

a. BPA Treatments Stop Dose Arm

Table 1. Summary of Animals with Vaginal Cytology Data for Bisphenol-A Stop-Dose

<i>Dose</i>	<i>($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)</i>	<i>N</i>
Stop BPA	0	26
	2.5	26
	25	26
	250	26
	2500	26
	25000	26

Table 2. Summary Statistics of Estrous Stage for Bisphenol-A Stop-Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)

<i>Dose</i>	<i>Estrous Stage</i>	<i>Count</i>	<i>Percent</i>
0	Diestrus	203	56.4
	Proestrus	47	13.1
	Estrus	110	30.6
2.5	Diestrus	217	60.3
	Proestrus	33	9.2
	Estrus	110	30.6
25	Diestrus	189	52.4
	Proestrus	52	14.4
	Estrus	120	33.2
250	Diestrus	186	51.2
	Proestrus	55	15.2
	Estrus	122	33.6
2500	Diestrus	211	58.3
	Proestrus	50	13.8
	Estrus	101	27.9
25000	Diestrus	211	58.8
	Proestrus	37	10.3
	Estrus	111	30.9

Table 3. Summary of Estrous Cycle Length (Days) for Bisphenol-A Stop-Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)¹

<i>0</i>			<i>2.5</i>			<i>25</i>			<i>250</i>			<i>2500</i>			<i>25000</i>		
<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>
20	4.08	0.12	22	4.23	0.13	23	4.17	0.12	25	4.47	0.23	26	4.42	0.15	24	4.38	0.17

¹ N includes animals with at least one uncensored cycle.

RR9: CLARITY-BPA Core Study
 Data from 27-Appendix XXVII Vaginal Cytology Statistical
 Report

Table 4. Comparison of Vaginal Cycling Abnormality by Animal Across Treatments

Bisphenol-A Stop-Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)																							
0				2.5				25				250				2500				25000			
Status	Count	Pct	P¹	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²
Diestrus																							
Abnormal	5	19.2	0.200	5	19.2	1.000	1.000	2	7.7	0.418	1.000	1	3.8	0.190	0.953	4	15.4	1.000	1.000	5	19.2	1.000	1.000
Normal	21	80.8	0.200	21	80.8	1.000	1.000	24	92.3	0.418	1.000	25	96.2	0.190	0.953	22	84.6	1.000	1.000	21	80.8	1.000	1.000
Estrus																							
Abnormal	5	19.2	0.384	2	7.7	0.418	1.000	3	11.5	0.703	1.000	5	19.2	1.000	1.000	2	7.7	0.418	1.000	3	11.5	0.703	1.000
Normal	21	80.8	0.384	24	92.3	0.418	1.000	23	88.5	0.703	1.000	21	80.8	1.000	1.000	24	92.3	0.418	1.000	23	88.5	0.703	1.000
Proestrus																							
Abnormal	2	7.7	0.153	1	3.8	1.000	1.000	1	3.8	1.000	1.000	0	0.0	0.490	1.000	0	0.0	0.490	1.000	0	0.0	0.490	1.000
Normal	24	92.3	0.153	25	96.2	1.000	1.000	25	96.2	1.000	1.000	26	100.0	0.490	1.000	26	100.0	0.490	1.000	26	100.0	0.490	1.000
Total																							
Abnormal	10	38.5	0.330	7	26.9	0.555	1.000	5	19.2	0.220	1.000	6	23.1	0.367	1.000	6	23.1	0.367	1.000	8	30.8	0.771	1.000
Normal	16	61.5	0.330	19	73.1	0.555	1.000	21	80.8	0.220	1.000	20	76.9	0.367	1.000	20	76.9	0.367	1.000	18	69.2	0.771	1.000

¹ P-values are relative to the control group, except p-value for trend shown below control.

² P-values were adjusted for multiple comparisons using Holm's method.

b. BPA Treatments Continuous Dose Arm

Table 5. Summary of Animals with Vaginal Cytology Data for Bisphenol-A Continuous

<i>Dose</i>	<i>($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)</i>	<i>N</i>
BPA	0	26
	2.5	25
	25	26
	250	25
	2500	26
	25000	25

Table 6. Summary Statistics of Estrous Stage for Bisphenol-A Continuous Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)

<i>Dose</i>	<i>Estrous Stage</i>	<i>Count</i>	<i>Percent</i>
0	Diestrus	209	57.7
	Proestrus	50	13.8
	Estrus	103	28.5
2.5	Diestrus	188	54.0
	Proestrus	52	14.9
	Estrus	108	31.0
25	Diestrus	198	55.2
	Proestrus	40	11.1
	Estrus	121	33.7
250	Diestrus	172	49.4
	Proestrus	60	17.2
	Estrus	116	33.3
2500	Diestrus	217	59.9
	Proestrus	50	13.8
	Estrus	95	26.2
25000	Diestrus	194	55.7
	Proestrus	44	12.6
	Estrus	110	31.6

Table 7. Summary of Estrous Cycle Length (Days) for Bisphenol-A Continuous Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)¹

<i>0</i>			<i>2.5</i>			<i>25</i>			<i>250</i>			<i>2500</i>			<i>25000</i>		
<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>
23	4.37	0.18	23	4.56	0.29	24	4.47	0.21	24	5.20	0.51	24	4.33	0.15	22	4.84	0.31

¹ N includes animals with at least one uncensored cycle.

