# MONSANTO COMPANY ENVIRONMENTAL HEALTH LABORATORY 645 S. NEWSTEAD ST. LOUIS, MISSOURI 63110

In Vivo Bone Marrow Cytogenetics Study of Glyphosate in Sprague-Dawley Rats

> Study Number: 830083 DMEH Project Number: ML-83-236

Submitted to: Monsanto Agricultural Products Company :, Senior Product Toxicologist Through:

Study Director:

Senior Research Toxicologist

10/20/83 , Study Director

Director EHL

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#### SUMMARY

The potential for glyphosate to induce chromosomal aberrations in the bone marrow cells of Sprague-Dawley rats was tested. Glyphosate was administered via intraperitoneal injection to male and female rats at a dosage of 1.0 g/kg body weight. Treatment periods were 6, 12 or 24 hrs. No significant increases in chromosomal aberrations were observed in the bone marrow cells at any CONTAINS TRADE SECRET OR
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INFORMATION OF of the time points tested. The results of this test suggest that glyphosate does not have the potential to produce clastogenic effects in mammalian cells.

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# INTRODUCTION

The study was designed to evaluate the potential of the test chemical, glyphosate, to induce morphological aberrations in the chromosomes of bone marrow cells. A well-established cytogenetics assay, the <u>in vivo</u> bone marrow chromosomal aberration assay, was used.

The <u>in vivo</u> bone marrow assay involves the administration of the <u>test</u> chemical in whole animals. At appropriate time intervals, the bone marrow cells were extracted and the morphology of the chromosomes in the mitotic cells are examined for aberrations. The advantage of this assay is the use of whole animals, therefore permitting normal metabolism (activation and detoxification) under a relevant <u>in vivo</u> situation.

The <u>in vivo</u> bone marrow cytogenetics assay has been found sensitive to a wide variety of chemicals. The assay has recently been reviewed by the EPA Gene-Tox program (Preston et al., 1981). The albino rat was used because it is a widely accepted animal species for toxicological studies.

The study was conducted at the Monsanto Company
Environmental Health Laboratory (645 S. Newstead, St.
Louis, MO 63110). Staining and scoring of the slides
were performed in Oak Ridge National Laboratory Biology
Division 's laboratory). The protocol
was signed by the study director on August 9, 1983.
Experimental work was initiated on August 8, 1983, and
completed on August 12, 1983. All rat data except
cytogenetic scores are stored in the archives of the
Environmental Health Laboratory. The raw data for scoring
are stored in Dr. 's laboratory, Biology
Division, Oak Ridge National Laboratory.

#### MATERIALS AND METHODS

#### Test Materials

Glyphosate (Environmental Health Laboratory sample no. T830044), a white powder, was submitted by the sponsor and received at EHL on June 20, 1983, and was indicated to have a purity of 98.7%. The material was stored at room temperature as recommended. Solutions of the material were made by resuspending the glyphosate in Hank's balanced salt solution (HBSS) (100 mg glyphosate/ml) and

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neutralized with 1 N sodium hydroxide to a pH of 7.0. The final solution was a clear solution. The positive control, cyclophosphamide, was purchased from Sigma Chemical Company, St. Louis, Missouri. Cyclophosphamide was dissolved also in HBSS for testing. The glyphosate test solutions were made within 24 hours of the day of testing.

# Animals

The animals used in this study were male and female Sprague-Dawley rats (Crl: CD®(SD)BR) (Trademark of Charles River Breeding Laboratories, Wilmington, MA) obtained from Charles River Breeding Laboratory, Portage, MI. Following delivery to the EHL by truck, the animals were quarantined for seven days, during which time individual ear tags were applied. The animals were housed in stainless steel mesh cages suspended over absorbant paper bedding. On the day of test material administration, the rats were approximately 9 weeks old. All animals were considered to be in excellent health at the initiation of the study.

Animals were selected for the different test (or control) groups by a computer-generated random number scheme. Each animal was identified by its ear tag and a corresponding bar-coded cage card. Water (supplied by the public water system of St. Louis, MO) was provided ad libitum via an automatic watering system. Purina Laboratory Rodent Chow® No. 5002 (Trademark of the Ralston-Purina Company, St. Louis, MO) was used as the diet and was provided ad libitum, except for a 14-24 hour fasting prior to dosing. This diet has been determined to be adequate for the maintenance of laboratory rodents used in acute studies. No contaminants were reported by the vendor that were likely to interfere with study conduct. The animals were housed in quarters designed to routinely maintain a 12-hour light cycle, a temperature between 70 and 74 degrees F, and relative humidity between 35 and 60%.

