**
48	Male	5	0.49 ± 0.04	0.48 ± 0.06		1.2 ± 2.2	1.0 ± 1.2	
	Female	5	0.53 ± 0.07	0.56 ± 0.03		0.8 ± 0.8	0.6 ± 0.9	
72	Male	5	0.54 ± 0.09	0.59 ± 0.11		2.4 ± 1.1	1.4 ± 1.7	
	Female	5	0.52 ± 0.10	0.61 ± 0.10		1.8 ± 1.3	1.0 ± 1.0	

* $p \leq 0.05$; ** $p \leq 0.01$ by one-sided t-test. Square root transformed data used for statistical analysis of micronucleated PCE.

APPENDIX I - TABLE 5
SUMMARY OF MICRONUCLEUS ASSAY RESULTS FOR ROUNDUP HERBICIDE FORMULATION
PCE RATIO AND MICRONUCLEUS DATA FOR HIGH DOSE ANIMALS

Harvest Time (Hours)	Sex	Number	Mean PCE / Total Erythrocyte Ratio ± Standard Deviation			Mean Micronucleated PCE / 1000 PCE ± Standard Deviation		
			Vehicle Control	Test Material	Positive Control	Vehicle Control	Test Material	Positive Control
24	Male	5	0.43 ± 0.04	0.40 ± 0.05	0.49 ± 0.06	1.4 ± 0.5	1.8 ± 3.0	29.2 ± 8.4**
	Female	5	0.48 ± 0.05	0.51 ± 0.05	0.51 ± 0.04	0.8 ± 1.1	1.4 ± 0.9	25.6 ± 7.8**
48	Male	5	0.49 ± 0.04	0.37 ± 0.02 **		1.2 ± 2.2	1.6 ± 1.5	
	Female	5	0.53 ± 0.07	0.49 ± 0.08		0.8 ± 0.8	0.8 ± 1.3	
72	Male	5	0.54 ± 0.09	0.56 ± 0.07		2.4 ± 1.1	2.0 ± 0.7	
	Female	5	0.52 ± 0.10	0.56 ± 0.17		1.8 ± 1.3	0.2 ± 0.4	

* $p \leq 0.05$; ** $p \leq 0.01$ by one-sided t-test. Square root transformed data used for statistical analysis of micronucleated PCE.

APPENDIX II
Individual Test Results

Table 1 Body Weight Table for Micronucleus Experiment with ROUNDUP Herbicide Formulation

Table 2 Slide Scoring Data for the Micronucleus Experiment with ROUNDUP Herbicide Formulation (PCE/erythrocyte Ratio and Micronucleated PCE's)

Table 3* Animal Number Assignments for the Micronucleus Experiment with ROUNDUP Herbicide Formulation

*Note: Animals were initially assigned individual animal lot numbers and those selected for study were subsequently also assigned study numbers. Appendix II, Table 1 reports individual weight data using the assigned study number (without the study number prefix). Slide scoring data were collected using the animal lot number to preclude knowledge of the treatment or control group by the scorers and the data in Appendix II, Table 2 are presented using the individual animal lot numbers (without the lot number prefix). Appendix II, Table 3 presents the lot number and corresponding assigned study number for the individual animals in Appendix II, Tables 1 and 2 to permit comparison of the data on an individual animal basis.

APPENDIX II - TABLE 1

BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH ROUNDUP® HERBICIDE FORMULATION

