NCTR PROTOCOL E0219001

TWO YEAR CHRONIC TOXICOLOGY STUDY OF BISPHENOL A (BPA) [CAS # 80-05-7] ADMINISTERED BY GAVAGE TO SPRAGUE-DAWLEY RATS (NCTR) FROM GESTATIONAL DAY 6 UNTIL BIRTH AND DIRECTLY TO F_1 PUPS FROM POSTNATAL DAY (PND) 1; CONTINUOUS AND STOP DOSE (PND 21) EXPOSURES

STATISTICAL REPORT

STATISTICAL ANALYSIS OF INTERIM SACRIFICE ORGAN WEIGHT DATA

PREPARED BY

BETH E. JULIAR
DIVISION OF BIOINFORMATICS AND BIOSTATISTICS

FOR

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH
3900 NCTR ROAD
JEFFERSON, ARKANSAS 72079

Signatures

Report prepared by Statistician: *Date*

Beth E. Juliar, M.A., M.S., Division of Bioinformatics and Biostatistics/NCTR/FDA

Report reviewed by Statistician: *Date*

Paul Felton, M.S., Division of Bioinformatics and Biostatistics /NCTR/FDA

Statistical Team Leader: *Date*

Paul Felton, M.S., Division of Bioinformatics and Biostatistics /NCTR/FDA

Table of Contents

1. Objectives 1
   1.1 Project Objectives 1
   1.2 Analysis Objectives 1
2. Experimental Design 1
3. Statistical Methods 1
4. Results 2
   4.1 BPA Treatments Stop Dose Arm 2
   4.2 BPA Treatments Continuous Dose Arm 3
   4.3 EE_2 Treatments Continuous Dose 4
5. Conclusions 5
   5.1 BPA Treatments Stop Dose Arm 5
   5.2 BPA Treatments Continuous Dose Arm 6
   5.3 EE_2 Treatments Continuous Dose 6

Appendices 8

A. Statistical Tables 8

a) BPA Treatments Stop Dose Arm 10

b) BPA Treatments Continuous Dose Arm 25

c) EE_2 Treatments Continuous Dose 40

B. Data 50

Quality Control 51

Statistical Analysis of Organ Weight Data

1. Objectives

1.1 Project Objectives

The goal of this two year chronic study is to characterize the long term toxicity of orally administered BPA, including developmental exposure, in the NCTR Sprague-Dawley (CD) rat over a broad dose range.

1.2 Analysis Objectives

The goal of this analysis is to evaluate the effects of exposure to BPA in Sprague-Dawley rats on organ weight data at one year sacrifice.

2. Experimental Design

The study design consisted of first generation female and male rats (F_0) for up to 600 mating pairs randomized to treatment groups in 5 loads. The goal of the F_0 matings was to obtain 352 study litters, 50 per dose group for vehicle controls and five BPA dose groups, 2.5, 25, 250, 2500, and 25000 µg/kg bw/day, and 26 for each of two EE_2 dose groups, 0.05 and 0.5 µg/kg bw/day. Dams were dosed daily from gestation day (GD) 6 until parturition. Dosing was by gavage for F_0 dams and F_1 pups, the second study generation. Litters were culled to 10 pups on PND 1.There were two study dosing arms of F_1 animals, daily continuous dosing to termination, and daily dose stopped at post-natal day (PND) 21. There was a vehicle control group and five BPA groups for each study dosing arm, and EE_2 daily dose groups for the continuous dosing arm only. From the F_1 litters, pups were allocated at weaning, PND 21, to the interim (1 year) and terminal (2 year) sacrifices for the core study. For vehicle and BPA terminal sacrifice groups, there were 50 pups each; for the interim sacrifice and the EE2 terminal sacrifice groups, there were 20-26 pups each. Pups within litter and sex were assigned to different dosing arms and sacrifice times.

Organ Weight Data

Organ weight data were collected for animals allocated to the interim sacrifice at one year that reached sacrifice.

3. Statistical Methods

Statistical analyses were performed separately for the BPA study arms, stop dose and continuous dose, and for the EE_2 continuous dose. Weights of paired organs were analyzed as combined weight. An analysis of variance (ANOVA) was performed for each sex and organ to determine the effect of treatment on organ weight. Analyses of covariance (ANOCOVA) were performed to determine the effect of treatment on organ weight adjusted for receiving weight or brain weight. Separate analyses were performed with each covariate. Comparisons of dosed groups versus vehicle control were performed using Dunnett's method for adjusted contrasts. Tests of trend, increasing treatment effect with increasing dose, were performed for the BPA and vehicle control treatments. Tests were conducted as two-sided at the 0.05 significance level.

For analysis of each compound and study arm, a sensitivity analysis was also performed for organ weight data collected from animals that reached interim sacrifice. During initial

preweaning, 129 pups later randomized to interim sacrifice were held in the same rooms as a special BPA 250,000 µg/kg bw/day high dose requested by an academic laboratory (20 vehicle control, 84 BPA 2.5, 25, 250, 2500, and 25000 µg/kg bw/day, and 25 EE_2 dose animals with organ weight data). In consultation with the Principal Investigator, to address the possibility of inadvertent exposure of the core study animals, a sensitivity analysis excluding these animals was also performed to test the robustness of the results. Additional statistically significant pairwise comparisons from the sensitivity analysis are reported in the text.

4. Results

Results of analyses are presented in Tables (Appendix A). Organ weight data excluded from the analysis of organ weight are listed in Table 1. Exclusions were determined by the Principal Investigator taking pathology reports and statistical distributions into consideration.

4.1 BPA Treatments Stop Dose Arm

Summary statistics for females are presented for the BPA stop dose arm in Table 2 for organ weight, Table 3 for organ relative to brain weight, and Table 4 for organ relative to receiving weight. Summary statistics for males are presented in Table 5 for organ weight, Table 6 for organ relative to brain weight, and Table 7 for organ relative to receiving weight.

The ANOVA omnibus test results for females and males are presented in Table 8 for the null hypothesis that all of the control and BPA stop dose treatment means for organ weights are equal. For females, there was a significant dose effect for spleen. Pairwise comparisons of least squares mean organ weight for females are presented in Table 9. For ovary, trend was significant (p=0.016) and there was a significant difference from control for the BPA stop dose 25000 µg/kg bw/day (p=0.037), with relatively lower mean weight in the dosed group (12.9% less than control). Pairwise comparisons of least squares mean organ weight for males are presented in Table 10. There were no statistically significant results in the analysis of organ weight for males.

In the sensitivity analysis of organ weight for female BPA stop dose, there were significant pairwise comparisons for BPA stop dose 25 µg/kg bw/day for ovarian/parametrial fat pad (p=0.010) and spleen (p=0.023), with lower mean weights in the dosed group relative to the control (25.7% and 14.2% lower, respectively). There were no statistically significant results in the sensitivity analysis of organ weight for males.

The ANOCOVA omnibus test results for females and males with covariate brain weight are presented in Table 11 for the null hypothesis that all of the control and BPA stop dose treatment means for organ weights are equal. For females, treatment effect was significant for spleen, and covariate brain weight was significant for adrenal gland, ovarian/parametrial fat pad, retroperitoneal fat pad, heart, kidney, liver, ovary, spleen, and thyroid gland. For males, covariate brain weight was significant for adrenal gland, kidney, liver, and spleen. Pairwise comparisons of least squares mean female organ weight adjusted for brain weight are presented in Table 12. For ovary, trend was significant (p=0.025) and the BPA stop dose 25000 µg/kg bw/day differed significantly from control (p=0.047), with relatively lower mean weight in the dosed group (11.9% less than control). Pairwise comparisons of least squares mean male organ weight adjusted for brain weight are presented in Table 13. There were no statistically significant results in the analysis of organ weight with covariate brain weight for males.

In the sensitivity analysis with covariate brain weight for female BPA stop dose, there was a significant pairwise comparison for BPA stop dose 2.5 µg/kg bw/day for spleen (p=0.039), with lower mean weight in the dosed group relative to the control (13.1% lower). For BPA stop dose

25 µg/kg bw/day, there were significant differences from control for ovarian/parametrial fat pad (p=0.010) and spleen (p=0.023), with relatively lower mean weights in the dosed group (25.0% and 13.7% lower than control, respectively). There were no statistically significant results in the sensitivity analysis with covariate brain weight for males.

The ANOCOVA omnibus test results for females and males with covariate receiving weight are presented in Table 14 for the null hypothesis that all of the control and BPA stop dose treatment means for organ weight are equal. For females, treatment effect was significant for spleen, and covariate receiving weight was significant for adrenal gland, ovarian/parametrial fat pad, retroperitoneal fat pad, heart, kidney, liver, ovary, pituitary gland, spleen, thymus, and thyroid gland. For males, covariate receiving weight was significant for adrenal gland, epididymis fat pad, retroperitoneal fat pad, heart, kidney, liver, pituitary gland, spleen, testes, thymus, and thyroid gland. Pairwise comparisons of least squares mean female organ weight adjusted for receiving weight are presented in Table 15. For ovary, trend was significant (p=0.019), but no pairwise comparisons for females were statistically significant. Pairwise comparisons of least squares mean male organ weight adjusted for receiving weight are presented in Table 16. For liver, trend was significant (p=0.027), but no pairwise comparisons for males were statistically significant.