### Administration of Test Chemical

A volume of 10 ml per kg of HBSS (solvent control) or the 100 mg/ml glyphosate solution was injected intraperitioneally into each of the experimental animals. The final treatment doses were 0 and 1000 mg glyphosate per kg body weight. A volume of 1 ml/kg of 25 mg/ml of cyclophosphamide was similarly injected as the positive control, yielding a final dose of 25 mg/kg.

The different treatment groups are tabulated below:

				f Animal	
			Sacrif	ice Time	
	6	hr	1	2 hr	24 hr
Treatment	Male	Female	Male	Female	Male Female
Solvent (HBSS)	6	6	6	6	6
l g/kg glyphosate	6	6	6	6	Ente Jing 6
25 mg/kg cyclophosphamid	e 6 ·	6	6	6	Portifies. My

The rats were fasted for 14-24 hours before the administration of test substances.

# Preparation of Bone Marrow Cells

The animals were injected with 2 mg/kg of colchicine 4, 10 and 22 hours after the administration of glyphosate, solvent or positive control. Two hours later (6, 12 or 24 hours after test chemical or solvent control administration), the animals were sacrificed by CO<sub>2</sub> asphyxiation and severance of the spinal cord. Marrow were aspirated from each femur into a 5 ml syringe containing 2 ml of HBSS. The contents of each syringe were added to 5 ml of HBSS in a plastic centrifuge tube. Syringes and centrifuge tubes containing HBSS were kept in an incubator at 37°C until shortly before use for slide preparation for the scoring of chromosomal aberrations.

#### Slide Preparation

The bone marrow cells were fixed for slide preparation. For fixation, cell suspensions were pelleted by centrifugation (700 x g, 10 min) and the supernatant solution discarded. One ml of 0.075 M KCl (warmed to 37°C) was added to each tube, the pellet was gently disrupted, another 3 ml of KCl was added, and gross debris removed. The tubes were incubated in a 37°C water bath for 30 min before 1 ml of chilled

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Cornoy's fixative (methanol/glacial acetic acid, 3/1, v/v) was added and mixed with the hypotonic solution. After pelleting the cells (700 x g, 10 min) and discarding the supernatant solution, 1 ml of chilled fixative was added and mixed with the pellet followed by addition of 4 ml of fixative solution. The fixed cells were stored refrigerated. One to two drops of the cell suspension in fixative were dropped on a clean wet slide and flamed to facilitate spreading the chromosomes. The air-dried slides were transported to Dr. 's laboratory where they were stained for 15-20 minutes in a 2% Giemsa solution. The slides were rinsed in water, air dried, and covered with cover-slips.

# Distribution of Slide for Scoring

Scoring was performed by Dr.

Biology Division, Oak Ridge National Laboratory. The three scorers were Dr.

associates Mr.

The analysis of each treatment group was equally divided between each of the three scorers. The slides from each animal were examined by two different scorers. This scheme was transmitted to Monsanto where the specific samples for each scorer were listed in terms of the previously assigned animal numbers. The numbers were re-listed in a random manner, to avoid identification by any scorer, and transmitted to Oak Ridge.

# Scoring of Chromosomal Aberrations

Approximately 50 mitotic cells (300 cells per treatment) were scored for chromosomal aberrations. The following information was recorded:

- 1. Number of cells scored
- Number of cells with normal numbers of chromosomes
- 3. Chromosome-type aberrations:
  - a) Dicentric
  - b) Ring
  - c) Chromosome deletions

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- 4. Chromatid-type aberrations:
  - a) Chromatid deletions
  - b) Isochromatid deletions
  - c) Chromatid interchanges
  - d) Chromatid intrachanges
- 5. Achromatic lesions (gaps)
- 6. Number of aneuploid cells
- Location of cells with aberrations

# Statistical Analysis

The student's t test was used for data analysis. Treatment samples were considered statistically different from controls if the probability value (p) to be the same as control was < 0.05.