24 HOUR MALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	M91 001	24	32.7	32.5	-0.2
Sterile Saline	M91 002	24	31.3	30.2	-1.1
Males	M91 003	24	35.1	33.9	-1.2
	M91 004	24	30.8	30.5	-0.3
	M91 005	24	32.0	32.3	0.3
140 mg/kg	M01 001	24	35.8	34.9	-0.9
ROUNDUP®	M01 002	24	38.2	36.6	-1.6
Males	M01 003	24	35.0	34.7	-0.3
	M01 004	24	32.5	31.9	-0.6
	M01 005	24	33.1	32.5	-0.6
278 mg/kg	M02 001	24	28.0	26.8	-1.2
ROUNDUP®	M02 002	24	32.7	32.1	-0.6
Males	M02 003	24	33.5	32.8	-0.7
	M02 004	24	30.1	29.5	-0.6
	M02 005	24	31.0	30.1	-0.9
555 mg/kg	M03 001	24	43.8	33.3	-10.5
ROUNDUP®	M03 002	24	30.8	29.6	-1.2
Males	M03 004	24	30.2	30.4	0.2
	M03 005	24	31.1	30.8	-0.3
	M03 006	24	32.4	30.6	-1.8
40 mg/kg	M04 001	24	33.8	32.4	-1.4
Cyclophosphamide	M04 002	24	35.6	33.6	-2.0
Males	M04 003	24	33.9	32.5	-1.4
	M04 004	24	36.3	35.1	-1.2
	M04 005	24	34.6	34.2	-0.4

[a] Hours after treatment.

APPENDIX II - TABLE 1 (continued)
BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

48 HOUR MALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	M91 006	48	33.3	32.3	-1.0
Sterile Saline	M91 007	48	33.8	32.6	-1.2
Males	M91 008	48	35.8	35.6	-0.2
	M91 009	48	33.0	32.7	-0.3
	M91 010	48	31.7	32.2	0.5
140 mg/kg	M01 006	48	32.9	32.5	-0.4
ROUNDUP®	M01 007	48	34.0	33.7	-0.3
Males	M01 008	48	35.8	34.1	-1.7
	M01 009	48	29.4	28.7	-0.7
	M01 010	48	37.9	36.3	-1.6
278 mg/kg	M02 006	48	34.5	32.5	-2.0
ROUNDUP®	M02 007	48	34.0	33.6	-0.4
Males	M02 008	48	30.4	30.1	-0.3
	M02 009	48	29.7	29.2	-0.5
	M02 010	48	33.5	32.5	-1.0
555 mg/kg	M03 007	48	32.1	28.7	-3.4
ROUNDUP®	M03 008	48	30.0	27.3	-2.7
Males	M03 012	48	33.7	31.9	-1.8
	M03 015	48	40.2	39.4	-0.8
	M03 017	48	33.1	29.6	-3.5

[a] Hours after treatment.

APPENDIX II - TABLE 1 (continued)
BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

72 HOUR MALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	M91 011	72	26.2	30.5	4.3
Sterile Saline	M91 012	72	29.9	29.5	-0.4
Males	M91 013	72	27.9	28.2	0.3
	M91 014	72	31.9	31.9	0.0
	M91 015	72	36.2	36.1	-0.1
140 mg/kg	M01 011	72	32.6	31.8	-0.8
ROUNDUP®	M01 012	72	30.4	29.4	-1.0
Males	M01 013	72	31.9	30.9	-1.0
	M01 014	72	32.3	31.7	-0.6
	M01 015	72	32.8	32.2	-0.6
278 mg/kg	M02 011	72	35.6	32.9	-2.7
ROUNDUP®	M02 012	72	35.7	33.7	-2.0
Males	M02 013	72	32.2	31.0	-1.2
	M02 014	72	30.1	29.4	-0.7
	M02 015	72	34.1	32.5	-1.6
555 mg/kg	M03 003	72	31.4	30.3	-1.1
ROUNDUP®	M03 009	72	33.2	31.7	-1.5
Males	M03 010	72	33.4	30.1	-3.3
	M03 011	72	32.9	33.2	0.3
	M03 014	72	31.3	30.7	-0.6

[a] Hours after treatment.