In the sensitivity analysis with covariate receiving weight, there was a significant pairwise comparison for female BPA stop dose 25 µg/kg bw/day compared to control for ovarian/parametrial fat pad (p=0.035), with relatively lower mean weight in the dosed group (13.7% lower than control). There were no additional statistically significant results for males.

4.2 BPA Treatments Continuous Dose Arm

Summary statistics for females are presented for the BPA continuous dose arm in Table 17 for organ weight, Table 18 for organ relative to brain weight, and Table 19 for organ relative to receiving weight. Summary statistics for males are presented in Table 20 for organ weight, Table 21 for organ relative to brain weight, and Table 22 for organ relative to receiving weight.

The ANOVA omnibus test results for females and males are presented in Table 23 for the null hypothesis that all of the control and BPA continuous dose treatment means for organ weights are equal. There was a significant dose effect for retroperitoneal fat pad and kidney for females and heart for males. Pairwise comparisons of least squares mean organ weight for females are presented in Table 24. There was a significant difference compared to control for the BPA continuous dose 2.5 µg/kg bw/day for retroperitoneal fat pad (p=0.025), with higher mean organ weight for the dosed group (40.3% greater than control). Pairwise comparisons of least squares mean organ weight for males are presented in Table 25. There were no statistically significant results in the analysis of organ weight for males.

In the sensitivity analysis of organ weight for the BPA continuous dose arm, there were no additional statistically significant results for females or males.

The ANOCOVA omnibus test results for females and males with covariate brain weight are presented in Table 26 for the null hypothesis that all of the control and BPA continuous dose treatment means for organ weights are equal. For females, treatment effect was significant for kidney, and the covariate brain weight was significant for ovarian/parametrial fat pad, retroperitoneal fat pad, heart, kidney, liver, ovary, pituitary gland, and spleen. For males, treatment effect was significant for heart; covariate brain weight was significant for adrenal gland, epididymis, retroperitoneal fat pad, heart, kidney, liver, seminal vesicles, spleen, and thyroid gland. Pairwise comparisons of least squares mean female organ weight adjusted for

brain weight are presented in Table 27. For retroperitoneal fat pad, there was a significant difference from control for the BPA continuous dose 2.5 µg/kg bw/day (p=0.033), with relatively higher mean weight in the dosed group (38.4% greater than control). Pairwise comparisons of least squares mean male organ weight adjusted for brain weight are presented in Table 28. There were no statistically significant results in the analysis of organ weight with covariate brain weight for males.

In the sensitivity analysis with covariate brain weight for the BPA continuous dose arm, there were no additional statistically significant results for females or males.

The ANOCOVA omnibus test results for females and males with covariate receiving weight are presented in Table 29 for the null hypothesis that all of the control and BPA continuous dose treatment means for organ weights are equal. For females, covariate receiving weight was significant for adrenal gland, ovarian/parametrial fat pad, retroperitoneal fat pad, heart, kidney, liver, ovary, spleen, thymus, and thyroid gland. For males, treatment effect was significant for heart and liver; covariate receiving weight was significant for adrenal gland, epididymis, epididymis fat pad, retroperitoneal fat pad, heart, kidney, liver, pituitary gland, spleen, and thyroid gland. Pairwise comparisons of least squares mean female organ weight adjusted for receiving weight are presented in Table 30. Trend for liver was significant (p=0.049), although no dosed group differed significantly from vehicle control. Pairwise comparisons of least squares mean male organ weight adjusted for receiving weight are presented in Table 31. There was a significant difference compared to control for liver for the BPA continuous dose 2.5 µg/kg bw/day (p=0.033), with relatively lower mean weight in the dosed group (7.7% less than control).

In the sensitivity analysis of BPA continuous dose organ weight with covariate receiving weight, there were no additional statistically pairwise comparisons for females or males.

4.3 EE_2 Treatments Continuous Dose

Summary statistics for females are presented for the EE_2 continuous dose in Table 32 for organ weight, Table 33 for organ relative to brain weight, and Table 34 for organ relative to receiving weight. Summary statistics for males are presented in Table 35 for organ weight, Table 36 for organ relative to brain weight, and Table 37 for organ relative to receiving weight.

The ANOVA omnibus test results for females and males are presented in Table 38 for the null hypothesis that all of the control and EE_2 continuous dose treatment means for organ weights are equal. For females, treatment effect was significant for adrenal gland, ovarian/parametrial fat pad, kidney, liver, ovary, and pituitary gland; for males, treatment effect was not significant for any organ. Pairwise comparisons of least squares mean organ weight for females are presented in Table 39. For the EE_2 0.5 µg/kg bw/day group, there were significant differences from control for adrenal gland, kidney, liver, ovary, and pituitary gland ($p<0.001$, =0.004, =0.006, =0.017, and =0.003, respectively). Mean weight was relatively lower in the dosed group for ovary (18.2% less than control); mean weights were relatively higher in the dosed group for adrenal gland, kidney, liver, and pituitary gland (27.4%, 15.2%, 19.5%, and 30.6% greater than control, respectively). Pairwise comparisons of least squares mean organ weight for males are presented in Table 40. There were no statistically significant results in the analysis of organ weight for males.

In the sensitivity analysis of organ weight for the EE_2 continuous dose, there were no additional statistically significant results for females or males.

The ANOCOVA omnibus test results for females and males with covariate brain weight are presented in Table 41 for the null hypothesis that all of the control and EE_2 continuous dose treatment means for organ weights are equal. For females, treatment effect was significant for adrenal gland, ovarian/parametrial fat pad, kidney, liver, ovary, and pituitary gland; covariate brain weight was significant for ovarian/parametrial fat pad, retroperitoneal fat pad, heart, liver, spleen, and thymus. For males, covariate brain weight was significant for epididymis, epididymis fat pad, retroperitoneal fat pad, heart, kidney, liver, pituitary gland, testes, and thyroid gland. Pairwise comparisons of least squares mean female organ weight adjusted for brain weight are presented in Table 42. For the EE_2 0.5 µg/kg bw/day group compared to control, there were significant differences for adrenal gland, kidney, liver, ovary, and pituitary gland ($p<0.001$, $=0.002$, $=0.001$, $=0.022$, and $=0.002$, respectively). Mean weight was relatively lower in the dosed group for ovary (17.8% less than control); mean weights were relatively higher in the dosed group for adrenal gland, kidney, liver, and pituitary gland (28.0%, 16.0%, 21.0%, and 31.4% greater than control, respectively). Pairwise comparisons of least squares mean male organ weight adjusted for brain weight are presented in Table 43. There were no statistically significant results in the analysis of organ weight with covariate brain weight for males.

In the sensitivity analysis for the EE_2 continuous dose with covariate brain weight, there were no additional statistically significant results for females or males.

The ANOCOVA omnibus test results for females and males with covariate receiving weight are presented in Table 44 for the null hypothesis that all of the control and EE_2 continuous dose treatment means for organ weights are equal. For females, treatment effect and covariate receiving weight were significant for adrenal gland, ovarian/parametrial fat pad, heart, kidney, liver, and pituitary gland; treatment effect was significant for ovary; and covariate receiving weight was significant for retroperitoneal fat pad, spleen, thymus, and thyroid gland. For males, treatment effect and covariate receiving weight were significant for thymus; covariate receiving weight was significant for adrenal gland, epididymis, epididymis fat pad, retroperitoneal fat pad, heart, kidney, liver, pituitary gland, spleen, testes, and thyroid gland. Pairwise comparisons of least squares mean female organ weight adjusted for receiving weight are presented in Table 45. For the EE_2 0.5 µg/kg bw/day group, there were significant differences from control for adrenal gland, ovarian/parametrial fat pad, heart, kidney, liver, ovary, and pituitary gland ($p<0.001$, <0.001, $=0.015$, <0.001, <0.001, $=0.021$, and $=0.002$, respectively). Mean weights were relatively lower in the dosed group for ovarian/parametrial fat pad and ovary (18.9% and 17.8% less than control, respectively); mean weights were relatively higher in the dosed group for adrenal gland, heart, kidney, liver, and pituitary gland (26.9%, 7.7%, 14.5%, 18.4%, and 29.9% greater than control, respectively). Pairwise comparisons of least squares mean male organ weight adjusted for receiving weight are presented in Table 46. There were no statistically significant results in the analysis of organ weight with covariate receiving weight for males.

In the sensitivity analysis for the EE_2 continuous dose with covariate receiving weight, there were no additional statistically significant results for females or males.

