Hypothesis test results for analysis of estrous cyclicity using the continuous-time Markov model (F1 generation)

Stage[a]	Comparison[b]	p-value[c]	Significance[d]	Stage Length Difference[e] (days)
Diestrus	Low-Control	1.000	None	0.1
Diestrus	Mid-Control	0.109	None	0.6
Diestrus	High-Control	< 0.001	p < 0.01	-2.2
Proestrus	Low-Control	0.323	None	-0.1
Proestrus	Mid-Control	0.516	None	0.1
Proestrus	High-Control	< 0.001	p < 0.01	0.3
Estrus	Low-Control	0.658	None	-0.1
Estrus	Mid-Control	1.000	None	-0.0
Estrus	High-Control	< 0.001	p < 0.01	11.7

a: Insufficient data to evaluate metestrus stage.

b: Sample sizes for the Control, Low, Mid, and High dose groups respectively were *n* = 53, 55, 53, 47. Dose levels were 0, 338, 1125, 3750 ppm respectively.

c: The p-values shown were calculated using a permutation null hypothesis testing method and have been adjusted for multiple comparisons using a Hommel correction within each stage.

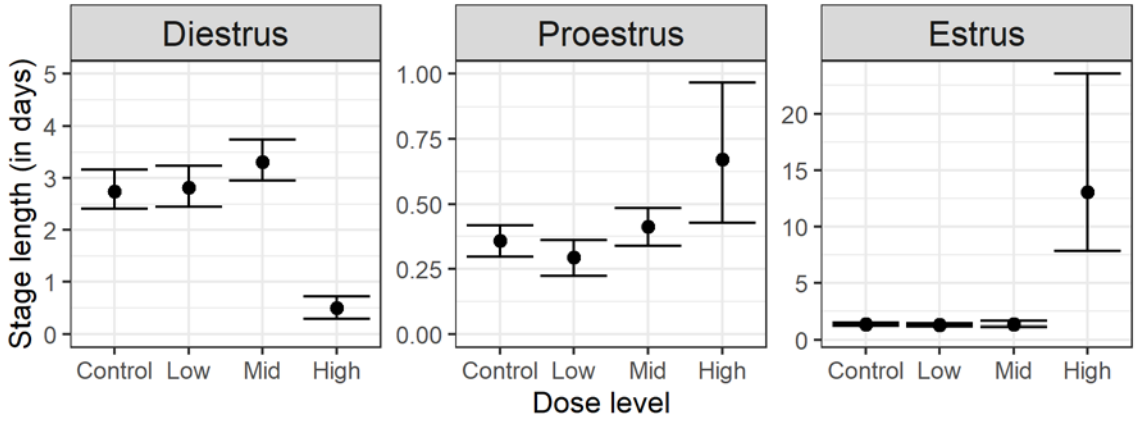
d: Significance is based on the adjusted p-value with a significance level of $\alpha = 0.05$.

e: A positive number indicates the estimated stage length in the treated group is longer than in the control group.

Markov model estimates of stage length and 95% confidence intervals (F1 generation)

	Control (0 ppm)		Low dose (338 ppm)		Mid dose (1125 ppm)		High dose (3750 ppm)	
	Stage Length (days)	95% CI	Stage Length (days)	95% CI	Stage Length (days)	95% CI	Stage Length (days)	95% CI
Diestrus	2.7	(2.4, 3.2)	2.8	(2.4, 3.2)	3.3	(3.0, 3.7)	0.5	(0.3, 0.7)
Proestrus	0.4	(0.3, 0.4)	0.3	(0.2, 0.4)	0.4	(0.3, 0.5)	0.7	(0.4, 1.0)
Estrus	1.4	(1.3, 1.5)	1.3	(1.2, 1.4)	1.4	(1.1, 1.7)	13.1	(7.8, 23.5)
Metestrus[a]	0.1	--	0.1	--	0.1	--	0.1	--

a: Due to a very low number of observations of metestrus, stage lengths were estimated using a profile likelihood approach. As a result, confidence intervals are not available for the metestrus stage length estimate.