APPENDIX II - TABLE 1 (continued)
BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH ROUNDUP® HERBICIDE FORMULATION

24 HOUR FEMALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	F91 001	24	25.5	24.6	-0.9
Sterile Saline	F91 002	24	27.4	26.0	-1.4
Females	F91 003	24	27.9	26.5	-1.4
	F91 004	24	30.1	28.6	-1.5
	F91 005	24	28.8	27.9	-0.9
140 mg/kg	F01 001	24	32.3	29.4	-2.9
ROUNDUP ®	F01 002	24	28.8	27.3	-1.5
Females	F01 003	24	28.2	27.4	-0.8
	F01 004	24	29.1	27.6	-1.5
	F01 005	24	26.9	25.9	-1.0
278 mg/kg	F02 001	24	26.5	24.7	-1.8
ROUNDUP ®	F02 002	24	27.3	26.9	-0.4
Females	F02 003	24	27.1	26.1	-1.0
	F02 004	24	27.5	26.8	-0.7
	F02 005	24	29.0	28.6	-0.4
555 mg/kg	F03 010	24	25.1	24.1	-1.0
ROUNDUP ®	F03 012	24	31.3	31.2	-0.1
Females	F03 013	24	29.2	28.5	-0.7
	F03 015	24	25.3	24.7	-0.6
	F03 018	24	27.4	25.2	-2.2
40 mg/kg	F04 001	24	28.7	28.5	-0.2
Cyclophosphamide	F04 002	24	29.0	28.7	-0.3
Females	F04 003	24	28.4	27.5	-0.9
	F04 004	24	29.0	28.4	-0.6
	F04 005	24	27.6	26.5	-1.1

[a] Hours after treatment.

APPENDIX II - TABLE 1 (continued)
BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

48 HOUR FEMALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	F91 006	48	27.4	26.5	-0.9
Sterile Saline	F91 007	48	26.5	26.0	-0.5
Females	F91 008	48	32.6	31.9	-0.7
	F91 009	48	24.7	23.5	-1.2
	F91 010	48	24.2	23.6	-0.6
140 mg/kg	F01 006	48	24.0	23.4	-0.6
ROUNDUP®	F01 007	48	28.8	27.8	-1.0
Females	F01 008	48	28.6	28.4	-0.2
	F01 009	48	26.6	28.1	1.5
	F01 010	48	29.5	28.4	-1.1
278 mg/kg	F02 006	48	30.6	30.5	-0.1
ROUNDUP®	F02 007	48	26.0	25.7	-0.3
Females	F02 008	48	24.7	24.6	-0.1
	F02 009	48	27.2	26.3	-0.9
	F02 010	48	29.3	28.8	-0.5
555 mg/kg	F03 001	48	25.8	25.2	-0.6
ROUNDUP®	F03 002	48	28.7	29.4	0.7
Females	F03 003	48	30.4	27.9	-2.5
	F03 005	48	29.3	28.9	-0.4
	F03 006	48	30.0	28.8	-1.2

[a] Hours after treatment.

APPENDIX II - TABLE 1 (continued)

BODY WEIGHT TABLE FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

72 HOUR FEMALES

Group	Animal Number	Time of Sacrifice [a] (hr)	Body Weight (g)		
			Pretest	Final	Difference
10 ml/kg	F91 011	72	27.0	27.0	0.0
Sterile Saline	F91 012	72	27.0	26.6	-0.4
Females	F91 013	72	30.4	29.5	-0.9
	F91 014	72	31.8	31.4	-0.4
	F91 015	72	25.6	25.5	-0.1
140 mg/kg	F01 011	72	26.1	26.1	0.0
ROUNDUP ®	F01 012	72	27.6	26.8	-0.8
Females	F01 013	72	25.9	26.1	0.2
	F01 014	72	30.9	30.7	-0.2
	F01 015	72	23.9	22.9	-1.0
278 mg/kg	F02 011	72	29.2	28.9	-0.3
ROUNDUP ®	F02 012	72	28.8	28.8	0.0
Females	F02 013	72	26.2	26.5	0.3
	F02 014	72	27.4	28.2	0.8
	F02 015	72	30.4	29.3	-1.1
555 mg/kg	F03 007	72	23.3	23.3	0.0
ROUNDUP ®	F03 008	72	24.4	25.0	0.6
Females	F03 009	72	25.4	26.1	0.7
	F03 011	72	31.9	28.3	-3.6
	F03 014	72	28.1	29.4	1.3

[a] Hours after treatment.

