

Experiment Number: 813361

Test Type: Genetic Toxicology - Micronucleus

Route: Intraperitoneal Injection

Species/Strain: Mouse/B6C3F1

**G04: In Vivo Micronucleus Summary Data**

Test Compound: Cyclophosphamide monohydrate

CAS Number: 6055-19-2

Date Report Requested: 09/19/2018

Time Report Requested: 20:26:13

**NTP Study Number:**

813361

**Study Duration:**

72 Hours

**Study Methodology:**

Slide Scoring

**Male Study Result:**

Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 1; Time interval between final treatment and cell sampling: 24 h

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	2.70 ± 0.37		43.70 ± 3.94
Vehicle Control <sup>1</sup>	5	2.70 ± 0.37		43.70 ± 3.94
9.375	5	11.50 ± 1.30	< 0.001 *	35.20 ± 8.16
9.375	5	11.50 ± 1.30	< 0.001 *	35.20 ± 8.16
18.75	5	18.20 ± 1.87	< 0.001 *	43.20 ± 5.13
18.75	5	18.20 ± 1.87	< 0.001 *	43.20 ± 5.13
37.5	5	18.20 ± 2.63	< 0.001 *	33.20 ± 5.08
37.5	5	18.20 ± 2.63	< 0.001 *	33.20 ± 5.08
75.0	5	23.00 ± 2.22	< 0.001 *	28.60 ± 2.50
75.0	5	23.00 ± 2.22	< 0.001 *	28.60 ± 2.50

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	2.30 ± 0.46		31.00 ± 3.71
Vehicle Control <sup>1</sup>	5	2.30 ± 0.46		31.00 ± 3.71
1.875	5	4.00 ± 0.16	0.0160	26.10 ± 3.62
1.875	5	4.00 ± 0.16	0.0160	26.10 ± 3.62
3.75	5	8.80 ± 1.63	< 0.001 *	35.30 ± 1.64
3.75	5	8.80 ± 1.63	< 0.001 *	35.30 ± 1.64
7.5	5	7.10 ± 1.20	< 0.001 *	33.00 ± 3.98
7.5	5	7.10 ± 1.20	< 0.001 *	33.00 ± 3.98
15.0	5	18.20 ± 1.24	< 0.001 *	27.70 ± 1.25
15.0	5	18.20 ± 1.24	< 0.001 *	27.70 ± 1.25

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 1; Time interval between final treatment and cell sampling: 48 h

Dose (mg/kg)	N	MN PCE/1000		% PCE	
		Mean ± SEM	p-Value	Mean ± SEM	
Vehicle Control <sup>1</sup>	5	1.80 ± 0.12		47.80 ± 2.01	
Vehicle Control <sup>1</sup>	5	1.80 ± 0.12		47.80 ± 2.01	
9.375	5	5.20 ± 0.75	< 0.001 *	32.70 ± 5.36	
9.375	5	5.20 ± 0.75	< 0.001 *	32.70 ± 5.36	
18.75	5	15.40 ± 1.65	< 0.001 *	42.60 ± 3.82	
18.75	5	15.40 ± 1.65	< 0.001 *	42.60 ± 3.82	
37.5	5	22.30 ± 1.07	< 0.001 *	26.80 ± 2.84	
37.5	5	22.30 ± 1.07	< 0.001 *	26.80 ± 2.84	
75.0	5	39.20 ± 3.12	< 0.001 *	18.40 ± 2.32	
75.0	5	39.20 ± 3.12	< 0.001 *	18.40 ± 2.32	

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 1; Time interval between final treatment and cell sampling: 48 h

Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	2.20 ± 0.25		30.70 ± 3.07
Vehicle Control <sup>1</sup>	5	2.20 ± 0.25		30.70 ± 3.07
1.875	5	3.00 ± 0.59	0.1333	25.60 ± 2.62
1.875	5	3.00 ± 0.59	0.1333	25.60 ± 2.62
3.75	5	7.40 ± 0.53	< 0.001 *	26.50 ± 3.09
3.75	5	7.40 ± 0.53	< 0.001 *	26.50 ± 3.09
7.5	5	12.40 ± 1.62	< 0.001 *	30.60 ± 4.77
7.5	5	12.40 ± 1.62	< 0.001 *	30.60 ± 4.77
15.0	5	28.60 ± 3.18	< 0.001 *	21.90 ± 3.47
15.0	5	28.60 ± 3.18	< 0.001 *	21.90 ± 3.47

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 3; Time interval between final treatment and cell sampling: 24 h

Dose (mg/kg)	N	MN PCE/1000		% PCE	
		Mean ± SEM	p-Value	Mean ± SEM	
Vehicle Control <sup>1</sup>	5	2.60 ± 0.33		36.20 ± 2.70	
Vehicle Control <sup>1</sup>	5	2.60 ± 0.33		36.20 ± 2.70	
9.375	5	10.70 ± 1.46	< 0.001 *	26.00 ± 2.82	
9.375	5	10.70 ± 1.46	< 0.001 *	26.00 ± 2.82	
37.5	3	34.83 ± 4.18	< 0.001 *	39.00 ± 2.02	
37.5	3	34.83 ± 4.18	< 0.001 *	39.00 ± 2.02	
75.0	5	35.20 ± 1.72	< 0.001 *	7.60 ± 0.87	
75.0	5	35.20 ± 1.72	< 0.001 *	7.60 ± 0.87	

