

**Study Number:** C00058B-04

**Test Type:** TOX

**Route:** Oral Gavage

**Species/Strain:** Mouse/B6C3F1/N

**C Number:**

**Study Gender:**

**PWG Approval Date**

**PA43: Hematology Summary**

**Test Compound:** Black Cohosh

**CAS Number:** 84776-26-1

C00058B-04

Female

See web page for date of PWG Approval

**Date Report Requested:** 10/31/2018

**Time Report Requested:** 11:56:07

**Lab:** NTP

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**Female: 3-Month Interim Fem**

	Phase Day	Treatment Groups (mg/kg)			
		0	30	100	300
Hematocrit (%)	SD 92	55.6 ± 1.2 (9)	56.3 ± 1.0 (10)	57.0 ± 1.6 (10)	56.5 ± 1.6 (10)
Percent of Control			101.2	102.4	101.7
Manual Hematocrit (%)	SD 92	53.2 ± 1.2 (9)	53.7 ± 1.3 (10)	54.2 ± 1.7 (10)	54.9 ± 1.6 (10)
Percent of Control			100.9	101.8	103.2
Hemoglobin (g/dL)	SD 92	17.1 ± 0.3 (9)	17.5 ± 0.3 (10)	17.7 ± 0.5 (10)	17.7 ± 0.5 (10)
Percent of Control			102.3	103.3	103.6
Erythrocytes (10 <sup>6</sup> /uL)	SD 92	11.42 ± 0.21 (9) **	11.42 ± 0.21 (10)	11.24 ± 0.30 (10)	10.76 ± 0.27 (10)
Percent of Control			99.92	98.34	94.18
Reticulocytes (10 <sup>3</sup> /uL)	SD 92	272.8 ± 11.8 (9)	275.7 ± 15.9 (10)	293.8 ± 14.5 (10)	282.2 ± 10.5 (10)
Percent of Control			101.1	107.7	103.5
Mean Cell Volume (fL)	SD 92	48.7 ± 0.2 (9) **	49.4 ± 0.2 (10) *	50.7 ± 0.2 (10) **	52.5 ± 0.3 (10) **
Percent of Control			101.4	104.2	107.9
Mean Cell Hemoglobin (pg)	SD 92	15.0 ± 0.1 (9) **	15.3 ± 0.0 (10) **	15.7 ± 0.0 (10) **	16.5 ± 0.2 (10) **
Percent of Control			102.3	105.1	110.2
Mean Cell Hemoglobin Concentration (g/dL)	SD 92	30.8 ± 0.2 (9)	31.1 ± 0.1 (10)	31.0 ± 0.1 (10)	31.4 ± 0.3 (10)
Percent of Control			100.8	100.8	101.9
Platelets (10 <sup>3</sup> /uL)	SD 92	803 ± 65 (9)	710 ± 39 (10)	662 ± 47 (10)	652 ± 50 (10)
Percent of Control			88	82	81
White Blood Cells (10 <sup>3</sup> /uL)	SD 92	4.45 ± 0.45 (9) **	3.95 ± 0.31 (10)	3.25 ± 0.19 (10)	3.61 ± 0.43 (10)
Percent of Control			88.88	72.96	81.19
Neutrophils (10 <sup>3</sup> /uL)	SD 92	0.62 ± 0.07 (9) **	0.51 ± 0.06 (10)	0.41 ± 0.04 (10) *	0.38 ± 0.04 (10) *
Percent of Control			83.05	66.57	61.40

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	Phase Day	Treatment Groups (mg/kg)			
		0	30	100	300
Lymphocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	3.66 ± 0.39 (9) **	3.28 ± 0.25 (10) 89.56	2.71 ± 0.15 (10) 73.98	3.14 ± 0.39 (10) 85.76
Total Lymphocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	3.67 ± 0.40 (9) **	3.29 ± 0.25 (10) 89.59	2.71 ± 0.15 (10) 73.88	3.15 ± 0.39 (10) 85.73
Monocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.09 ± 0.01 (9) **	0.07 ± 0.01 (10) 85.38	0.08 ± 0.02 (10) 92.31	0.04 ± 0.01 (10) ** 41.54
Basophils (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.02 ± 0.00 (9)	0.02 ± 0.00 (10) 114.00	0.01 ± 0.00 (10) 66.00	0.02 ± 0.00 (10) 114.00
Eosinophils (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.05 ± 0.01 (9)	0.06 ± 0.02 (10) 107.23	0.03 ± 0.01 (10) 55.53	0.03 ± 0.01 (10) 57.45
Large Unstained Cells (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.02 ± 0.00 (9)	0.02 ± 0.00 (10) 96.43	0.01 ± 0.00 (10) 51.43	0.01 ± 0.00 (10) 77.14

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**Female: 3-Month Interim Fem**