#### RESULTS

Chromatid-type aberrations were observed both in the solvent control and glyphosate groups at low frequencies. Chromatid deletions, the most frequent category, was observed at a frequency of approximately 1%. At the 6 hr sampling time, glyphosate treatment did not induce higher frequency of chromatid deletions above the solvent There were 7 chromatid deletions in 600 cells control. (male and female) in the solvent control group and 6 in 600 cells in the test compound group (Appendix I, Table 1). For the 12 hr sampling times 2 chromatid deletions per 575 cells and 5 per 577 cells were observed for solvent control and glyphosate treatment, respectively (Appendix I, Table 1). At the 24 hr sampling time, 4 chromatid deletions per 565 cells and 7 per 492 cells were observed for the solvent control and glyphosate treatment, respectively (Appendix I, Table 1). The slightly higher frequencies for the glyphosate treatment group at the 12 hr and 24 hr sampling times were not statistically significant (p > 0.05) from the control frequencies (Appendix I, Table 2).

Achromatic lesions are not considered to be chromosome aberrations, but were recorded to show that they were distinguished from chromatid aberrations (Appendix I, Tables 1-3; Appendix II, Tables 1-3). However, the

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frequencies were still compared in test compound and solvent control groups. There were no significant differences in achromatic lesion frequency between the glyphosate and solvent treated groups for any of the sampling times (Appendix I, Table 2).

The response to the positive control was scored at the 24 hr sampling time. Because of the apparently high cytotoxicity of cyclophosphamide towards bone marrow cells, only 256 cells were available for scoring in the male animals and only 21 cells were scored in the female animals. Nevertheless, high frequencies of chromosomal aberrations induced by cyclophosphamide were observed (Appendix I, Table 1).

No chromosomal-type aberrations were observed in the glyphosate-treated groups (Appendix II, Tables 1-3).

#### DISCUSSION

A high concentration of glyphosate (1 g per kg body weight) was administered via an effective route for absorption, intraperitoneal injection, into male and female Sprague-Dawley rats. No significant induction of chromosomal aberrations was observed.

The present study therefore suggests that glyphosate does not have significant clastogenic effects in mammalian cells.

The dose used in this study (1.0~g/kg) was the maximum one could effectively administer into the test animals based on the solubility of glyphosate and the amount of fluid to be injected into a rat.

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# REFERENCE

The determinate and the deciding for the first and the deciding for the deciding Preston, R. J., W. Au, M. A. Bender, J. G. Brewen, A. V. Carrano, J. A. Heddle, A. F. McFee, S. Wolff and J. S.

## DMEH QUALITY ASSURANCE AUDIT STATEMENT

Study Number:

830083 ML-83-236

Protocol Amendments:

None

Study Title:

In Vivo Bone Marrow Cytogenetics Study in Sprague-Dawley Rats with Glyphosate

Communication of Findings:

Quality Assurance Review Conducted by:

Results:

Sprague-Dawley Rats with Glyphosate

August 11, 24, 1983
October 18, 19, 20, 1983

The Quality Assurance review indicates the final report accurately presents auring the
no significant deviation
moratory Practice regulations
affected study quality or integrity.
The study appears to have been conducted
in general compliance with 21 CFR Part 58,
Monsanto Standard Operating Procedures and
study protocol. the final report accurately presents study. There were no significant deviations

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#### APPENDIX I

## Summary of Results

Chromosomal Aberration Frequencies Observed in Rat Bone Marrow Cells Treated with Solvent Control, Glyphosate (1) went of the content o Table 1 

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Table 1

Chromosomal Aberration Frequencies Observed in Rat Bone Marrow Cells
Treated with Solvent Control, Glyphosate (1 g/kg) or Positive
Control Cyclophosphamide (25 mg/kg)

