

Table 1: Effect of Vehicle Exposure on Estrous Stage Prevalence

		Vehicle	Naïve	Total
Organ	Stage	f (%)	f (%)	f (%)
Ovaries	P	7 (41%)	5 (28%)	12 (34%)
	E	9 (53%)	12 (67%)	21 (60%)
	D	1 (6%)	1 (6%)	2 (6%)
	pPreg	3	2	5
	Total	17 7 9 0 1	18 5 12 0 1	35
Uterus	P	4 (24%)	3 (17%)	7 (20%)
	E	11 (65%)	13 (72%)	24 (69%)
	M	1 (6%)	1 (6%)	2 (6%)
	D	1 (6%)	1 (6%)	2 (6%)
	pPreg	3	2	5
	Total	17 4 11 1 1	18 3 13 1 1	35
Vagina	P	3 (18%)	2 (11%)	5 (14%)
	E	11 (65%)	12 (67%)	23 (66%)
	M	1 (6%)	3 (17%)	4 (11%)
	D	2 (12%)	1 (6%)	3 (9%)
	pPreg	3	2	5
	Total	17 3 11 1 2	18 2 12 3 1	35

Table 2: Effect of Low-Dose BPA Exposure on Estrous Stage Prevalence

Organ	Stage	Vehicle	BPA 2.5	BPA 8.0	BPA 25
		f (%)	f (%)	f (%)	f (%)
Ovaries	P	7 (41%)	4 (19%)	6 (33%)	2 (10%)
	E	9 (53%)	15 (71%)	11 (61%)	13 (65%)
	M	0 (0%)	0 (0%)	1 (6%)	2 (10%)
	D	1 (6%)	2 (10%)	0 (0%)	3 (15%)
	pPreg	3	2		1
	*				
	Total	17 7 9 0 1	21 4 15 0 2	18 6 11 1 0	20 2 13 2 3
Uterus	P	4 (24%)	4 (19%)	6 (33%)	2 (10%)
	E	11 (65%) *	16 (76%)	11 (61%)	12 (60%)
	M	1 (6%)	0 (0%)	1 (6%)	3 (15%)
	D	1 (6%)	1 (5%)	0 (0%)	3 (15%)
	N	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	pPreg	3	2		1
	Total	17 4 11 1 1 0	21 4 16 0 1 0	18 6 11 1 0 0	20 2 12 3 3 0
Vagina	P	3 (18%)	2 (10%)	5 (28%)	1 (5%)
	E	11 (65%)	8 (38%)	7 (39%)	4 (20%)
	M	1 (6%)	10 (48%) *	6 (33%)	11 (55%) **
	D	2 (12%)	1 (5%)	0 (0%)	4 (20%)
	N	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	pPreg	3	2		1
	Total	17 3 11 1 2 0	21 2 8 10 1 0	18 5 7 6 0 0	20 1 4 11 4 0 **

Organ	Stage	BPA 80	BPA 260	BPA 840	BPA 2700	Total
		f (%)	f (%)	f (%)	f (%)	f (%)
Ovaries	P	6 (33%)	8 (44%)	7 (41%)	6 (35%)	46 (32%)
	E	8 (44%)	8 (44%)	8 (47%)	8 (47%)	80 (55%)
	M	2 (11%)	0 (0%)	1 (6%)	2 (12%)	8 (5%)
	D	2 (11%)	2 (11%)	1 (6%)	1 (6%)	12 (8%)
	pPreg	1	1	3	3	14
	*		1			1
	Total	18 6 8 2 2	18 8 8 0 2	17 7 8 1 1	17 6 8 2 1	146
Uterus	P	7 (39%)	7 (37%)	7 (41%)	7 (41%)	44 (30%)
	E	8 (44%)	8 (42%)	8 (47%)	7 (41%)	81 (55%)
	M	1 (6%)	0 (0%)	0 (0%)	1 (6%)	7 (5%)
	D	2 (11%)	3 (16%)	2 (12%)	2 (12%)	14 (10%)
	N	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (1%)
	pPreg	1	1	3	3	14
	Total	18 7 8 1 2 0	19 7 8 0 3 1	17 7 8 0 2 0	17 7 7 1 2 0	147
Vagina	P	4 (22%)	4 (21%)	6 (35%)	3 (18%)	28 (19%)
	E	5 (28%)	8 (42%)	8 (47%)	9 (53%)	60 (41%)
	M	7 (39%)	3 (16%)	1 (6%)	4 (24%)	43 (29%)
	D	2 (11%)	3 (16%)	2 (12%)	1 (6%)	15 (10%)
	N	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (1%)
	pPreg	1	1	3	3	14
	Total	18 4 5 7 2 0	19 4 8 3 3 1	17 6 8 1 2 0	17 3 9 4 1 0	147