APPENDIX II - TABLE 2

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** Herbicide Formulation
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
24 Hour Males

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]			
			Sld. 1	Sld. 2	Mean	Sld. 1	Sld. 2	Combined	
10 ml/kg	M 038	24	0.456	0.510	0.483	0	2	2	
Sterile Saline	M 177	24	0.352	0.396	0.374	1	0	1	
Males	M 202	24	0.464	0.372	0.418	1	0	1	
	M 209	24	0.476	0.432	0.454	0	1	1	
	M 232	24	0.442	0.370	0.406	1	1	2	
140 mg/kg	M 140	24	0.516	0.522	0.519	0	0	0	
ROUNDUP®	M 187	24	0.454	0.508	0.481	0	0	0	
Males	M 234	24	0.488	0.560	0.524	1	0	1	
	M 255	24	0.438	0.538	0.488	1	0	1	c
	M 304	24	0.442	0.452	0.447	2	0	2	
278 mg/kg	M 135	24	0.488	0.596	0.542	2	1	3	
ROUNDUP®	M 227	24	0.464	0.474	0.469	3	0	3	
Males	M 245	24	0.482	0.434	0.458	1	1	2	
	M 261	24	0.496	0.582	0.539	0	1	1	
	M 290	24	0.488	0.472	0.480	0	2	2	
555 mg/kg	M 189	24	0.414	0.458	0.436	0	0	0	
ROUNDUP®	M 205	24	0.340	0.336	0.338	0	0	0	
Males	M 217	24	0.380	0.344	0.362	1	1	2	
	M 268	24	0.384	0.442	0.413	3	4	7	c
	M 287	24	0.442	0.444	0.443	0	0	0	
40 mg/kg	M 112	24	0.400	0.434	0.417	7	9	16	
Cyclophosphamide	M 179	24	0.544	0.602	0.573	13	18	31	
Males	M 194	24	0.434	0.452	0.443	21	18	39	
	M 233	24	0.510	0.560	0.535	12	20	32	c
	M 240	24	0.472	0.474	0.473	18	10	28	

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - TABLE 2 (continued)

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** Herbicide Formulation
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
48 Hour Males

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]			
			Sld. 1	Sld. 2	Mean	Sld.1	Sld. 2	Combined	
10 ml/kg	M 066	48	0.436	0.404	0.420	0	0	0	
Sterile Saline	M 117	48	0.484	0.462	0.473	0	0	0	
Males	M 161	48	0.510	0.508	0.509	0	0	0	
	M 257	48	0.558	0.500	0.529	2	3	5	
	M 294	48	0.542	0.502	0.522	0	1	1	
140 mg/kg	M 171	48	0.476	0.496	0.486	0	1	1	
ROUNDUP®	M 198	48	0.552	0.500	0.526	0	0	0	
Males	M 223	48	0.432	0.404	0.418	0	0	0	
	M 242	48	0.560	0.530	0.545	3	3	6	
	M 249	48	0.594	0.496	0.545	0	1	1	c
278 mg/kg	M 147	48	0.572	0.512	0.542	0	0	0	
ROUNDUP®	M 247	48	0.482	0.426	0.454	1	2	3	
Males	M 251	48	0.544	0.412	0.478	0	0	0	
	M 260	48	0.360	0.430	0.395	1	0	1	
	M 298	48	0.510	0.516	0.513	1	0	1	
555 mg/kg	M 047	48	0.360	0.436	0.398	0	0	0	
ROUNDUP®	M 219	48	0.374	0.326	0.350	0	1	1	
Males	M 222	48	0.366	0.338	0.352	2	2	4	
	M 282	48	0.298	0.446	0.372	1	1	2	
	M 293	48	0.410	0.378	0.394	1	0	1	

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - TABLE 2 (continued)

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** Herbicide Formulation
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
72 Hour Males