	Number of Cells	Normal1	Chromatid Deletions <sup>2</sup>	Chromatid Interchanges	Chromat1d Intrachanges	Achromatic Lesions <sup>3</sup>	Aneuploid Cells <sup>4</sup>
A. 6 hr Sampl	ing Time			, of 9 <sup>11</sup>	Sy cition logicity	Ø.	
Vehicle Contro	1			idhanda	of course on		
Male	300	296	3	WE HELD	To On the	0	13
Female	300	292	4	1,10 00, 19,0,00	0, 4,	5	22
Tota1	600	588	7	Hoce of I'm as	or cio	5	35
Test Compound			III	ectife of the Ethics	le ill		
Male	300	293	3,1100,40	1010 0 0 1010 PO 11010	0	6	21
Female	300	291	3 6	96,910, 10,00	0	6	22
Tota1	600	584	60,60	13/16/10/00 St.	0	12	43
B. 12 hr Samp	ling Time	and is or	Chule to the court	Chromatid Interchanges  0 0 0 0 0 0 0			
Vehicle Contro	1	6 101, AZ.	O' illo of legion				
Male	300	29,7	100 out 1100,	0	0	2	1.7
Female	275 👌	271	I'm of	0	0	1	31
Tota1	275 575 300 277	568	ocities 2	0	0	3	48
Test Compound	& big ing lift	Olica illia	illie				
Male	300	294	3	0	0	3	21
Female	277 mg	270	2	0	0	6	21
Total 💉	5,7,7	<b>₹</b> 564	5	0	0	9	42
Total	of the	-					

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Table 1 (Cont.)

Chromosomal Aberration Frequencies Observed in Rat Bone Marrow Cells Treated with Solvent Control, Glyphosate (1 g/kg) or Positive Control Cyclophosphamide (25 mg/kg)

		Number of Cells	Normal <sup>1</sup>	Chromatid Deletions <sup>2</sup>	Chromatid Interchanges	Chromatid Intrachanges	Achromatic Lesions <sup>3</sup>	Aneuploid Cells <sup>4</sup>
c.	24 hr Sampli	ng Time			idio:	intis continue		
Veh	icle Control				NOT OR	Cijo, Ulus, of Mus		
	Male	300	296	1		CO (01) 15	3	19
	<b>Female</b>	265	259	3	1609 150 S	100 m	5	27
	Total	565	555	4	Still Of Odd Miles		8	46
Tes	t Compound			and the second	ingly angle thing is sign	ille		
	Male	192	190	2 10110		0	0	13
	Female	300	289	:511 in 1011	(8, 6), 00 6, 1/0, 1/0, 1/0, 1/0, 1/0, 1/0, 1/0, 1/0	0	6	22
	Total	492	479	101 07 05 111 de	O, Tir O'lle	0	6	35
Pos	itive Control		;;	sed such tallion	driftiolied 2			
	Male	256	148	1217 NO 1	76	6	34	22
	Female	21	₹6	Sect 140 City	2 2	0	3	1
	Total	277	164	JI 231 5 (8)	77	6	37	23

1 Number of normal cells includes aneuploid cells.

Note: Chromosome-type interchanges and intrachanges not observed.

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<sup>&</sup>lt;sup>2</sup>This category includes chromatid deletions, isochromatid deletions, and chromosome-type terminal deletions (indistinguishable from isochromatid deletions).

<sup>3</sup>Achromatic lesions are not considered to be aberrations. They are recorded to indicate that a distinction was made between deletions and achromatic lesions.

<sup>4</sup>Almost all aneuploids were minus one chromosome, and since slides had been flamed these cells were considered to be technical artifacts.

Table 2 Statistical Analysis of Datal

# Chromatid Deletions

# Observed Frequencies2

Sampling Time	Control	Glyphosate	<u>6</u> 3
12 hr	0.0035	0.0087	0.26
24 hr	0.0071	0.0142	0.26

#### В. Achromatic Lesions

# Observed Frequencies2

Sampling Time	Control Glyp	hosate <u>p</u> 3	\$
6 hr	0.0083	20 000 000	8 (
12 hr	0.0052	16 0.0	8

lperformed only on data where the observed frequency for glyphosate treatment was higher than that of the cions - no
y to be the sai
ed by the student

2No. of aberrations - no of cells scored.

3Probability to be the same as solvent control as determined by the student's t test.