5. Conclusions

5.1 BPA Treatments Stop Dose Arm

In pairwise comparisons of least squares mean organ weight for females, there was a significant difference for the BPA stop dose 25000 µg/kg bw/day compared to control for ovary, with relatively lower mean weight in the dosed group. In the sensitivity analysis for female BPA stop dose, there were significant pairwise comparisons for BPA stop dose 25 µg/kg bw/day for

ovarian/parametrial fat pad and spleen, with lower mean weights in the dosed group relative to the control. There were no statistically significant results in the analysis of organ weight for male BPA stop dose.

In the analysis of female organ weight adjusted for brain weight, ovary differed significantly from control for the BPA stop dose 25000 µg/kg bw/day, with relatively lower mean weight in the dosed group. In the sensitivity analysis, there was a significant pairwise comparison for BPA stop dose 2.5 µg/kg bw/day for spleen, with lower mean weight in the dosed group relative to the control. For BPA stop dose 25 µg/kg bw/day, there were significant differences from control for ovarian/parametrial fat pad and spleen, with lower mean weights in the dosed group relative to control. There were no statistically significant results in the analysis of organ weight with covariate brain weight for male BPA stop dose.

In the analysis of organ weight adjusted for receiving weight, there were no significant pairwise comparisons for female or male BPA stop dose. In the sensitivity analysis with covariate receiving weight, there was a significant pairwise comparison to control for female BPA stop dose 25 µg/kg bw/day for ovarian/parametrial fat pad, with relatively lower mean weight in the dosed group.

5.2 BPA Treatments Continuous Dose Arm

In pairwise comparisons of least squares mean organ weight for females, there was a significant difference compared to control for the BPA continuous dose 2.5 µg/kg bw/day for retroperitoneal fat pad, with relatively higher mean organ weight for the dosed group. There were no statistically significant results in the analysis of organ weight for male BPA continuous dose.

In analysis of female organ weight adjusted for brain weight, retroperitoneal fat pad was significantly different from control for the BPA continuous dose 2.5 µg/kg bw/day, with relatively higher mean weight in the dosed group. For BPA continuous dose males, there were no statistically significant results in the analysis of organ weight with covariate brain weight.

For BPA continuous dose female organ weight adjusted for receiving weight, there were no statistically significant pairwise comparisons to control. For males, there was a significant difference compared to control for liver for the BPA continuous dose 2.5 µg/kg bw/day, with lower mean weight in the dosed group relative to control.

5.3 EE_2 Treatments Continuous Dose

For the female EE_2 0.5 µg/kg bw/day group, there were significant comparisons to control for adrenal gland, kidney, liver, ovary, and pituitary gland, with lower mean weight in the dosed group for ovary and higher mean weight for adrenal gland, kidney, liver, and pituitary gland relative to control. There were no statistically significant results in the analysis of organ weight for male EE_2 dose groups.

In pairwise comparisons of least squares mean female organ weight adjusted for brain weight, the EE_2 0.5 µg/kg bw/day group differed significantly from control for adrenal gland, kidney, liver, ovary, and pituitary gland. Mean weight was relatively lower in the EE_2 0.5 µg/kg bw/day group for ovary and higher in the dosed group for adrenal gland, kidney, liver, and pituitary gland compared to control. For male organ weight adjusted for brain weight, there were no statistically significant differences compared to control for male EE_2 dose groups.

For female organ weight with covariate receiving weight, pairwise comparisons to control for adrenal gland, ovarian/parametrial fat pad, heart, kidney, liver, ovary, and pituitary gland were significant for the EE_2 0.5 µg/kg bw/day group. Compared to control, mean weights were

relatively lower in the dosed group for ovarian/parametrial fat pad and ovary, and relatively higher for adrenal gland, heart, kidney, liver, and pituitary gland. There were no statistically significant pairwise comparisons to control in the analysis of organ weight with covariate receiving weight for male EE_2 dose groups.

Appendices

A. Statistical Tables

Table 1. Organ Weight Exclusions

Compound	*Sex*	*Dose*	*CID*	*UIN*	*Organ*	*Weight (g)*	*Reason*[1]
Stop BPA	F	2.5	21900301511	23000528957	Thymus	0.627	Outlier
			21900305842	23000533708	Kidney	2.711	All organs with gross cysts will be excluded
		250	21900301841	23000533932	Uterus	4.677	Only uterus noted as fluid filled
			21900308032	23000535435	Kidney	2.427	All organs with gross cysts will be excluded
	M	2500	21900034071	23000530435	Epidid Fat Pad	14.728	All organs with gross cysts will be excluded
		25000	21900302071	23000528744	Kidney	11.552	Outlier
			21900306381	23000533115	Kidney	11.920	Outlier
Continuous BPA	F	0	21900300162	23000529217	Ovary	0.456	Outlier
		25	21900300471	23000529095	Ovary	0.557	Outlier
			21900304792	23000534826	Ovary	5.070	All organs with gross cysts will be excluded
			21900306902	23000535711	Ovary	1.471	All organs with gross cysts will be excluded
			21900308732	23000536210	Ovary	0.162	All organs with gross cysts will be excluded
			21900308732	23000536210	Uterus	2.906	Outlier
		250	21900302801	23000532773	Ovary	0.238	All organs with gross cysts will be excluded
		2500	21900300802	23000529379	Ovary	0.623	Outlier
			21900305102	23000532714	Ovary	0.658	All organs with gross cysts will be excluded
		25000	21900300961	23000530323	Kidney	5.282	Outlier
			21900307321	23000535770	Ovary	0.071	All organs with gross cysts will be excluded
			21900307322	23000535723	Ovary	0.241	All organs with gross cysts will be excluded
			21900309151	23000536139	Ovary	0.186	All organs with gross cysts will be excluded
	M	0	21900308391	23000535588	Kidney	4.301	All organs with gross cysts will be excluded
		25	21900308662	23000536176	Kidney	4.043	All organs with gross cysts will be excluded
		2500	21900305031	23000533335	Kidney	3.800	All organs with gross cysts will be excluded
EE2	F	0.5	21900303341	23000529390	Ovary	0.552	Outlier
			21900305501	23000530846	Ovary	2.592	All organs with gross cysts will be excluded
			21900305522	23000533418	Ovary	1.212	All organs with gross cysts will be excluded
		0.05	21900305391	23000533458	Kidney	2.373	All organs with gross cysts will be excluded
			21900309241	23000535579	Ovary	0.177	All organs with gross cysts will be excluded
	M	0.05	21900305331	23000533450	Kidney	4.267	All organs with gross cysts will be excluded
			21900305342	23000533940	Adrenal Gl	0.235	Outlier

[1] Exclusions were determined by the Principle Investigator taking pathology reports and statistical distributions into consideration.

a) BPA Treatments Stop Dose Arm

Table 2. Summary Statistics of Female Organ Weight (g) Bisphenol-A Stop-Dose (µg/kg'BW'/day)

	0.0			2.5			25			250			2500			25000	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	20	0.0731	0.0029	22	0.0700	0.0016	20	0.0716	0.0027	22	0.0712	0.0024	20	0.0685	0.0029	20	0.0756	0.0031
Brain	20	2.091	0.023	22	2.095	0.017	20	2.090	0.027	22	2.049	0.021	20	2.090	0.018	20	2.071	0.017
Fat Pad Ov/Pm	20	17.20	1.23	22	16.18	0.72	20	14.31	0.95	22	15.33	1.07	20	16.31	1.13	20	14.97	0.87
Fat Pad Retro	20	18.24	1.55	22	15.41	1.53	20	16.96	1.84	22	17.10	1.53	20	16.18	1.33	20	16.44	1.41
Heart	20	1.433	0.049	22	1.359	0.023	20	1.350	0.045	22	1.366	0.042	20	1.377	0.045	20	1.347	0.038
Kidney	20	2.47	0.11	21	2.30	0.09	20	2.28	0.09	21	2.41	0.10	20	2.35	0.09	20	2.38	0.08
Liver	20	12.30	0.68	22	11.54	0.40	20	11.25	0.59	22	12.10	0.57	20	11.95	0.57	20	11.65	0.41
Ovary	20	0.157	0.006	22	0.149	0.004	20	0.148	0.006	22	0.147	0.004	20	0.147	0.006	20	0.136	0.005
Pituitary Gland	20	0.0211	0.0010	22	0.0203	0.0008	20	0.0199	0.0013	22	0.0201	0.0007	20	0.0190	0.0009	20	0.0203	0.0011
Spleen	20	0.678	0.030	22	0.618	0.016	20	0.612	0.024	22	0.693	0.024	20	0.659	0.030	20	0.611	0.017
Thymus	20	0.154	0.007	21	0.139	0.006	20	0.142	0.010	22	0.164	0.014	20	0.150	0.011	20	0.167	0.012
Thyroid Gland	20	0.0378	0.0022	22	0.0360	0.0016	20	0.0363	0.0017	22	0.0363	0.0013	20	0.0382	0.0023	20	0.0369	0.0017
Uterus	20	0.744	0.046	22	0.699	0.045	20	0.795	0.080	21	0.843	0.076	20	0.747	0.054	20	0.789	0.051
Receiving Weight	20	464.88	18.94	22	454.94	14.16	20	437.22	18.85	22	453.05	19.34	20	454.04	18.57	20	443.83	13.88

