

Hypothesis test results for analysis of estrous cyclicity using the continuous-time Markov model

Stage ^a	Comparison ^b	p-value ^c	Significance ^d	Stage Length Difference ^e (days)
Diestrus	Low-Control	0.847	None	-0.1
Diestrus	Mid-Control	1.000	None	-0.0
Diestrus	High-Control	0.054	None	-0.3
Proestrus	Low-Control	1.000	None	0.0
Proestrus	Mid-Control	0.011	p < 0.05	-0.1
Proestrus	High-Control	0.469	None	0.1
Estrus	Low-Control	1.000	None	0.0
Estrus	Mid-Control	0.007	p < 0.01	0.2
Estrus	High-Control	0.119	None	0.2
Diestrus	Pos. Control - Control	0.550	None	0.1
Proestrus	Pos. Control – Control	0.438	None	0.0
Estrus	Pos. Control - Control	0.081	None	-0.1

a: Insufficient data to evaluate metestrus stage.

b: Sample sizes for the Control, Low, Mid, High dose, and positive control groups respectively were $n = 42, 40, 40, 30$. The positive control group was compared to control separately from the other treated groups, with no correction for multiple comparisons. Dose levels were 0, 3000, 10000, 30000 ppm respectively for the treated groups, and 0.05 ppm EE for the positive control group.

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 $\alpha = 0.05$.

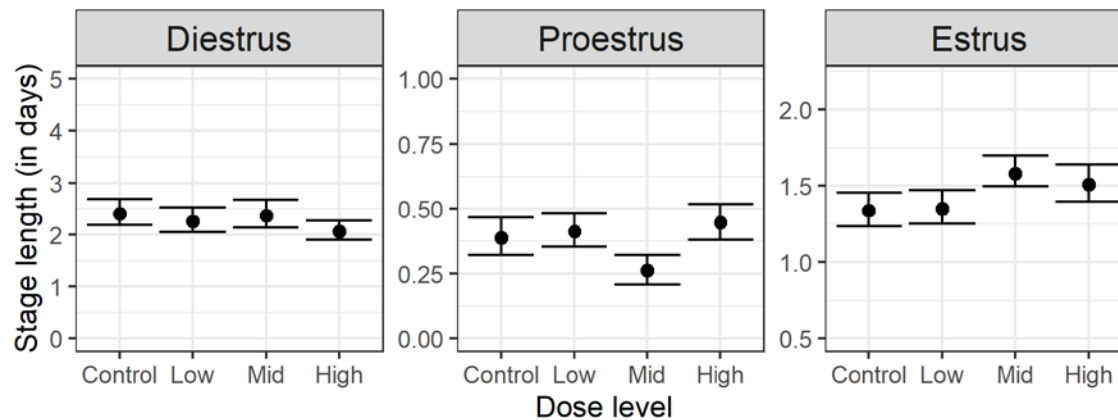
e: A positive number indicates the estimated stage length in the treated group is longer than in the control group.

Markov model estimates of stage length and 95% confidence intervals

Treated groups vs. control

	Control (0 ppm)		Low dose (3000 ppm)		Mid dose (10,000 ppm)		High dose (30,000 ppm)	
	Stage Length (days)	95% CI	Stage Length (days)	95% CI	Stage Length (days)	95% CI	Stage Length (days)	95% CI
Diestrus	2.4	(2.2, 2.7)	2.3	(2.0, 2.5)	2.4	(2.1, 2.7)	2.1	(1.9, 2.3)
Proestrus	0.4	(0.3, 0.5)	0.4	(0.3, 0.5)	0.3	(0.2, 0.3)	0.4	(0.4, 0.5)
Estrus	1.3	(1.2, 1.5)	1.4	(1.2, 1.5)	1.6	(1.5, 1.7)	1.5	(1.4, 1.6)
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.



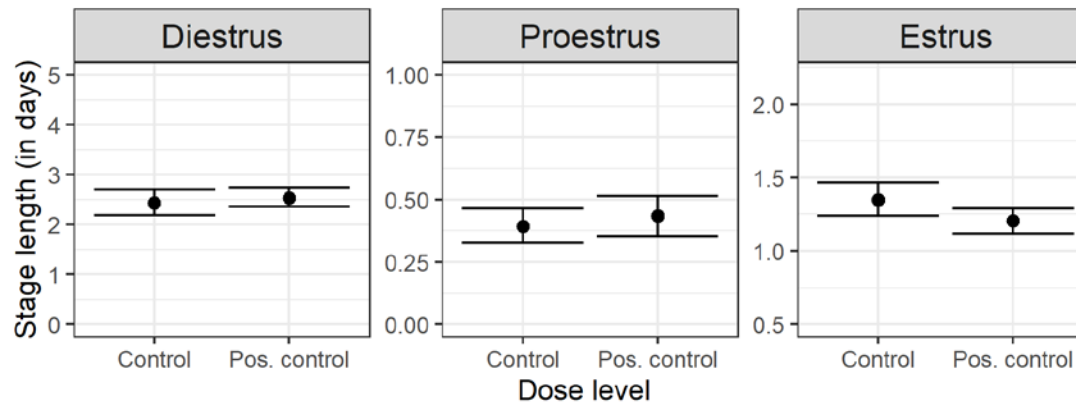
Estimates of stage length shown as dots, with bars indicating 95% confidence intervals. Estimates for lengths of metestrus are not shown here due to very low numbers of observations of this stage.

Markov model estimates of stage length and 95% confidence intervals

Positive control group vs. control

	Control (0 ppm)		Positive control (0.05 ppm EE)	
	Stage Length (days)	95% CI	Stage Length (days)	95% CI
Diestrus	2.4	(2.2, 2.7)	2.5	(2.4, 2.8)
Proestrus	0.4	(0.3, 0.5)	0.4	(0.3, 0.5)
Estrus	1.4	(1.2, 1.5)	1.2	(1.1, 1.3)
Metestrus ^a	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.