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- ADIX II

  idual Animal Data

  ...al Aberration Frequencies Observe
  ...r Sampling Time

  ...nromosomal Aberration Frequencies Observed
  the 12 hr Sampling Time

  able 3 Chromosomal Aberration Frequencies Observed at
  the 24 hr Sampling Time

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Table 1 Chromosomal Aberration Frequencies Observed at the 6 hr Sampling Time

	A	В	c	D	E	F	G_	<u>H</u>	I	J	K	L	
A. Solve	ent Contro	1	49(50) 47(50) 48(50) 43(48) 47(49) 49(49) 45(47) 45(48) 44(49) 46(50) 44(48) 46(50) eatment 48(50) 47(49) 45(49) 41(47) 45(49) 46(49) 47(48) 43(49)									134.	
Male:	M0001	 50	49(50)	0	O	0	0	0	0	0	. SO	1	
	M0003	50	47(50)	0	0	0	0	0	0	0 <	0	3	
	M0004	50	48(50)	0	0	O	0	0	0	0/2	0	_2	
	M0019	50	43(48)	0	0	0	1	0	1 .	0 0	0	5°5	
	M0024	50	47(49)	0	0	0	1	0	<b>0</b> 00	O	00	2	
	M0025	50	49(49)	0	0	0	1	0	100,0	Ø 0	000	0	
Female:	F0002	50	45(47)	0	0	0	1	Tops	410	Ollo	1	2	
	<b>F</b> 6003	50	45(48)	0	0	1	0 🐇	ૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢૢ	<u> </u>	045	1	3	
	F0004	50	44(49)	0	0	0	0%	(0)	600 W	0	1	5	
	F0011	50	46(50)	0	0	0	60°C	100,1	CO.	0	0	4	
	F0013	50	44(48)	0	0	0,%	(,000)	n Po	/, '6s, '	0/20	2	4	
	F0018	50	46(50)	0	0	O	30,00	2,00	02040	0	0	4	
					*(	ill of the	70,07	Sill, Fille	150				
B. 1 g/k	kg glyphos	ate tr	eatment		Kect.	orogon/	od sile	ion id					
				(1)	(S. 17) (S.)	Willow St	III	illo					
Male:	M0002	50	48(50)	0	160 (		S 0 0	0	0	0	0	2	
	M0005	50	47(49)	JI ONE		(20°)	( O )	0	0	0	1	2	
	M0007	50	45(49)	એ <b>ું</b>	100 09/1	(1)0 ×	0 0	0	0	0	1	4	
	8000M	50	41(47)	30 81	_	<i>\</i> 00000	1	0	0	0	3	6	
	M0009	50	45(49)	40 W	0//	0'0	1	1	0	0	0	4	
	M0011	50	46(49)		3/10/0	0	0	0	0	0	1	3	
Female:	F0001	50	47(48)	9,00	0	0	0	0	0	0	2	1	
	F0005	50	43(49)	60	0	0	0	0	0	0	1	6	
	F0008	× 50°	45(49)	, © O	0	0	0	0	0	0	1	4	
	F0009	50	44(47)	<u>``</u> 0	0	0	1	0	0	0	2	3	
	F0012	Ø 50°	46(49)	0	0	0	0	1	0	0	0	4 3 3 5	
	F0014	50	44(49)	0	0	0	1	0	0	0	0	5	
	N NO X	D Co 1	11. 10.										

Animal Number

BNo. of Cells Scored CNormal (Normal + Aneuploid)

DDicentric

ERing

ERing FChromosome Deletions

GChromatid Deletions

HIsochromatid Deletions

IChromatid Interchanges JChromatid Intrachanges

KAchromatic Lesions LAneuploid

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Table 2 Chromosomal Aberration Frequencies Observed at the 12 hr Sampling Time