Estimates of stage length shown as dots, with bars indicating 95% confidence intervals. Estimates for lengths of metestrus are not shown here due to very low numbers of observations of this stage.

Hypothesis test results for analysis of estrous cyclicity using the continuous-time Markov model (F2 generation)

Stage[a]	Comparison[b]	p-value[c]	Significance[d]	Stage Length Difference[e] (days)
Diestrus	Low-Control	1.000	None	0.1
Diestrus	Mid-Control	0.639	None	0.3
Proestrus	Low-Control	< 0.001	$p < 0.01$	-0.2
Proestrus	Mid-Control	0.205	None	-0.1
Estrus	Low-Control	0.010	$p < 0.05$	-0.2
Estrus	Mid-Control	0.444	None	-0.1

a: Insufficient data to evaluate metestrus stage.

b: Sample sizes for the Control, Low, and Mid dose groups respectively were *n* = 78, 77, 20. Dose levels were 0, 338, 1125 ppm respectively. No high dose group was analyzed for the F2 generation in this study.

c: The p-values shown were calculated using a permutation null hypothesis testing method and have been adjusted for multiple comparisons using a Hommel correction within each stage.

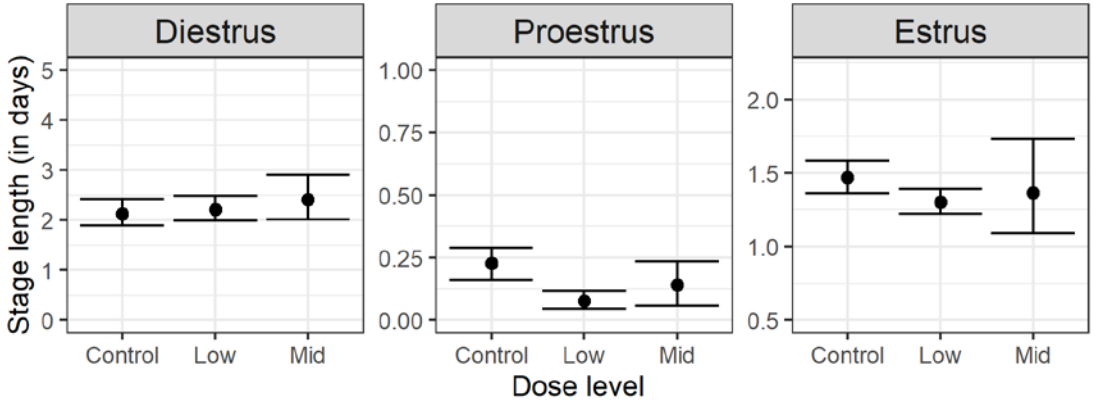
d: Significance is based on the adjusted p-value with a significance level of $\alpha = 0.05$.

e: A positive number indicates the estimated stage length in the treated group is longer than in the control group.

Markov model estimates of stage length and 95% confidence intervals (F2 generation)

	Control (0 ppm)		Low dose (338 ppm)		Mid dose (1125 ppm)	
	Stage Length (days)	95% CI	Stage Length (days)	95% CI	Stage Length (days)	95% CI
Diestrus	2.1	(1.9, 2.4)	2.2	(2.0, 2.5)	2.4	(2.0, 2.9)
Proestrus	0.2	(0.2, 0.3)	0.1	(0.0, 0.1)	0.1	(0.1, 0.2)
Estrus	1.5	(1.4, 1.6)	1.3	(1.2, 1.4)	1.4	(1.1, 1.7)
Metestrus[a]	0.2	--	0.2	--	0.2	--

a: Due to a very low number of observations of metestrus, stage lengths were estimated using a profile likelihood approach. As a result, confidence intervals are not available for the metestrus stage length estimate.



Estimates of stage length shown as dots, with bars indicating 95% confidence intervals. Estimates for lengths of metestrus are not shown here due to very low numbers of observations of this stage.