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	<b>Phase Day</b>	<b>Treatment Groups</b>
		<b>1000</b>
Hematocrit (%)	SD 92	53.4 ± 1.0 (10)
Percent of Control		96.0
Manual Hematocrit (%)	SD 92	51.2 ± 1.4 (10)
Percent of Control		96.2
Hemoglobin (g/dL)	SD 92	16.4 ± 0.3 (10)
Percent of Control		95.8
Erythrocytes (10 <sup>6</sup> /uL)	SD 92	9.73 ± 0.19 (10) **
Percent of Control		85.19
Reticulocytes (10 <sup>3</sup> /uL)	SD 92	255.5 ± 17.6 (10)
Percent of Control		93.7
Mean Cell Volume (fL)	SD 92	54.9 ± 0.3 (10) **
Percent of Control		112.7
Mean Cell Hemoglobin (pg)	SD 92	16.9 ± 0.1 (10) **
Percent of Control		112.7
Mean Cell Hemoglobin Concentration (g/dL)	SD 92	30.7 ± 0.1 (10)
Percent of Control		99.7
Platelets (10 <sup>3</sup> /uL)	SD 92	748 ± 60 (10)
Percent of Control		93
White Blood Cells (10 <sup>3</sup> /uL)	SD 92	2.85 ± 0.36 (10) **
Percent of Control		64.11
Neutrophils (10 <sup>3</sup> /uL)	SD 92	0.42 ± 0.12 (10) **
Percent of Control		67.70

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**Female: 3-Month Interim Fem**

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	<b>Phase Day</b>	<b>Treatment Groups</b>
		<b>1000</b>
Lymphocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	2.32 ± 0.25 (10) ** 63.43
Total Lymphocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	2.33 ± 0.25 (10) ** 63.40
Monocytes (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.05 ± 0.01 (10) ** 60.00
Basophils (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.01 ± 0.00 (10) 78.00
Eosinophils (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.04 ± 0.01 (10) 76.60
Large Unstained Cells (10 <sup>3</sup> /uL) Percent of Control	SD 92	0.01 ± 0.00 (10) 57.86

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Female: 1-Year Interim Fem

	Phase Day	Treatment Groups (mg/kg)			
		0	30	100	300
Hematocrit (%)	SD 365	52.5 ± 0.6 (10) **	51.2 ± 0.5 (10) *	51.3 ± 0.6 (10) *	49.6 ± 0.6 (10) **
Percent of Control			97.6	97.7	94.6
Manual Hematocrit (%)	SD 365	51.4 ± 0.8 (10) *	48.9 ± 1.0 (9)	48.9 ± 1.2 (10)	48.5 ± 1.2 (10)
Percent of Control			95.1	95.1	94.4
Hemoglobin (g/dL)	SD 365	15.4 ± 0.2 (10) **	15.3 ± 0.1 (10)	15.2 ± 0.2 (10)	14.8 ± 0.2 (10) *
Percent of Control			98.9	98.7	95.7
Erythrocytes (10 <sup>6</sup> /uL)	SD 365	10.34 ± 0.10 (10) **	10.02 ± 0.10 (10) *	9.77 ± 0.16 (10) **	9.22 ± 0.13 (10) **
Percent of Control			96.91	94.45	89.21
Reticulocytes (10 <sup>3</sup> /uL)	SD 365	247.4 ± 16.6 (10)	290.0 ± 25.0 (10)	276.6 ± 14.9 (10)	230.8 ± 15.0 (10)
Percent of Control			117.2	111.8	93.3
Mean Cell Volume (fL)	SD 365	50.7 ± 0.3 (10) **	51.1 ± 0.2 (10)	52.6 ± 0.4 (10) **	53.8 ± 0.3 (10) **
Percent of Control			100.7	103.6	106.1
Mean Cell Hemoglobin (pg)	SD 365	14.9 ± 0.1 (10) **	15.2 ± 0.1 (10) *	15.6 ± 0.1 (10) **	16.0 ± 0.1 (10) **
Percent of Control			102.1	104.8	107.3
Mean Cell Hemoglobin Concentration (g/dL)	SD 365	29.4 ± 0.1 (10)	29.8 ± 0.2 (10)	29.7 ± 0.2 (10)	29.7 ± 0.2 (10)
Percent of Control			101.4	101.1	101.2
Platelets (10 <sup>3</sup> /uL)	SD 365	789 ± 40 (10)	768 ± 27 (10)	714 ± 42 (10)	715 ± 64 (10)
Percent of Control			97	91	91
Mean Platelet Volume (fL)	SD 365	6.6 ± 0.2 (10)	6.2 ± 0.2 (10)	7.0 ± 0.2 (10)	6.4 ± 0.3 (10)
Percent of Control			93.8	107.2	97.6
White Blood Cells (10 <sup>3</sup> /uL)	SD 365	4.02 ± 0.35 (10)	3.65 ± 0.27 (10)	3.39 ± 0.23 (10)	3.89 ± 0.28 (10)
Percent of Control			90.96	84.46	96.84

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**Female: 1-Year Interim Fem**