- <del></del>	A	В	C	D	E	F	G	H	1	J	K	L	
A. Solv	ent Contro	<u> </u>									0 1 1 0	1914.	
Male:	M0032	50	47(50)	0	0	0	0	0	0	0	(a) (b)	3	
	M0033	~ ~	10/101	_	^	_	^	_	Ō	0.4	,00 1	3	
	M0038	50	43(48)	Ô	Ô	7	Ô	0	Ô	ંલ	1	5	
	M0041	50	47(50)	Ö	Ö	ō	Õ	ō	0 0	O O	Ö.	5° 3	
	M0043	50	49(50)	Ō	Ō	Ď	Ō	Ō	acil)	. 60	0	1	
	M0045	50	48(50)	Ŏ	Ö	ŏ	Ö	ŏ,	.000 r	0	100	2	
Female:	F0026	50	46(49)	0	0	0	0	. OS :	ililo	Ö	1	3	
	F0028	50	44(47)	0	0	0	1	3000°	`(O)	t <sub>2</sub> ,0	0	3	
	F0029	50	43(50)	0	0	0	00	000	0)	0	0	7	
	F0039	50	47(50)	0	0	0	100	0	S Ô	Ø.	0	3	
	F0040	25	20(25)	0	0	0,0	00%	COM	Ø	W O	0	5	
	F0045	50	40(50)	0	0	(O)	1000	ઁ <b>૦</b> ૦ે (	3N QS	0	0	10	
					, O	ine in	2000	UA THE	SOI				
B. <u>1 g/l</u>	cg glyphos	ate tr	46(49) 43(48) 47(50) 48(50) 48(50) 46(49) 44(47) 43(50) 47(50) 20(25) 40(50)  eatment  47(49) 42(48) 42(49) 49(50) 44(49) 45(48) 48(50) 22(25) 46(49)		stect to	Sioble of	ig allo	10,40					
Male:	M0012	50	47(49)	0111	~;;;o.	Julio Brill	110,10	0	0	0	1	2	
	M0013	50	42(48)	11000	0.	000	9	1	0	0	1	6	
	M0015	50	42(49)	00	<sub>96,</sub> 0/0,	6	0	Ō	Ō	Ö	ī	7	
	M0016	50	49(49)	( D. D. 1)	ે જે0	ON B ON	Ö	ì	Ō	Ō	ō	Ö	
	M0018	50	49(50)	` (°0)	Oil	O	Ō	ō	0	ō	ō	i	
	M0022	50	44(49)	184 Oct.	100%	0	1	0	0	0	0	1 5	
Female:	E0010	E0 .	20 10 10 V	of or the	00 D	_	_	_	_	_	_		
remare:	F0019	50	42(48)	. S. J. C	0	0	0	1	0	0	1	4	
	F0025	50	× 48(50)	11. 00.	0	0	0	O	0	0	0	2	
	F0027	S2731	22(25)	0	0	0	0	0	0	0	3	4	
	F0030	50	46(49)	0	0	0	0	0	0	0	1	3	
	F0032	50	45(48)	0	0	0	1	0	0	0	1	3 3 5	
	F0033	50,0	45(50)	0	0	0	0	0	0	0	0	5	
	VI V V	5 1 6 7 8											

AAnimal Number
BNo. of Cells Scored
CNormal (Normal + Aneuploid)

D<sub>Dicentric</sub>

ERing

Chromosome Deletions

GChromatid Deletions

HIsochromatid Deletions

IChromatid Interchanges

JChromatid Intrachanges

KAchromatic Lesions

LAneuploid

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Table 3 Chromosomal Aberration Frequencies Observed at the 24 hr Sampling Time

A. Solve	ent Contro	<u>,1</u>										10
Male:	M0048	50	48(50)	0	0	0	0	0	0	0	\d)	
	M0049	50	45(48)	n	0	n	3	0	0	0 .	( <sup>O</sup> 1	
	M0056	50	45(50)	Ô	Ô	Ô	õ	Ô	Õ	as)	Ô	
	M0058	50	46(50)	0	0	n	ñ	0	0	200	Ô	.6
	M0059	50	40(50)	0	0	0	0	0	n d	Miles.	0.8	0.
-	M0059	50 50	40(JU) 45(49)	0	0	0	0	0	20	NINO.	9000	
	MOUBU	30	43(46)	U	U	U	U	ي ر	6,6	jo u	Onz	
Female:	F0048	33	32(33)	0	0	0	0	05	0	0//0	0	
	F0054	50	46(50)	n	Ō	Ô	ñ	~ 20. c.	J. We.	490	n	
	F0056	50	48(49)	0	n	ñ	0.0	C dila	000	, O	Ô	
	F0057	50	40(43)	Ô	0	0	( D) .	11/19		0.4	1	
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B. <u>1 g/k</u>	g glyphos	ate	45(50) 46(50) 48(50) 45(48) 32(33) 4. (50) 48(49) 40(48) 26(29) 43(50) 9(10) 3(5) 26(27) 49(49) 43(49) 47(50) 45(48) 46(49) 40(46) 46(50) 43(48) 47(48)	Ū	offect.	orobeity	data d	on of the	nis of in	J 000000 0000 0000	Ü	
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Table 3 (Cont.)