Table 3. Summary Statistics of Female Relative Organ to Brain Weight (g/g) Bisphenol-A Stop Dose (µg/kg$_{'BW}$/day)

	0.0			***2.5***			***25***			***250***			***2500***			***25000***	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	20	0.0349	0.0013	22	0.0334	0.0007	20	0.0343	0.0013	22	0.0348	0.0012	20	0.0328	0.0013	20	0.0365	0.0014
Fat Pad Ov/Pm	20	8.17	0.53	22	7.72	0.33	20	6.84	0.45	22	7.47	0.51	20	7.79	0.53	20	7.22	0.41
Fat Pad Retro	20	8.66	0.67	22	7.36	0.73	20	8.10	0.87	22	8.28	0.69	20	7.71	0.61	20	7.93	0.68
Heart	20	0.684	0.019	22	0.649	0.011	20	0.647	0.022	22	0.666	0.018	20	0.658	0.020	20	0.651	0.019
Kidney	20	1.18	0.04	21	1.10	0.04	20	1.09	0.04	21	1.17	0.04	20	1.12	0.04	20	1.15	0.04
Liver	20	5.86	0.28	22	5.52	0.19	20	5.38	0.27	22	5.89	0.26	20	5.70	0.25	20	5.63	0.20
Ovary	20	0.075	0.003	22	0.071	0.002	20	0.071	0.003	22	0.072	0.002	20	0.070	0.003	20	0.066	0.003
Pituitary Gland	20	0.0100	0.0004	22	0.0097	0.0004	20	0.0096	0.0007	22	0.0098	0.0003	20	0.0091	0.0004	20	0.0098	0.0005
Spleen	20	0.323	0.011	22	0.295	0.007	20	0.293	0.011	22	0.339	0.012	20	0.315	0.014	20	0.295	0.008
Thymus	20	0.074	0.003	21	0.067	0.003	20	0.068	0.005	22	0.080	0.007	20	0.072	0.005	20	0.080	0.006
Thyroid Gland	20	0.0180	0.0010	22	0.0172	0.0008	20	0.0174	0.0008	22	0.0177	0.0006	20	0.0183	0.0011	20	0.0178	0.0008
Uterus	20	0.356	0.022	22	0.334	0.022	20	0.382	0.040	21	0.410	0.035	20	0.360	0.028	20	0.381	0.024

Table 4. Summary Statistics of Female Relative Organ to Receiving Weight (mg/g) Bisphenol-A Stop Dose (µg/kg'BW'/day)

	0.0			2.5			25			250			2500			25000	
Organ	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**
Adrenal Gland	20	0.1592	0.0058	22	0.1573	0.0061	20	0.1658	0.0054	22	0.1629	0.0085	20	0.1546	0.0077	20	0.1721	0.0072
Brain	20	4.604	0.145	22	4.684	0.128	20	4.930	0.197	22	4.677	0.184	20	4.747	0.195	20	4.749	0.145
Fat Pad Ov/Pm	20	36.29	1.33	22	35.45	0.96	20	32.35	1.14	22	33.31	1.55	20	35.59	1.68	20	33.28	1.09
Fat Pad Retro	20	38.14	1.75	22	33.30	2.56	20	36.99	2.69	22	36.29	2.12	20	34.79	2.01	20	36.01	2.31
Heart	20	3.111	0.076	22	3.023	0.071	20	3.130	0.086	22	3.071	0.097	20	3.064	0.069	20	3.060	0.078
Kidney	20	5.34	0.12	21	5.17	0.23	20	5.24	0.12	21	5.38	0.15	20	5.22	0.14	20	5.39	0.15
Liver	20	26.43	0.78	22	25.42	0.55	20	25.72	0.59	22	26.83	0.77	20	26.36	0.86	20	26.31	0.58
Ovary	20	0.342	0.015	22	0.331	0.011	20	0.346	0.018	22	0.332	0.015	20	0.329	0.014	20	0.312	0.014
Pituitary Gland	20	0.0463	0.0025	22	0.0452	0.0021	20	0.0464	0.0029	22	0.0457	0.0022	20	0.0425	0.0020	20	0.0463	0.0028
Spleen	20	1.471	0.046	22	1.372	0.039	20	1.414	0.042	22	1.562	0.055	20	1.475	0.067	20	1.395	0.051
Thymus	20	0.340	0.019	21	0.311	0.017	20	0.325	0.019	22	0.368	0.030	20	0.341	0.028	20	0.376	0.023
Thyroid Gland	20	0.0820	0.0047	22	0.0800	0.0037	20	0.0851	0.0044	22	0.0814	0.0028	20	0.0850	0.0046	20	0.0839	0.0039
Uterus	20	1.667	0.140	22	1.584	0.123	20	1.868	0.187	21	1.928	0.203	20	1.737	0.165	20	1.829	0.145

Table 5. Summary Statistics of Male Organ Weight (g) Bisphenol-A Stop-Dose (µg/kg$_{BW}$/day)																		
	0.0			***2.5***			***25***			***250***			***2500***			***25000***		
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	20	0.0634	0.0020	20	0.0657	0.0021	19	0.0679	0.0033	19	0.0689	0.0027	20	0.0654	0.0035	22	0.0683	0.0033
Brain	20	2.325	0.021	20	2.331	0.019	19	2.325	0.026	19	2.303	0.031	20	2.275	0.021	22	2.304	0.029
Epididymis (Paired)	20	1.310	0.030	20	1.282	0.031	19	1.300	0.030	19	1.320	0.031	20	1.260	0.041	22	1.373	0.022
Fat Pad Epidid	20	13.901	0.697	20	15.990	0.927	19	14.852	1.040	19	13.452	0.643	19	14.850	0.994	22	14.625	0.713
Fat Pad Retro	20	25.01	2.29	20	27.78	2.01	19	25.65	2.29	19	23.03	1.69	20	23.43	2.69	22	24.97	2.12
Heart	20	2.269	0.066	20	2.451	0.088	19	2.395	0.082	19	2.248	0.078	20	2.225	0.071	22	2.354	0.098
Kidney	20	4.38	0.15	20	4.43	0.15	19	4.54	0.11	19	4.32	0.11	20	4.17	0.15	20	4.33	0.10
Liver	20	23.58	0.86	20	24.41	0.73	19	25.10	1.02	19	23.23	0.77	20	24.84	0.99	22	25.12	0.93
Pituitary Gland	20	0.0151	0.0006	20	0.0165	0.0009	19	0.0153	0.0003	19	0.0156	0.0006	20	0.0145	0.0004	22	0.0151	0.0005
Sem Ves	20	1.222	0.049	20	1.233	0.057	19	1.269	0.092	19	1.118	0.052	20	1.120	0.070	22	1.169	0.044
Spleen	20	0.999	0.029	20	1.043	0.044	19	1.015	0.034	19	1.031	0.053	20	1.071	0.063	22	1.058	0.060
Testes (Paired)	20	3.640	0.070	20	3.593	0.079	19	3.633	0.093	19	3.486	0.091	20	3.546	0.148	22	3.710	0.060
Thymus	20	0.137	0.009	20	0.123	0.005	19	0.154	0.010	19	0.130	0.008	20	0.134	0.009	22	0.145	0.008
Thyroid Gland	20	0.0431	0.0019	20	0.0434	0.0025	19	0.0449	0.0018	19	0.0412	0.0019	20	0.0422	0.0024	22	0.0454	0.0027
Receiving Weight	20	734.61	26.05	20	787.19	22.81	19	759.68	22.50	19	732.61	21.05	20	737.79	21.34	22	743.24	16.97

Table 6. Summary Statistics of Male Relative Organ to Brain Weight (mg/g) Bisphenol-A Stop Dose (µg/kg·BW/day)