Table 3: Effect of High-Dose BPA Exposure on Estrous Stage Prevalence

Organ	Stage	Vehicle	BPA 100K	BPA 300K	Total
		f (%)	f (%)	f (%)	f (%)
Ovaries	P	7 (41%) *	9 (45%)	2 (11%)	18 (32%)
	E	9 (53%) ***	8 (40%)	0 (0%) ***	17 (30%)
	M	0 (0%)	0 (0%)	3 (16%)	3 (5%)
	D	1 (6%)	2 (10%)	1 (5%)	4 (7%)
	N	0 (0%) ***	1 (5%)	13 (68%) ***	14 (25%)
	pPreg	3			3
	Total	17 7 9 0 1 0 ***	20 9 8 0 2 1	19 2 0 3 1 13 ***	56
Uterus	P	4 (24%)	9 (45%)	3 (16%)	16 (29%)
	E	11 (65%)	9 (45%)	10 (53%)	30 (54%)
	M	1 (6%)	(0%)	4 (21%)	5 (9%)
	D	1 (6%)	2 (10%)	2 (11%)	5 (9%)
	pPreg	3			3
	Total	17 4 11 1 1	20 9 9 0 2	19 3 10 4 2	56
Vagina	P	3 (18%)	3 (15%)	1 (5%)	7 (13%)
	E	11 (65%)	12 (60%)	12 (63%)	35 (63%)
	M	1 (6%)	3 (15%)	5 (26%)	9 (16%)
	D	2 (12%)	2 (10%)	1 (5%)	5 (9%)
	pPreg	3			3
	Total	17 3 11 1 2	20 3 12 3 2	19 1 12 5 1	56

Table 4: Effect of Ethinyl Estradiol Exposure on Estrous Stage Prevalence

Organ	Stage	Vehicle	EE 0.5	EE 5.0	Total
		f (%)	f (%)	f (%)	f (%)
Ovaries	P	7 (41%) ***	0 (0%) **	0 (0%) **	7 (13%)
	E	9 (53%) ***	1 (6%) **	0 (0%) ***	10 (19%)
	D	1 (6%)	0 (0%)	0 (0%)	1 (2%)
	N	0 (0%) ***	16 (94%) ***	19 (100%) ***	35 (66%)
	pPreg	3	2		5
	*		1	1	2
	Total	17 7 9 1 0 ***	17 0 1 0 16 ***	19 0 0 0 19 ***	53
Uterus	P	4 (24%)	(0%)	1 (5%)	5 (9%)
	E	11 (65%)	12 (67%)	13 (65%)	36 (65%)
	M	1 (6%)	4 (22%)	2 (10%)	7 (13%)
	D	1 (6%)	1 (6%)	4 (20%)	6 (11%)
	N	0 (0%)	1 (6%)	0 (0%)	1 (2%)
	pPreg	3	2		5
	Total	17 4 11 1 1	18 0 12 4 1	20 1 13 2 4	55
Vagina	P	3 (18%)	0 (0%)	0 (0%)	3 (5%)
	E	11 (65%)	8 (44%)	15 (75%)	34 (62%)
	M	1 (6%)	8 (44%) *	4 (20%)	13 (24%)
	D	2 (12%)	1 (6%)	1 (5%)	4 (7%)
	N	0 (0%)	1 (6%)	0 (0%)	1 (2%)
	pPreg	3	2		5
	Total	17 3 11 1 2	18 0 8 8 1 *	20 0 15 4 1	55

Table 5: Effect of Treatments on Reproductive Organ Synchrony

			Scoring Method ^o								
			Method 1		Method 2		Method 4			Method 3	
Analysis	Dose	(N)	RTE ¹	P-Value ²	RTE ¹	P-Value ²	RTE ¹	P-Value ²	(N) ³	RTE ¹	P-Value ²
Naïve Control	Vehicle	(20)	0.48	0.545	0.48	0.546	0.50	0.921	(17)	0.48	0.609
	Naïve	(20)	0.52	0.545	0.52	0.546	0.50	0.921	(18)	0.52	0.609
Low Bisphenol A	Vehicle	(20)	0.42	0.590	0.42	0.586	0.46	0.973	(17)	0.42	0.715
	BPA 2.5	(23)	0.60	0.140	0.60	0.135	0.59	0.973	(21)	0.61	0.165
	BPA 8.0	(18)	0.47	0.590	0.47	0.586	0.41	0.973	(18)	0.45	0.715
	BPA 25	(21)	0.59	0.151	0.59	0.162	0.55	0.973	(20)	0.59	0.273
	BPA 80	(19)	0.58	0.274	0.58	0.270	0.54	0.973	(18)	0.57	0.461
	BPA 260	(20)	0.46	0.590	0.46	0.586	0.47	0.973	(18)	0.46	0.715
	BPA 840	(20)	0.36	0.590	0.36	0.586	0.41	0.973	(17)	0.35	0.715
	BPA 2700	(20)	0.51	0.590	0.51	0.586	0.55	0.973	(17)	0.53	0.715
High Bisphenol A	Vehicle	(20)	0.39	0.018 *	0.41	0.145	0.42	0.005 **	(17)	0.36	<.001 ***
	BPA 100K	(20)	0.51	0.137	0.55	0.145	0.42	0.988	(20)	0.44	0.290
	BPA 300K	(19)	0.61	0.018 *	0.54	0.145	0.67	0.005 **	(19)	0.69	<.001 ***
Ethinyl Estradiol	Vehicle	(20)	0.31	<.001 ***	0.36	0.013 *	0.24	<.001 ***	(17)	0.18	<.001 ***
	EE 0.5	(20)	0.57	<.001 ***	0.53	0.028 *	0.63	<.001 ***	(17)	0.64	<.001 ***
	EE 5.0	(20)	0.63	<.001 ***	0.60	0.007 **	0.63	<.001 ***	(20)	0.65	<.001 ***