Chromosomal Aberration Frequencies Observed at the 24 hr Sampling Time

C. Positive Control (25 mg/kg cyclophosphamide)  Male: M0046 50 21(25) 0 0 0 25 13 25 1 5 M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	C. Positive Control (25 mg/kg cyclophosphamide)  Male: M0046 50 21(25) 0 0 0 25 13 25 1 5 M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 0 F0043 6 6(6) 0 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	C. Positive Control (25 mg/kg cyclophosphamide)  Male: M0046 50 21(25) 0 0 0 25 13 25 1 5 M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Male: M0046 50 21(25) 0 0 0 25 13 25 1 5 M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 0 F0054 4 0(0) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0								25 8 22 19 40 24	13 5 8 6 25 22	25 2 7 7 20 15	1 1 0 0 0 3 1	5 3 2 4 9
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M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 F0043 6 6(6) 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 10 4 1 0 2 F0053 1 0(0) 0 0 0 0 0 0 0 0 1 F0059 8 8(8) 0 0 0 0 0 0 0 0 0 0  Annimal Number BNo. of Cells Scored CNormal (Normal + Aneuploid) Dicentric ERing FChromosome Deletions GChromatid Interchanges KAchromatid Interchanges KAchromatic Lesions LAneuploid  CCNTAINS TRADE SECKET CK OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY	M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 0 F0059 8 8(8) 0 0 0 0 0 0 0 0 0  Animal Number BNo. of Cells Scored CNormal (Normal + Aneuploid) Dicentric ERing FChromatid Deletions Ichromatid Interchanges JChromatid Interchanges JChromatid Interchanges KAchromatic Lesions LAneuploid  CCNTAINS TRADE SECKET CR OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY	M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 022 8 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 0 F0043 6 6(6) 0 0 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 10 4 1 0 2 F0053 1 0(0) 0 0 0 0 0 0 0 0 0 0 F0059 8 8(8) 0 0 0 0 0 0 0 0 0 0  Animal Number BNo. of Cells Scored CNormal (Normal + Aneuploid) Dicentric ERing FChromosome Deletions GChromatid Interchanges JChromatid Interchanges JChromatid Interchanges JChromatid Intrachanges KAchromatic Lesions LAneuploid  CONTAINS TRADE SECRET CR OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY	M0047 23 13(14) 0 0 0 8 5 2 1 3 M0050 50 30(35) 0 0 0 22 8 7 0 2 M0051 50 31(35) 0 0 0 19 6 7 0 4 M0053 51 24(28) 0 0 0 40 25 20 3 9 M0054 32 10(11) 0 0 0 24 22 15 1 11  Female: F0041 1 0(1) 0 0 0 0 0 0 0 0 0 0 F0043 6 6(6) 0 0 0 0 0 0 0 0 0 F0047 1 1(1) 0 0 0 0 0 0 0 0 0 0 F0050 4 0(0) 0 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 F0053 1 0(0) 0 0 0 0 0 0 0 0 F0059 8 8(8) 0 0 0 0 0 0 0 0 0  Annimal Number BNo. of Cells Scored CNormal (Normal + Aneuploid) Dicentric ERing FChromosome Deletions GChromatid Deletions IIsochromatid Deletions IChromatid Intrachanges JChromatid Intrachanges JChromatid Intrachanges JChromatid Intrachanges KAchromatic Lesions LAneuploid  CONTAINS TRADE SECRET CA OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY	Female:  Animal Num BNo. of Ce	M0047 M0050 M0051 M0053 M0054 F0041 F0043 F0047 F0050 F0053 F0059	23 50 50 51 32 1 6	13(14) 30(35) 31(35) 24(28) 10(11) 0(1) 6(6) 1(1)	0 0 0 0 0 0 0 0 0	0 0 0 0	0 0 0 0	8 22 19 40 24	5 8 6 25 22	2 7 7 20 15	1 0 0 0 3 1	3 2 4 9
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