	0.0			2.5			25			250			2500			25000	
Organ	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**
Adrenal Gland	20	0.0273	0.0008	20	0.0282	0.0009	19	0.0293	0.0015	19	0.0300	0.0013	20	0.0287	0.0014	22	0.0296	0.0013
Epididymis (Paired)	20	0.564	0.014	20	0.551	0.015	19	0.560	0.014	19	0.574	0.015	20	0.556	0.020	22	0.598	0.012
Fat Pad Epididymis	20	5.994	0.313	20	6.850	0.376	19	6.384	0.435	19	5.824	0.255	20	6.521	0.411	22	6.381	0.331
Fat Pad Retro	20	10.79	1.02	20	11.90	0.84	19	11.04	0.98	19	10.01	0.73	20	10.30	1.17	22	10.90	0.94
Heart	20	0.978	0.030	20	1.052	0.038	19	1.033	0.037	19	0.974	0.026	20	0.980	0.033	22	1.025	0.046
Kidney	20	1.89	0.07	20	1.90	0.06	19	1.95	0.05	19	1.88	0.05	20	1.83	0.06	20	1.89	0.04
Liver	20	10.16	0.38	20	10.47	0.30	19	10.79	0.41	19	10.07	0.28	20	10.92	0.43	22	10.93	0.43
Pituitary Gland	20	0.0065	0.0002	20	0.0071	0.0004	19	0.0066	0.0001	19	0.0068	0.0002	20	0.0064	0.0002	22	0.0066	0.0002
Seminal Vesicles	20	0.526	0.021	20	0.529	0.024	19	0.544	0.037	19	0.485	0.022	20	0.494	0.032	22	0.511	0.022
Spleen	20	0.430	0.012	20	0.448	0.019	19	0.437	0.014	19	0.449	0.024	20	0.470	0.026	22	0.458	0.024
Testes (Paired)	20	1.568	0.032	20	1.544	0.037	19	1.568	0.047	19	1.517	0.043	20	1.562	0.066	22	1.615	0.033
Thymus	20	0.059	0.004	20	0.053	0.002	19	0.066	0.004	19	0.057	0.003	20	0.059	0.004	22	0.063	0.004
Thyroid Gland	20	0.0186	0.0008	20	0.0186	0.0011	19	0.0194	0.0008	19	0.0180	0.0009	20	0.0186	0.0010	22	0.0197	0.0011

Table 7. Summary Statistics of Male Relative Organ to Receiving Weight (mg/g) Bisphenol-A Stop Dose (µg/kg·BW·/day)

	0.0			2.5			25			250			2500			25000	
Organ	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**
Adrenal Gland	20	0.0879	0.0037	20	0.0841	0.0028	19	0.0900	0.0043	19	0.0955	0.0050	20	0.0891	0.0044	22	0.0931	0.0052
Brain	20	3.241	0.119	20	3.004	0.083	19	3.105	0.091	19	3.174	0.067	20	3.128	0.087	22	3.132	0.078
Epididymis (Paired)	20	1.826	0.075	20	1.649	0.055	19	1.728	0.046	19	1.828	0.068	20	1.730	0.066	22	1.868	0.051
Fat Pad Epididymis	20	18.821	0.538	20	20.263	0.924	19	19.240	0.909	19	18.335	0.703	20	19.844	0.921	22	19.561	0.691
Fat Pad Retro	20	33.12	2.09	20	34.67	1.64	19	32.95	2.34	19	31.26	1.96	20	31.00	2.91	22	32.97	2.18
Heart	20	3.120	0.081	20	3.128	0.093	19	3.178	0.108	19	3.086	0.097	20	3.037	0.095	22	3.199	0.157
Kidney	20	5.98	0.09	20	5.62	0.09	19	6.01	0.13	19	5.94	0.15	20	5.64	0.08	20	5.78	0.09
Liver	20	32.12	0.39	20	31.07	0.52	19	33.07	0.98	19	31.79	0.75	20	33.56	0.71	22	33.93	1.25
Pituitary Gland	20	0.0207	0.0007	20	0.0212	0.0012	19	0.0205	0.0006	19	0.0214	0.0008	20	0.0198	0.0006	22	0.0205	0.0007
Seminal Vesicles	20	1.694	0.081	20	1.579	0.073	19	1.696	0.127	19	1.537	0.071	20	1.524	0.092	22	1.588	0.067
Spleen	20	1.381	0.046	20	1.333	0.057	19	1.344	0.039	19	1.415	0.068	20	1.455	0.080	22	1.440	0.095
Testes (Paired)	20	5.053	0.172	20	4.617	0.132	19	4.819	0.131	19	4.824	0.180	20	4.840	0.184	22	5.043	0.136
Thymus	20	0.188	0.010	20	0.157	0.006	19	0.204	0.014	19	0.179	0.010	20	0.185	0.013	22	0.196	0.012
Thyroid Gland	20	0.0597	0.0029	20	0.0548	0.0023	19	0.0596	0.0025	19	0.0569	0.0029	20	0.0570	0.0024	22	0.0615	0.0039

Table 8. ANOVA Results for Organ Weight[1] for Bisphenol-A Stop-Dose (µg/kg'BW'/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Dose	5	118	0.877	0.499
	Brain	Dose	5	118	0.763	0.578
	Fat Pad Ov/Pm	Dose	5	118	1.048	0.393
	Fat Pad Retro	Dose	5	118	0.391	0.854
	Heart	Dose	5	118	0.587	0.710
	Kidney	Dose	5	116	0.615	0.688
	Liver	Dose	5	118	0.506	0.771
	Ovary	Dose	5	118	1.449	0.211
	Pituitary Gland	Dose	5	118	0.485	0.786
	Spleen	Dose	5	118	2.349	**0.045**
	Thymus	Dose	5	117	1.200	0.313
	Thyroid Gland	Dose	5	118	0.235	0.946
	Uterus	Dose	5	117	0.721	0.609
M	Adrenal Gland	Dose	5	114	0.542	0.744
	Brain	Dose	5	114	0.716	0.612
	Epididymis (Paired)	Dose	5	114	1.623	0.159
	Fat Pad Epididymis	Dose	5	114	1.083	0.373
	Fat Pad Retro	Dose	5	114	0.584	0.711
	Heart	Dose	5	114	1.193	0.316
	Kidney	Dose	5	112	0.890	0.490
	Liver	Dose	5	114	0.805	0.548
	Pituitary Gland	Dose	5	114	1.542	0.182
	Seminal Vesicles	Dose	5	114	0.996	0.423
	Spleen	Dose	5	114	0.294	0.915
	Testes (Paired)	Dose	5	114	0.710	0.617
	Thymus	Dose	5	114	1.737	0.131
	Thyroid Gland	Dose	5	114	0.484	0.787

[1] Analyses were conducted separately for females and males.

Table 9. Comparisons of Least Squares Mean Female Organ Weight for Bisphenol-A Stop-Dose (µg/kg'BW'/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.073	0.003	0.724	0.070	0.003	95.8	0.871	0.072	0.003	98.0	0.993	0.071	0.003	97.4	0.979	0.069	0.003	93.7	0.617	0.076	0.003	103.5	0.938
Brain	2.091	0.021	0.379	2.095	0.020	100.2	0.999	2.090	0.021	100.0	0.999	2.049	0.020	98.0	0.458	2.090	0.021	100.0	0.999	2.071	0.021	99.1	0.943
Fat Pad Ov/Pm	17.197	1.021	0.254	16.176	0.974	94.1	0.921	14.314	1.021	83.2	0.174	15.327	0.974	89.1	0.539	16.307	1.021	94.8	0.958	14.973	1.021	87.1	0.395
Fat Pad Retro	18.240	1.566	0.616	15.407	1.494	84.5	0.551	16.960	1.566	93.0	0.967	17.099	1.494	93.7	0.978	16.175	1.566	88.7	0.814	16.441	1.566	90.1	0.882
Heart	1.433	0.041	0.297	1.359	0.040	94.9	0.566	1.350	0.041	94.2	0.481	1.366	0.040	95.3	0.654	1.377	0.041	96.1	0.798	1.347	0.041	94.0	0.445
Kidney	2.473	0.093	0.806	2.298	0.091	92.9	0.526	2.279	0.093	92.1	0.441	2.413	0.091	97.6	0.987	2.348	0.093	94.9	0.802	2.378	0.093	96.2	0.924
Liver	12.300	0.554	0.797	11.542	0.528	93.8	0.776	11.248	0.554	91.4	0.526	12.103	0.528	98.4	0.999	11.950	0.554	97.2	0.989	11.648	0.554	94.7	0.870
Ovary	0.157	0.005	**0.016**	0.149	0.005	95.1	0.741	0.148	0.005	94.2	0.634	0.147	0.005	93.6	0.526	0.147	0.005	93.6	0.539	0.136	0.005	87.1	**0.037**
Pituitary Gland	0.021	0.001	0.349	0.020	0.001	96.3	0.966	0.020	0.001	94.6	0.876	0.020	0.001	95.3	0.918	0.019	0.001	90.0	0.410	0.020	0.001	96.3	0.972
Spleen	0.678	0.024	0.511	0.618	0.023	91.0	0.251	0.612	0.024	90.2	0.195	0.693	0.023	102.2	0.990	0.659	0.024	97.1	0.970	0.611	0.024	90.0	0.184
Thymus	0.154	0.011	0.192	0.139	0.010	90.1	0.745	0.142	0.011	92.0	0.873	0.164	0.010	106.5	0.934	0.150	0.011	96.9	0.997	0.167	0.011	107.9	0.878
Thyroid Gland	0.038	0.002	0.899	0.036	0.002	95.3	0.933	0.036	0.002	96.2	0.973	0.036	0.002	96.0	0.965	0.038	0.002	101.1	0.999	0.037	0.002	97.6	0.996
Uterus	0.744	0.061	0.409	0.699	0.058	93.9	0.976	0.795	0.061	106.9	0.964	0.843	0.060	113.3	0.657	0.747	0.061	100.4	0.999	0.789	0.061	106.1	0.978