RR9: CLARITY-BPA Core Study
 Data from 27-Appendix XXVII Vaginal Cytology Statistical Report

Table 8. Comparison of Vaginal Cycling Abnormality by Animal Across Treatments

Bisphenol-A Continuous Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)																									
		0				2.5				25				250				2500				25000			
Status	Count	Pct	P¹	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²		
Diestrus																									
Abnormal	4	15.4	0.121	2	8.0	0.667	1.000	4	15.4	1.000	1.000	1	4.0	0.349	1.000	4	15.4	1.000	1.000	5	20.0	0.726	1.000		
Normal	22	84.6	0.121	23	92.0	0.667	1.000	22	84.6	1.000	1.000	24	96.0	0.349	1.000	22	84.6	1.000	1.000	20	80.0	0.726	1.000		
Estrus																									
Abnormal	3	11.5	0.345	3	12.0	1.000	1.000	4	15.4	1.000	1.000	4	16.0	0.703	1.000	2	7.7	1.000	1.000	4	16.0	0.703	1.000		
Normal	23	88.5	0.345	22	88.0	1.000	1.000	22	84.6	1.000	1.000	21	84.0	0.703	1.000	24	92.3	1.000	1.000	21	84.0	0.703	1.000		
Proestrus																									
Abnormal	0	0.0	0.182	0	0.0	-	-	0	0.0	-	-	1	4.0	0.490	1.000	1	3.8	1.000	1.000	1	4.0	0.490	1.000		
Normal	26	100.0	0.182	25	100.0	-	-	26	100.0	-	-	24	96.0	0.490	1.000	25	96.2	1.000	1.000	24	96.0	0.490	1.000		
Total																									
Abnormal	7	26.9	0.125	5	20.0	0.743	1.000	8	30.8	1.000	1.000	5	20.0	0.743	1.000	7	26.9	1.000	1.000	9	36.0	0.555	1.000		
Normal	19	73.1	0.125	20	80.0	0.743	1.000	18	69.2	1.000	1.000	20	80.0	0.743	1.000	19	73.1	1.000	1.000	16	64.0	0.555	1.000		

¹ P-values are relative to the control group, except p-value for trend shown below control.

² P-values were adjusted for multiple comparisons using Holm's method.

c. EE₂ Treatments Continuous Dose

Table 9. Summary of Animals with Vaginal Cytology Data for Ethinyl Estradiol

<i>Dose</i>	<i>($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)</i>	<i>N</i>
	0	26
EE2	0.05	26
	0.5	26

Table 10. Summary Statistics of Estrous Stage for Ethinyl Estradiol ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)

<i>Dose</i>	<i>Estrous Stage</i>	<i>Count</i>	<i>Percent</i>
0	Diestrus	209	57.7
	Proestrus	50	13.8
	Estrus	103	28.5
0.05	Diestrus	197	54.3
	Proestrus	40	11.0
	Estrus	126	34.7
0.5	Diestrus	56	15.5
	Proestrus	3	0.8
	Estrus	302	83.7

Table 11. Summary of Estrous Cycle Length (Days) for Ethinyl Estradiol Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)¹

<i>0</i>			<i>0.05</i>			<i>0.5</i>		
<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>	<i>N</i>	<i>Mean</i>	<i>SE</i>
23	4.37	0.18	23	4.72	0.33	12	5.58	0.64

¹ N includes animals with at least one uncensored cycle.

Table 12. Comparison of Vaginal Cycling Abnormality by Animal Across Treatments										
Ethinyl Estradiol Dose ($\mu\text{g}/\text{kg}_{\text{BW}}/\text{day}$)										
	0		0.05				0.5			
Status	Count	Pct	Count	Pct	P¹	P_{adj}²	Count	Pct	P¹	P_{adj}²
Diestrus										
Abnormal	4	15.4	6	23.1	0.726	1.000	2	7.7	0.667	1.000
Normal	22	84.6	20	76.9	0.726	1.000	24	92.3	0.667	1.000
Estrus										
Abnormal	3	11.5	4	15.4	1.000	1.000	25	96.2	<.001	<.001
Normal	23	88.5	22	84.6	1.000	1.000	1	3.8	<.001	<.001
Total										
Abnormal	7	26.9	10	38.5	0.555	0.555	26	100.0	<.001	<.001
Normal	19	73.1	16	61.5	0.555	0.555	0	0.0	<.001	<.001

¹ P-values are relative to the control group.

² P-values were adjusted for multiple comparisons using Holm's method.