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]		
			Sld. 1	Sld. 2	Mean	Sld.1	Sld. 2	Combined
10 ml/kg	M 125	72	0.616	0.598	0.607	3	1	4
Sterile Saline	M 203	72	0.514	0.436	0.475	1	1	2
Males	M 225	72	0.674	0.534	0.604	3	0	3
	M 266	72	0.440	0.420	0.430	0	1	1
	M 306	72	0.612	0.596	0.604	1	1	2
140 mg/kg	M 087	72	0.444	0.618	0.531	1	0	1
ROUNDUP®	M 151	72	0.580	0.856	0.718	0	0	0
Males	M 206	72	0.476	0.470	0.473	1	0	1
	M 241	72	0.576	0.654	0.615	1	0	1
	M 258	72	0.686	0.724	0.705	1	0	1
278 mg/kg	M 100	72	0.672	0.810	0.741	2	0	2
ROUNDUP®	M 173	72	0.594	0.626	0.610	0	1	1
Males	M 182	72	0.524	0.572	0.548	1	3	4
	M 208	72	0.500	0.400	0.450	0	0	0
	M 281	72	0.596	0.642	0.619	0	0	0
555 mg/kg	M 012	72	0.646	0.642	0.644	2	1	3
ROUNDUP®	M 168	72	0.512	0.648	0.580	2	0	2
Males	M 180	72	0.492	0.418	0.455	1	0	1
	M 191	72	0.554	0.536	0.545	2	0	2
	M 277	72	0.570	0.568	0.569	2	0	2

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - TABLE 2 (continued)

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** Herbicide Formulation
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
24 Hour Females

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]		
			Sld. 1	Sld. 2	Mean	Sld. 1	Sld. 2	Combined
10 ml/kg	F 195	24	0.536	0.482	0.509	0	0	0
Sterile Saline	F 213	24	0.543 d	0.408	0.476	2	0	2
Females	F 217	24	0.602	0.508	0.555	0	0	0
	F 234	24	0.436	0.468	0.452	0	0	0
	F 303	24	0.406	0.446	0.426	0	2	2
140 mg/kg	F 154	24	0.475 d	0.460	0.467	1	2	3
ROUNDUP®	F 162	24	0.430	0.462	0.446	0	2	2
Females	F 170	24	0.558	0.466	0.512	0	0	0
	F 216	24	0.710	0.582	0.646	0	0	0
	F 230	24	0.498	0.544	0.521	0	0	0
278 mg/kg	F 209	24	0.548	0.498	0.523	0	0	0
ROUNDUP®	F 219	24	0.566	0.526	0.546	0	0	0
Females	F 229	24	0.426	0.502	0.464	1	0	1
	F 287	24	0.618	0.612	0.615	0	0	0
	F 305	24	0.496	0.456	0.476	0	0	0
555 mg/kg	F 168	24	0.396	0.472	0.434	2	0	2
ROUNDUP®	F 243	24	0.534	0.536	0.535	0	0	0
Females	F 260	24	0.584	0.526	0.555	0	2	2
	F 296	24	0.468	0.538	0.503	0	1	1 c
	F 297	24	0.540	0.542	0.541	2	0	2
40 mg/kg	F 220	24	0.598	0.490	0.544	18	16	34
Cyclophosphamide	F 245	24	0.478	0.482	0.480	5	10	15 c
Females	F 256	24	0.572	0.498	0.535	19	13	32 c
	F 264	24	0.418	0.474	0.446	10	11	21 c
	F 269	24	0.536	0.534	0.535	15	11	26 c

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - TABLE 2 (continued)

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** Herbicide Formulation
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
48 Hour Females