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 10. Comparisons of Least Squares Mean Male Organ Weight for Bisphenol-A Stop-Dose (µg/kg'BW'/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.063	0.003	0.295	0.066	0.003	103.6	0.970	0.068	0.003	107.2	0.704	0.069	0.003	108.7	0.536	0.065	0.003	103.2	0.982	0.068	0.003	107.8	0.603
Brain	2.325	0.025	0.154	2.331	0.025	100.3	0.999	2.325	0.026	100.0	1.000	2.303	0.026	99.1	0.962	2.275	0.025	97.8	0.472	2.304	0.024	99.1	0.964
Epididymis (Paired)	1.310	0.031	0.288	1.282	0.031	97.9	0.954	1.300	0.032	99.3	0.999	1.320	0.032	100.8	0.999	1.260	0.031	96.2	0.688	1.373	0.030	104.9	0.436
Fat Pad Epidid	13.901	0.840	0.862	15.990	0.840	115.0	0.277	14.852	0.862	106.8	0.895	13.452	0.862	96.8	0.995	14.850	0.862	106.8	0.896	14.625	0.801	105.2	0.957
Fat Pad Retro	25.007	2.209	0.386	27.777	2.209	111.1	0.844	25.654	2.267	102.6	0.999	23.030	2.267	92.1	0.956	23.433	2.209	93.7	0.982	24.974	2.107	99.9	0.999
Heart	2.269	0.082	0.552	2.451	0.082	108.0	0.384	2.395	0.084	105.5	0.725	2.248	0.084	99.1	0.999	2.225	0.082	98.0	0.994	2.354	0.078	103.7	0.914
Kidney	4.383	0.129	0.246	4.426	0.129	101.0	0.999	4.538	0.133	103.5	0.874	4.320	0.133	98.6	0.997	4.168	0.129	95.1	0.650	4.330	0.129	98.8	0.998
Liver	23.579	0.891	0.333	24.406	0.891	103.5	0.947	25.104	0.914	106.5	0.637	23.234	0.914	98.5	0.998	24.840	0.891	105.3	0.774	25.117	0.850	106.5	0.598
Pituitary Gland	0.015	0.001	0.193	0.017	0.001	109.6	0.241	0.015	0.001	101.7	0.997	0.016	0.001	103.3	0.959	0.014	0.001	95.8	0.889	0.015	0.001	100.0	1.000
Sem Ves	1.222	0.062	0.143	1.233	0.062	100.9	0.999	1.269	0.064	103.9	0.978	1.118	0.064	91.5	0.652	1.120	0.062	91.6	0.657	1.169	0.059	95.7	0.959
Spleen	0.999	0.049	0.333	1.043	0.049	104.3	0.957	1.015	0.051	101.6	0.999	1.031	0.051	103.2	0.989	1.071	0.049	107.2	0.755	1.058	0.047	105.9	0.858
Testes (Paired)	3.640	0.094	0.937	3.593	0.094	98.7	0.996	3.633	0.096	99.8	0.999	3.486	0.096	95.8	0.670	3.546	0.094	97.4	0.928	3.710	0.089	101.9	0.976
Thymus	0.137	0.008	0.499	0.123	0.008	89.5	0.606	0.154	0.008	112.3	0.472	0.130	0.008	95.0	0.968	0.134	0.008	97.6	0.998	0.145	0.008	105.3	0.954
Thyroid Gland	0.043	0.002	0.836	0.043	0.002	100.5	0.999	0.045	0.002	104.1	0.975	0.041	0.002	95.6	0.966	0.042	0.002	97.8	0.998	0.045	0.002	105.2	0.928

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 11. ANOCOVA Results for Organ Weight with Covariate Brain Weight[1] for Bisphenol-A Stop-Dose (µg/kg$_{BW}$/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Brain Weight	1	117	9.860	**0.002**
		Dose	5	117	1.130	0.348
	Fat Pad Ov/Pm	Brain Weight	1	117	11.149	**0.001**
		Dose	5	117	0.999	0.421
	Fat Pad Retro	Brain Weight	1	117	11.202	**0.001**
		Dose	5	117	0.563	0.728
	Heart	Brain Weight	1	117	17.905	**<.001**
		Dose	5	117	0.651	0.661
	Kidney	Brain Weight	1	115	26.464	**<.001**
		Dose	5	115	1.093	0.368
	Liver	Brain Weight	1	117	17.498	**<.001**
		Dose	5	117	0.845	0.520
	Ovary	Brain Weight	1	117	12.983	**<.001**
		Dose	5	117	1.380	0.236
	Pituitary Gland	Brain Weight	1	117	0.051	0.822
		Dose	5	117	0.482	0.789
	Spleen	Brain Weight	1	117	10.755	**0.001**
		Dose	5	117	2.975	**0.014**
	Thymus	Brain Weight	1	116	0.273	0.602
		Dose	5	116	1.106	0.360
	Thyroid Gland	Brain Weight	1	117	4.506	**0.035**
		Dose	5	117	0.223	0.951
	Uterus	Brain Weight	1	116	0.028	0.866
		Dose	5	116	0.681	0.638
M	Adrenal Gland	Brain Weight	1	113	4.539	**0.035**
		Dose	5	113	0.621	0.684
	Epididymis (Paired)	Brain Weight	1	113	0.146	0.702
		Dose	5	113	1.621	0.159
	Fat Pad Epididymis	Brain Weight	1	113	2.236	0.137
		Dose	5	113	1.052	0.391
	Fat Pad Retro	Brain Weight	1	113	0.133	0.716
		Dose	5	113	0.537	0.747
	Heart	Brain Weight	1	113	1.961	0.164
		Dose	5	113	1.029	0.404
	Kidney	Brain Weight	1	111	8.962	**0.003**
		Dose	5	111	0.558	0.731
	Liver	Brain Weight	1	113	5.751	**0.018**
		Dose	5	113	0.931	0.463
	Pituitary Gland	Brain Weight	1	113	2.284	0.133
		Dose	5	113	1.337	0.253
	Seminal Vesicles	Brain Weight	1	113	0.876	0.351
		Dose	5	113	0.855	0.514
	Spleen	Brain Weight	1	113	7.543	**0.007**
		Dose	5	113	0.523	0.758
	Testes (Paired)	Brain Weight	1	113	0.022	0.882
		Dose	5	113	0.708	0.618
	Thymus	Brain Weight	1	113	0.387	0.535
		Dose	5	113	1.736	0.132
	Thyroid Gland	Brain Weight	1	113	0.653	0.420
		Dose	5	113	0.452	0.810

[1] Analyses were conducted separately for females and males.

Table 12. Comparisons of Least Squares Mean Female Organ Weight with Covariate Brain Weight for Bisphenol-A Stop-Dose (µg/kg'BW'/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.073	0.003	0.537	0.070	0.002	95.6	0.833	0.071	0.003	98.0	0.993	0.072	0.002	99.4	0.999	0.068	0.003	93.8	0.592	0.076	0.003	104.5	0.837
Fat Pad Ov/Pm	17.050	0.981	0.360	15.975	0.936	93.7	0.891	14.180	0.981	83.2	0.149	15.780	0.944	92.6	0.816	16.175	0.981	94.9	0.953	15.109	0.981	88.6	0.489
Fat Pad Retro	18.014	1.504	0.801	15.097	1.436	83.8	0.485	16.754	1.504	93.0	0.964	17.796	1.448	98.8	0.999	15.972	1.504	88.7	0.796	16.650	1.504	92.4	0.951
Heart	1.425	0.039	0.441	1.349	0.037	94.6	0.469	1.343	0.039	94.2	0.425	1.389	0.037	97.4	0.939	1.370	0.039	96.1	0.764	1.354	0.039	95.0	0.555
Kidney	2.453	0.085	0.927	2.282	0.083	93.0	0.460	2.260	0.085	92.1	0.355	2.469	0.083	100.7	0.999	2.329	0.085	94.9	0.748	2.396	0.085	97.7	0.986
Liver	12.203	0.519	0.948	11.408	0.495	93.5	0.695	11.160	0.519	91.4	0.472	12.403	0.500	101.6	0.998	11.863	0.519	97.2	0.987	11.738	0.519	96.2	0.953
Ovary	0.156	0.005	**0.025**	0.148	0.005	94.8	0.675	0.147	0.005	94.2	0.599	0.149	0.005	95.8	0.819	0.146	0.005	93.6	0.502	0.137	0.005	88.1	**0.047**
Pituitary Gland	0.021	0.001	0.362	0.020	0.001	96.2	0.966	0.020	0.001	94.6	0.879	0.020	0.001	95.5	0.934	0.019	0.001	90.0	0.414	0.020	0.001	96.4	0.975
Spleen	0.675	0.023	0.676	0.613	0.022	90.8	0.203	0.608	0.023	90.1	0.170	0.704	0.023	104.3	0.846	0.656	0.023	97.2	0.968	0.614	0.023	90.9	0.235
Thymus	0.155	0.011	0.208	0.139	0.010	90.1	0.746	0.142	0.011	92.0	0.874	0.164	0.010	105.9	0.959	0.150	0.011	96.9	0.997	0.166	0.011	107.6	0.896
Thyroid Gland	0.038	0.002	0.765	0.036	0.002	95.1	0.919	0.036	0.002	96.2	0.973	0.037	0.002	97.9	0.998	0.038	0.002	101.1	0.999	0.037	0.002	98.5	0.999
Uterus	0.744	0.061	0.420	0.699	0.058	93.9	0.977	0.795	0.061	106.8	0.965	0.842	0.060	113.1	0.684	0.747	0.061	100.4	0.999	0.789	0.061	106.0	0.980