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	3.60 ± 0.48		34.70 ± 4.74
Vehicle Control <sup>1</sup>	5	3.60 ± 0.48		34.70 ± 4.74
1.875	5	5.10 ± 0.80	0.2286	26.00 ± 5.86
1.875	5	5.10 ± 0.80	0.2286	26.00 ± 5.86
3.75	5	7.90 ± 1.33	0.0318	21.40 ± 2.71
3.75	5	7.90 ± 1.33	0.0318	21.40 ± 2.71
7.5	5	16.90 ± 2.53	< 0.001 *	21.10 ± 1.44
7.5	5	16.90 ± 2.53	< 0.001 *	21.10 ± 1.44
15.0	5	19.50 ± 5.44	< 0.001 *	7.70 ± 1.14
15.0	5	19.50 ± 5.44	< 0.001 *	7.70 ± 1.14

Trend p-Value

< 0.001 \*

Trial Summary: Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 1; Time interval between final treatment and cell sampling: 24 h

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	1.90 ± 0.51		31.70 ± 3.48
25.0	5	13.50 ± 2.74	< 0.001 *	32.20 ± 1.79
50.0	5	14.10 ± 2.50	< 0.001 *	33.10 ± 4.21
100.0	5	10.40 ± 2.09	< 0.001 *	25.50 ± 3.10
Trend p-Value		0.0100 *		

Trial Summary: Positive

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Tissue: Bone marrow; Sex: Male; Number of Treatments: 1; Time interval between final treatment and cell sampling: 48 h

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>1</sup>	5	1.90 ± 0.43		30.50 ± 3.08
25.0	5	21.70 ± 2.47	< 0.001 *	25.00 ± 1.85
50.0	4	42.50 ± 8.22	< 0.001 *	16.75 ± 2.36
100.0	5	37.60 ± 4.77	< 0.001 *	15.90 ± 2.23
Trend p-Value		< 0.001 *		

---

Trial Summary: Positive

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		MN PCE/1000		% PCE	
Dose (mg/kg)	N	Mean ± SEM	p-Value	Mean ± SEM	
Vehicle Control <sup>2</sup>	5	0.90 ± 0.33		24.70 ± 2.96	
25.0	4	16.13 ± 6.52	< 0.001 *	12.88 ± 3.35	
Trend p-Value		< 0.001 *			

Trial Summary: Positive

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		MN PCE/1000		% PCE	
Dose (mg/kg)	N	Mean ± SEM	p-Value	Mean ± SEM	
Vehicle Control <sup>2</sup>	5	1.30 ± 0.34		40.40 ± 1.22	
25.0	5	8.00 ± 1.92	< 0.001 *	34.70 ± 2.55	
50.0	4	15.38 ± 1.42	< 0.001 *	40.25 ± 1.39	
100.0	5	17.80 ± 2.64	< 0.001 *	36.50 ± 2.06	
Trend p-Value		< 0.001 *			

Trial Summary: Positive

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Dose (mg/kg)	N	MN PCE/1000	p-Value	% PCE
		Mean ± SEM		Mean ± SEM
Vehicle Control <sup>2</sup>	5	1.50 ± 0.27		24.10 ± 4.65
25.0	5	23.40 ± 1.53	< 0.001 *	21.00 ± 2.86
50.0	5	29.30 ± 1.30	< 0.001 *	15.70 ± 2.96
100.0	5	22.20 ± 3.04	< 0.001 *	21.30 ± 2.54
Trend p-Value		< 0.001 *		

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Trial Summary: Positive

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	MN PCE/1000		% PCE
Dose (mg/kg)	N	Mean ± SEM	Mean ± SEM
Vehicle Control <sup>1</sup>	5	0.90 ± 0.24	26.50 ± 2.56

Trend p-Value < 0.001 \*

Trial Summary: Positive

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LEGEND

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MN = micronucleated, PCE = polychromatic erythrocyte, NCE = normochromatic erythrocyte

CAS Number = Chemical Abstracts Service registry number

N = Number of subjects

Values given as Mean or Mean  $\pm$  Standard Error Mean

Results were tabulated as the mean of the pooled results from all animals within a treatment group, plus or minus the standard error of the mean

Pairwise comparison to the concurrent control, dosed groups significant at  $p = 0.025/\text{number of treatment groups}$ ; positive control value is significant at  $p = 0.05$

Cochran-Armitage trend test, significant at  $p = 0.025$

\* Statistically significant pairwise or trend test

1: Vehicle Control: Phosphate Buffered Saline

2: Vehicle Control: Corn Oil

**\*\* END OF REPORT \*\***