	Phase Day	Treatment Groups (mg/kg)			
		0	30	100	300
Neutrophils (10 <sup>3</sup> /uL)	SD 365	0.80 ± 0.07 (10)	0.57 ± 0.09 (10) *	0.57 ± 0.04 (10)	0.66 ± 0.04 (10)
Percent of Control			70.89	71.02	82.18
Lymphocytes (10 <sup>3</sup> /uL)	SD 365	3.05 ± 0.30 (10)	2.95 ± 0.19 (10)	2.75 ± 0.22 (10)	3.07 ± 0.23 (10)
Percent of Control			96.82	90.12	100.59
Total Lymphocytes (10 <sup>3</sup> /uL)	SD 365	3.05 ± 0.30 (10)	2.96 ± 0.19 (10)	2.75 ± 0.22 (10)	3.08 ± 0.23 (10)
Percent of Control			96.99	90.14	100.85
Monocytes (10 <sup>3</sup> /uL)	SD 365	0.10 ± 0.03 (10)	0.10 ± 0.03 (10)	0.06 ± 0.02 (10)	0.11 ± 0.01 (10)
Percent of Control			93.14	54.90	103.92
Basophils (10 <sup>3</sup> /uL)	SD 365	0.00 ± 0.00 (10)	0.00 ± 0.00 (10)	0.00 ± 0.00 (10)	0.00 ± 0.00 (10)
Percent of Control			200.00	100.00	300.00
Eosinophils (10 <sup>3</sup> /uL)	SD 365	0.06 ± 0.04 (10)	0.03 ± 0.01 (10)	0.02 ± 0.01 (10)	0.05 ± 0.01 (10)
Percent of Control			47.62	28.57	73.02
Large Unstained Cells (10 <sup>3</sup> /uL)	SD 365	0.00 ± 0.00 (10)	0.01 ± 0.00 (10)	0.00 ± 0.00 (10)	0.01 ± 0.00 (10)
Percent of Control			225.00	100.00	300.00

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**Female: 1-Year Interim Fem**

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		Treatment Groups	
	Phase Day	1000	
Hematocrit (%)	SD 365	50.1 ± 0.4	(10) **
Percent of Control		95.5	
Manual Hematocrit (%)	SD 365	48.4 ± 1.3	(10)
Percent of Control		94.2	
Hemoglobin (g/dL)	SD 365	14.9 ± 0.1	(10) *
Percent of Control		96.7	
Erythrocytes (10 <sup>6</sup> /uL)	SD 365	9.00 ± 0.08	(10) **
Percent of Control		87.01	
Reticulocytes (10 <sup>3</sup> /uL)	SD 365	256.9 ± 22.5	(10)
Percent of Control		103.8	
Mean Cell Volume (fL)	SD 365	55.7 ± 0.2	(10) **
Percent of Control		109.7	
Mean Cell Hemoglobin (pg)	SD 365	16.6 ± 0.1	(10) **
Percent of Control		111.3	
Mean Cell Hemoglobin Concentration (g/dL)	SD 365	29.8 ± 0.1	(10)
Percent of Control		101.4	
Platelets (10 <sup>3</sup> /uL)	SD 365	671 ± 52	(10)
Percent of Control		85	
Mean Platelet Volume (fL)	SD 365	6.4 ± 0.2	(10)
Percent of Control		98.2	
White Blood Cells (10 <sup>3</sup> /uL)	SD 365	3.58 ± 0.44	(10)
Percent of Control		89.24	



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**Female: 1-Year Interim Fem**

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		<b>Treatment Groups</b>
	<b>Phase Day</b>	<b>1000</b>
Neutrophils (10 <sup>3</sup> /uL)	SD 365	0.71 ± 0.09 (10)
Percent of Control		89.21
Lymphocytes (10 <sup>3</sup> /uL)	SD 365	2.74 ± 0.35 (10)
Percent of Control		89.99
Total Lymphocytes (10 <sup>3</sup> /uL)	SD 365	2.75 ± 0.35 (10)
Percent of Control		90.20
Monocytes (10 <sup>3</sup> /uL)	SD 365	0.06 ± 0.01 (10)
Percent of Control		62.75
Basophils (10 <sup>3</sup> /uL)	SD 365	0.00 ± 0.00 (10)
Percent of Control		200.00
Eosinophils (10 <sup>3</sup> /uL)	SD 365	0.05 ± 0.01 (10)
Percent of Control		80.95
Large Unstained Cells (10 <sup>3</sup> /uL)	SD 365	0.01 ± 0.00 (10)
Percent of Control		250.00

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#### LEGEND

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Values given as mean  $\pm$  SEM (N) with Percent of Control calculated by (dosed group mean / control group mean) x 100

SD – Study Day; GD – Gestation Day; LD – Lactation Day; PND – Postnatal Day, adults post-weaning

Hematology for gestation phase includes pregnant females only

Statistical analysis performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests (unless otherwise noted).

Statistical significance for the control group indicates a significant trend test

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

\* Statistically significant at  $P \leq 0.05$

\*\* Statistically significant at  $P \leq 0.01$

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