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 13. Comparisons of Least Squares Mean Male Organ Weight with Covariate Brain Weight for Bisphenol-A Stop-Dose (µg/kg$_{BW}$/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.063	0.003	0.182	0.065	0.003	103.4	0.976	0.068	0.003	107.2	0.694	0.069	0.003	109.5	0.442	0.066	0.003	105.1	0.895	0.068	0.003	108.6	0.506
Epididymis (Paired)	1.310	0.031	0.318	1.283	0.031	97.9	0.956	1.301	0.032	99.3	0.999	1.319	0.032	100.7	0.999	1.259	0.031	96.1	0.662	1.373	0.030	104.8	0.456
Fat Pad Epidid	13.832	0.837	0.972	15.890	0.838	114.9	0.286	14.781	0.859	106.9	0.894	13.484	0.858	97.5	0.998	15.036	0.866	108.7	0.778	14.652	0.797	105.9	0.929
Fat Pad Retro	24.963	2.221	0.419	27.714	2.225	111.0	0.850	25.609	2.279	102.6	0.999	23.052	2.276	92.3	0.963	23.541	2.238	94.3	0.989	24.992	2.115	100.1	1.000
Heart	2.263	0.082	0.685	2.442	0.082	107.9	0.395	2.389	0.084	105.5	0.723	2.251	0.084	99.5	0.999	2.240	0.082	99.0	0.999	2.356	0.078	104.1	0.877
Kidney	4.360	0.125	0.479	4.393	0.125	100.8	0.999	4.514	0.128	103.5	0.860	4.328	0.128	99.3	0.999	4.218	0.126	96.8	0.895	4.351	0.125	99.8	0.999
Liver	23.466	0.874	0.196	24.242	0.876	103.3	0.955	24.988	0.897	106.5	0.622	23.290	0.896	99.2	0.999	25.122	0.881	107.1	0.540	25.165	0.833	107.2	0.487
Pituitary Gland	0.015	0.001	0.272	0.016	0.001	109.5	0.248	0.015	0.001	101.7	0.997	0.016	0.001	103.7	0.931	0.015	0.001	96.8	0.963	0.015	0.001	100.4	0.999
Sem Ves	1.219	0.062	0.184	1.228	0.062	100.8	0.999	1.266	0.064	103.9	0.978	1.119	0.064	91.8	0.692	1.127	0.063	92.5	0.753	1.171	0.059	96.1	0.972
Spleen	0.992	0.048	0.177	1.032	0.048	104.0	0.965	1.008	0.049	101.6	0.999	1.035	0.049	104.3	0.959	1.089	0.048	109.7	0.483	1.061	0.046	106.9	0.749
Testes (Paired)	3.641	0.094	0.954	3.594	0.094	98.7	0.996	3.634	0.097	99.8	0.999	3.486	0.097	95.7	0.669	3.544	0.095	97.3	0.924	3.710	0.090	101.9	0.978
Thymus	0.138	0.008	0.558	0.123	0.008	89.6	0.617	0.154	0.009	112.3	0.475	0.130	0.009	94.7	0.960	0.133	0.008	96.9	0.996	0.144	0.008	105.0	0.964
Thyroid Gland	0.043	0.002	0.754	0.043	0.002	100.4	0.999	0.045	0.002	104.1	0.975	0.041	0.002	95.9	0.976	0.042	0.002	98.6	0.999	0.045	0.002	105.5	0.911

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 14. ANOCOVA Results for Organ Weight with Covariate Receiving Weight[1] for Bisphenol-A Stop-Dose Dose (µg/kg'BW'/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Receiving Weight	1	117	10.954	**0.001**
		Dose	5	117	1.045	0.394
	Fat Pad Ov/Pm	Receiving Weight	1	117	283.111	**<.001**
		Dose	5	117	1.215	0.306
	Fat Pad Retro	Receiving Weight	1	117	335.986	**<.001**
		Dose	5	117	1.703	0.139
	Heart	Receiving Weight	1	117	144.094	**<.001**
		Dose	5	117	0.521	0.759
	Kidney	Receiving Weight	1	115	109.310	**<.001**
		Dose	5	115	0.617	0.687
	Liver	Receiving Weight	1	117	214.147	**<.001**
		Dose	5	117	0.513	0.765
	Ovary	Receiving Weight	1	117	18.287	**<.001**
		Dose	5	117	1.334	0.254
	Pituitary Gland	Receiving Weight	1	117	8.563	**0.004**
		Dose	5	117	0.463	0.803
	Spleen	Receiving Weight	1	117	52.038	**<.001**
		Dose	5	117	2.601	**0.028**
	Thymus	Receiving Weight	1	116	5.246	**0.023**
		Dose	5	116	1.258	0.286
	Thyroid Gland	Receiving Weight	1	117	21.692	**<.001**
		Dose	5	117	0.224	0.951
	Uterus	Receiving Weight	1	116	3.833	0.052
		Dose	5	116	0.699	0.625
M	Adrenal Gland	Receiving Weight	1	113	4.601	**0.034**
		Dose	5	113	0.605	0.696
	Epididymis (Paired)	Receiving Weight	1	113	1.744	0.189
		Dose	5	113	1.724	0.134
	Fat Pad Epididymis	Receiving Weight	1	113	134.052	**<.001**
		Dose	5	113	0.605	0.696
	Fat Pad Retro	Receiving Weight	1	113	142.030	**<.001**
		Dose	5	113	0.224	0.951
	Heart	Receiving Weight	1	113	23.425	**<.001**
		Dose	5	113	0.664	0.651
	Kidney	Receiving Weight	1	111	207.403	**<.001**
		Dose	5	111	2.001	0.084
	Liver	Receiving Weight	1	113	135.960	**<.001**
		Dose	5	113	1.915	0.097
	Pituitary Gland	Receiving Weight	1	113	12.671	**<.001**
		Dose	5	113	1.126	0.350
	Seminal Vesicles	Receiving Weight	1	113	3.355	0.069
		Dose	5	113	0.830	0.531
	Spleen	Receiving Weight	1	113	12.623	**<.001**
		Dose	5	113	0.408	0.842
	Testes (Paired)	Receiving Weight	1	113	10.231	**0.001**
		Dose	5	113	0.778	0.567
	Thymus	Receiving Weight	1	113	6.357	**0.013**
		Dose	5	113	2.010	0.082
	Thyroid Gland	Receiving Weight	1	113	17.080	**<.001**
		Dose	5	113	0.513	0.766

[1] Analyses were conducted separately for females and males.

Table 15. Comparisons of Least Squares Mean Female Organ Weight with Covariate Receiving Weight for Bisphenol-A Stop-Dose (µg/kg$_{BW}$/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.072	0.003	0.578	0.070	0.002	96.4	0.913	0.072	0.003	99.6	0.999	0.071	0.002	98.1	0.993	0.068	0.003	94.3	0.676	0.076	0.003	104.8	0.796
Fat Pad Ov/Pm	16.545	0.556	0.257	16.005	0.529	96.7	0.929	15.002	0.556	90.7	0.188	15.247	0.529	92.2	0.308	16.180	0.555	97.8	0.987	15.341	0.555	92.7	0.401
Fat Pad Retro	17.215	0.801	0.944	15.138	0.762	87.9	0.219	18.040	0.802	104.8	0.920	16.974	0.762	98.6	0.999	15.975	0.800	92.8	0.704	17.019	0.800	98.9	0.999
Heart	1.409	0.028	0.390	1.353	0.027	96.0	0.443	1.375	0.028	97.5	0.849	1.363	0.027	96.7	0.630	1.372	0.028	97.4	0.805	1.360	0.028	96.5	0.597
Kidney	2.423	0.067	0.839	2.293	0.066	94.7	0.502	2.330	0.067	96.2	0.787	2.403	0.066	99.2	0.999	2.337	0.067	96.4	0.830	2.405	0.067	99.3	0.999
Liver	11.962	0.331	0.681	11.453	0.315	95.7	0.691	11.605	0.331	97.0	0.905	12.062	0.315	100.8	0.999	11.884	0.330	99.3	0.999	11.838	0.331	99.0	0.999
Ovary	0.155	0.005	**0.019**	0.148	0.005	95.7	0.798	0.149	0.005	96.1	0.867	0.146	0.005	94.4	0.594	0.146	0.005	94.3	0.594	0.137	0.005	88.5	0.054
Pituitary Gland	0.021	0.001	0.425	0.020	0.001	96.9	0.983	0.020	0.001	96.5	0.974	0.020	0.001	96.1	0.955	0.019	0.001	90.7	0.454	0.020	0.001	97.8	0.996
Spleen	0.668	0.020	0.710	0.615	0.019	92.0	0.214	0.622	0.020	93.2	0.371	0.692	0.019	103.5	0.867	0.657	0.020	98.3	0.994	0.616	0.020	92.3	0.258
Thymus	0.153	0.010	0.143	0.138	0.010	90.6	0.775	0.144	0.010	94.1	0.960	0.164	0.010	107.5	0.885	0.149	0.010	97.7	0.999	0.168	0.010	109.7	0.765
Thyroid Gland	0.037	0.002	0.686	0.036	0.002	96.3	0.967	0.037	0.002	99.2	0.999	0.036	0.002	97.3	0.991	0.038	0.002	102.3	0.996	0.037	0.002	99.9	0.999
Uterus	0.752	0.060	0.467	0.700	0.057	93.2	0.958	0.786	0.060	104.5	0.993	0.846	0.059	112.6	0.687	0.748	0.060	99.5	0.999	0.784	0.060	104.3	0.994