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]		
			Sld. 1	Sld. 2	Mean	Sld. 1	Sld. 2	Combined
10 ml/kg	F 167	48	0.552	0.534	0.543	0	1	1
Sterile Saline	F 187	48	0.612	0.564	0.588	0	0	0
Females	F 200	48	0.428	0.434	0.431	1	1	2
	F 248	48	0.500	0.524	0.512	0	0	0
	F 255	48	0.614	0.574	0.594	1	0	1
140 mg/kg	F 164	48	0.498	0.544	0.521	0	0	0
ROUNDUP®	F 191	48	0.444	0.450	0.447	1	0	1
Females	F 196	48	0.502	0.476	0.489	1	0	1
	F 204	48	0.534	0.526	0.530	3	0	3
	F 231	48	0.470	0.474	0.472	0	0	0
278 mg/kg	F 173	48	0.526	0.538	0.532	0	0	0
ROUNDUP®	F 178	48	0.560	0.634	0.597	0	1	1
Females	F 266	48	0.540	0.636	0.588	0	0	0
	F 283	48	0.512	0.550	0.531	0	0	0
	F 295	48	0.548	0.556	0.552	0	2	2
555 mg/kg	F 155	48	0.446	0.444	0.445	1	2	3
ROUNDUP®	F 166	48	0.570	0.444	0.507	0	0	0
Females	F 176	48	0.410	0.450	0.430	0	0	0
	F 271	48	0.588	0.642	0.615	0	1	1
	F 293	48	0.430	0.426	0.428	0	0	0

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - TABLE 2 (continued)

Slide Scoring Data for the Micronucleus Experiment with **ROUNDUP®** HERBICIDE FORMULATION
(PCE/Erythrocyte Ratio and Micronucleated PCE's)
72 Hour Females

Group	Animal Number	Time Hrs.	PCE/Erythrocyte Ratio [a]			Micronucleated PCE [b]		
			Sld. 1	Sld. 2	Mean	Sld.1	Sld. 2	Combined
10 ml/kg	F 235	72	0.396	0.384	0.390	1	2	
Sterile Saline	F 240	72	0.544	0.542	0.543	1	0	1
Females	F 241	72	0.564	0.478	0.521	1	0	1
	F 281	72	0.614	0.720	0.667	0	1	1
	F 290	72	0.500	0.450	0.475	1	3	4
140 mg/kg	F 160	72	0.610	0.580	0.595	1	1	2
ROUNDUP®	F 253	72	0.476	0.512	0.494	2	0	2
Females	F 286	72	0.632	0.682	0.657	0	2	2
	F 300	72	0.674	0.666	0.670	1	0	1
	F 309	72	0.570	0.530	0.550	0	1	1 [c]
278 mg/kg	F 156	72	0.636	0.678	0.657	1	1	2
ROUNDUP®	F 163	72	0.654	0.720	0.687	0	0	0
Females	F 169	72	0.604	0.596	0.600	0	1	1
	F 233	72	0.406	0.474	0.440	0	0	0
	F 299	72	0.622	0.670	0.646	0	2	2
555 mg/kg	F 157	72	0.688	0.700	0.694	0	1	1
ROUNDUP®	F 171	72	0.598	0.540	0.569	0	0	0
Females	F 172	72	0.332	0.342	0.337	0	0	0
	F 189	72	0.450	0.404	0.427	0	0	0
	F 251	72	0.734	0.770	0.752	0	0	0

Note: Refer to the end of APPENDIX II Table 2 for all footnote codes.

APPENDIX II - Table 2 (Footnotes)

a Ratio scored per 500 erythrocytes (PCEs and NCEs) for each slide except as noted in (d) and mean ratio of both slides (equivalent to ratio for 1000 erythrocytes).
b Micronucleated PCE scored per 500 PCEs for each slide and combined micronucleated PCEs for 1000 PCEs scored.
c Significantly discordant scoring results observed in initial scoring, slides were re-scored and rescored value used in analysis.
d Total PCE/NCE not equal to 500, but between 490 and 510. Ratio was calculated to reflect the actual number of PCE/NCE counted.