⁰ See text for a detailed discussion about the different scoring methods.

¹ Relative Treatment Effect - Value is "relative" to the treatment groups within the analysis and so Vehicle is not required to be the same for each analysis.

² P-Values are adjusted for multiple comparisons using Hochberg's method.

³ Method 3 excludes pseudo-pregnant animals and so the sample size is not the same.

Table 6: Desynchrony Results and Scoring of Reproductive Organ Synchrony

Desynchrony Status	OUV	Naïve	Vehicle	BPA 2.5	BPA 8.0	BPA 25.0	BPA 80.0	BPA 260	BPA 840	BPA 2700	BPA 100K	BPA 300K	EE 0.5	EE 5.0	Row Total	Method 1 Scoring	Method 2 Scoring	Method 3 Scoring	Method 4 Scoring
Synchronous	PPP	2	3	1	5	1	3	4	6	2	3	1			31				
	EEE	8	8	6	6	3	2	5	7	5	5		1		56				
	MMM				1	1	1				3				6	0	0	0	0
	DDD	1	1	1		3	1	2	1		2	1			13				
	Total	11	12	8	12	8	7	11	14	7	10	5	1		106				
Synchronous w/missing	*EE												1		1	0	0	0	0
	Total												1		1				
F/L Consistent Desynchrony	PEE	2	2								1				5				
	PPE	1	1	2	1	1	3	3	1	4	5	1			23				
	MDD						1		1	1					3	1	1	1	1
	MDM									1					1				
	MMD					1									1				
	Total	3	3	2	1	2	4	3	2	6	6	1			33				
F/L Inconsistent Adjacent Stage Desynchrony	PDD							1							1				
	EEM	3		9	5	9	6	3	1	2	3				41				
	EME	1													1	2	2	2	2
	EMM					1				1					2				
	DPP			1			1			1					3				
	Total	4		10	5	10	7	4	1	4	3				48				
Oppositional Desynchrony	PMM		1												1				
	EED		1												1	3	3	3	3
	Total		2												2				
Complete Desynchrony	PEM		1												1	4	4	4	4
	Total		1												1				
Non-Anestrus Total		18	17	21	18	20	18	18	17	17	19	6	1	1	191				
Anestrus Synchrony ¹	NNN	2	3	2		1	1	1	3	3			2		18	0	0	--	5
	Total	2	3	2		1	1	1	3	3			2		18				
Anestrus in 1 - Synchronous in 2	NEE										9		7	12	28				
	NMM										1		4	1	6	1	0.5	5	5
	NDD												1	1	2				
	Total										10		12	14	36				
Anestrus Synchrony w/missing	*NN						1						1		2	0	0	--	5
	Total						1						1		2				
Anestrus in 1 - F/L Consistent Desynchrony in 2	NPE										1	1	1		3				
	NDM												3		3	2	0.5	5	5
	Total										1	1	4		6				
Anestrus in 1 - F/L Inconsistent Desynchrony in 2	NEM										1		4		5				
	NME												1		1	3	0.5	5	5
	Total										1		4	1	6				
Anestrus in 1 - Desynchrony in 2	NDE										1				1				
	Total										1				1	4	0.5	5	5
Anestrus Total		2	3	2		1	1	2	3	3	1	13	19	19	69				
Grand Total		20	20	23	18	21	19	20	20	20	20	19	20	20	260				

¹All 18 animals in this group were also found to be pseudo-pregnant histopathologically based on simultaneous presence of ovary, corpus luteum * hypertrophy, uterus, endometrium * cytoplasmic vacuolization, and vagina, mucocyte * hyperplasia.