APPENDIX II - TABLE 3

ANIMAL NUMBER ASSIGNMENTS FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

Group	Study Number	Lot Number
10 ml/kg	F91 001	F 234
Sterile Saline	F91 002	F 217
Females	F91 003	F 213
	F91 004	F 303
	F91 005	F 195
	F91 006	F 255
	F91 007	F 167
	F91 008	F 200
	F91 009	F 248
	F91 010	F 187
	F91 011	F 241
	F91 012	F 240
	F91 013	F 235
	F91 014	F 290
	F91 015	F 281
140 mg/kg	F01 001	F 154
ROUNDUP®	F01 002	F 162
Females	F01 003	F 170
	F01 004	F 216
	F01 005	F 230
	F01 006	F 204
	F01 007	F 231
	F01 008	F 164
	F01 009	F 196
	F01 010	F 191
	F01 011	F 300
	F01 012	F 160
	F01 013	F 286
	F01 014	F 309
	F01 015	F 253
278 mg/kg	F02 001	F 209
ROUNDUP®	F02 002	F 305
Females	F02 003	F 229
	F02 004	F 287
	F02 005	F 219
	F02 006	F 173
	F02 007	F 283
	F02 008	F 178
	F02 009	F 266
	F02 010	F 295

APPENDIX II - TABLE 3 (Continued)
ANIMAL NUMBER ASSIGNMENTS FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

Group	Study Number	Lot Number
	F02 011	F 233
	F02 012	F 156
	F02 013	F 299
	F02 014	F 163
	F02 015	F 169
555 mg/kg	F03 001	F 271
ROUNDUP®	F03 002	F 155
Females	F03 003	F 166
	F03 005	F 293
	F03 006	F 176
	F03 007	F 172
	F03 008	F 189
	F03 009	F 157
	F03 010	F 297
	F03 011	F 171
	F03 012	F 168
	F03 013	F 260
	F03 014	F 251
	F03 015	F 296
	F03 018	F 243
40 mg/kg	F04 001	F 264
Cyclophosphamide	F04 002	F 269
Females	F04 003	F 220
	F04 004	F 256
	F04 005	F 245
10 ml/kg	M91 001	M 232
Sterile Saline	M91 002	M 202
Males	M91 003	M 038
	M91 004	M 177
	M91 005	M 209
	M91 006	M 117
	M91 007	M 066
	M91 008	M 257
	M91 009	M 294
	M91 010	M 161
	M91 011	M 225
	M91 012	M 306
	M91 013	M 203
	M91 014	M 125
	M91 015	M 266

APPENDIX II - TABLE 3 (Continued)
ANIMAL NUMBER ASSIGNMENTS FOR THE MICRONUCLEUS EXPERIMENT WITH ROUNDUP® HERBICIDE FORMULATION

Group	Study Number	Lot Number
140 mg/kg ROUNDUP® Males	M01 001	M 234
	M01 002	M 140
	M01 003	M 304
	M01 004	M 187
	M01 005	M 255
	M01 006	M 249
	M01 007	M 198
	M01 008	M 242
	M01 009	M 171
	M01 010	M 223
	M01 011	M 206
	M01 012	M 151
	M01 013	M 087
	M01 014	M 258
	M01 015	M 241
278 mg/kg ROUNDUP® Males	M02 001	M 135
	M02 002	M 227
	M02 003	M 245
	M02 004	M 261
	M02 005	M 290
	M02 006	M 251
	M02 007	M 298
	M02 008	M 147
	M02 009	M 260
	M02 010	M 247
	M02 011	M 182
	M02 012	M 173
	M02 013	M 100
	M02 014	M 208
	M02 015	M 281
555 mg/kg ROUNDUP® Males	M03 001	M 217
	M03 002	M 287
	M03 003	M 012
	M03 004	M 205
	M03 005	M 268
	M03 006	M 189
	M03 007	M 219
	M03 008	M 222
	M03 009	M 168

APPENDIX II - TABLE 3 (Continued)
ANIMAL NUMBER ASSIGNMENTS FOR THE MICRONUCLEUS EXPERIMENT WITH **ROUNDUP®** HERBICIDE FORMULATION

Group	Study Number	Lot Number
	M03 010	M 277
	M03 011	M 180
	M03 012	M 282
	M03 014	M 191
	M03 015	M 047
	M03 017	M 293
40 mg/kg	M04 001	M 233
Cyclophosphamide	M04 002	M 112
Males	M04 003	M 194
	M04 004	M 240
	M04 005	M 179