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 16. Comparisons of Least Squares Mean Male Organ Weight with Covariate Receiving Weight for Bisphenol-A Stop-Dose (µg/kg·BW/day)

	0.0			2.5				25				250				2500				25000			
Organ	**Mean**	**SE**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**
Adrenal Gland	0.064	0.003	0.228	0.065	0.003	101.5	0.999	0.068	0.003	106.1	0.803	0.069	0.003	108.7	0.513	0.066	0.003	103.1	0.984	0.068	0.003	107.4	0.631
Epididymis (Paired)	1.312	0.031	0.249	1.275	0.031	97.2	0.872	1.298	0.032	98.9	0.998	1.323	0.032	100.8	0.999	1.262	0.031	96.2	0.677	1.374	0.030	104.7	0.457
Fat Pad Epidid	14.308	0.572	0.576	14.911	0.578	104.2	0.918	14.551	0.586	101.7	0.998	13.916	0.587	97.3	0.985	15.206	0.586	106.3	0.707	14.788	0.544	103.4	0.961
Fat Pad Retro	26.104	1.480	0.632	24.903	1.497	95.4	0.970	24.857	1.517	95.2	0.966	24.279	1.519	93.0	0.858	24.290	1.479	93.0	0.854	25.419	1.409	97.4	0.997
Heart	2.292	0.075	0.751	2.391	0.076	104.3	0.820	2.379	0.077	103.8	0.887	2.274	0.077	99.2	0.999	2.243	0.075	97.8	0.987	2.363	0.071	103.1	0.938
Kidney	4.459	0.077	0.210	4.251	0.078	95.3	0.216	4.494	0.079	100.8	0.997	4.405	0.079	98.8	0.984	4.228	0.077	94.8	0.134	4.329	0.077	97.1	0.634
Liver	24.018	0.604	**0.027**	23.258	0.611	96.8	0.848	24.786	0.619	103.2	0.844	23.733	0.620	98.8	0.997	25.182	0.604	104.8	0.515	25.295	0.575	105.3	0.404
Pituitary Gland	0.015	0.001	0.262	0.016	0.001	106.7	0.532	0.015	0.001	100.3	0.999	0.016	0.001	103.4	0.944	0.015	0.001	95.7	0.851	0.015	0.001	99.5	0.999
Sem Ves	1.229	0.062	0.176	1.214	0.062	98.8	0.999	1.264	0.063	102.9	0.993	1.126	0.063	91.6	0.652	1.125	0.062	91.5	0.636	1.172	0.059	95.4	0.943
Spleen	1.010	0.047	0.209	1.015	0.048	100.6	0.999	1.008	0.048	99.8	0.999	1.043	0.048	103.3	0.984	1.079	0.047	106.9	0.744	1.062	0.045	105.2	0.885
Testes (Paired)	3.658	0.090	0.764	3.546	0.091	96.9	0.854	3.620	0.093	99.0	0.998	3.506	0.093	95.8	0.652	3.560	0.090	97.3	0.904	3.717	0.086	101.6	0.986
Thymus	0.139	0.008	0.388	0.119	0.008	86.2	0.336	0.153	0.008	110.6	0.585	0.132	0.008	95.2	0.968	0.135	0.008	97.5	0.998	0.145	0.008	104.7	0.967
Thyroid Gland	0.044	0.002	0.614	0.042	0.002	96.0	0.969	0.045	0.002	101.9	0.998	0.042	0.002	95.8	0.963	0.043	0.002	97.5	0.996	0.046	0.002	104.4	0.950

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

b) BPA Treatments Continuous Dose Arm

Table 17. Summary Statistics of Female Organ Weight (g) Bisphenol-A Continuous Dose (µg/kg'BW'/day)

	0.0			*2.5*			*25*			*250*			*2500*			*25000*	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.0724	0.0020	22	0.0764	0.0028	21	0.0749	0.0038	22	0.0754	0.0047	20	0.0765	0.0038	24	0.0733	0.0031
Brain	21	2.086	0.017	22	2.112	0.030	21	2.102	0.025	22	2.083	0.019	20	2.048	0.027	24	2.076	0.029
Fat Pad Ov/Pm	21	14.06	1.16	22	17.12	0.98	21	14.41	0.80	22	14.43	0.84	20	14.84	0.98	24	14.20	0.87
Fat Pad Retro	21	14.09	1.51	22	19.78	1.97	21	16.06	1.41	22	14.12	1.13	20	14.13	1.21	24	14.70	1.17
Heart	21	1.308	0.048	22	1.435	0.045	21	1.415	0.041	22	1.289	0.032	20	1.313	0.043	24	1.379	0.041
Kidney	21	2.27	0.07	22	2.54	0.08	21	2.51	0.10	22	2.23	0.06	20	2.31	0.08	23	2.30	0.07
Liver	21	10.69	0.52	22	12.42	0.71	21	12.16	0.48	22	10.79	0.34	20	11.26	0.49	24	11.65	0.68
Ovary	20	0.140	0.008	22	0.147	0.007	17	0.142	0.006	21	0.138	0.005	18	0.140	0.007	21	0.140	0.005
Pituitary Gland	21	0.0206	0.0011	22	0.0212	0.0013	21	0.0235	0.0018	22	0.0204	0.0015	20	0.0202	0.0014	24	0.0216	0.0011
Spleen	21	0.598	0.025	22	0.648	0.027	21	0.638	0.017	22	0.600	0.020	20	0.642	0.023	24	0.638	0.026
Thymus	21	0.150	0.011	22	0.185	0.016	21	0.155	0.012	22	0.135	0.012	20	0.142	0.009	24	0.151	0.010
Thyroid Gland	21	0.0382	0.0017	22	0.0374	0.0016	21	0.0372	0.0015	22	0.0358	0.0012	20	0.0378	0.0020	24	0.0385	0.0015
Uterus	21	0.773	0.045	22	0.742	0.052	20	0.872	0.060	22	0.757	0.058	20	0.831	0.051	24	0.832	0.061
Receiving Weight	21	420.41	18.98	22	476.93	21.94	21	445.22	14.85	22	411.06	13.91	20	421.82	12.96	24	424.53	17.38

Table 18. Summary Statistics of Female Relative Organ to Brain Weight (g/g) Bisphenol-A Continuous Dose (µg/kg$_{BW}$/day)																		
	0.0			***2.5***			***25***			***250***			***2500***			***25000***		
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.0348	0.0010	22	0.0362	0.0014	21	0.0356	0.0017	22	0.0362	0.0022	20	0.0374	0.0019	24	0.0354	0.0015
Fat Pad Ov/Pm	21	6.72	0.54	22	8.13	0.47	21	6.83	0.35	22	6.93	0.40	20	7.21	0.44	24	6.83	0.40
Fat Pad Retro	21	6.72	0.70	22	9.41	0.97	21	7.64	0.67	22	6.76	0.52	20	6.84	0.55	24	7.09	0.56
Heart	21	0.628	0.023	22	0.682	0.024	21	0.674	0.020	22	0.619	0.014	20	0.641	0.019	24	0.664	0.017
Kidney	21	1.09	0.03	22	1.21	0.04	21	1.20	0.05	22	1.07	0.03	20	1.12	0.03	23	1.11	0.03
Liver	21	5.12	0.24	22	5.90	0.36	21	5.81	0.25	22	5.18	0.16	20	5.49	0.21	24	5.60	0.30
Ovary	20	0.067	0.003	22	0.070	0.004	17	0.068	0.003	21	0.066	0.002	18	0.068	0.003	21	0.068	0.003
Pituitary Gland	21	0.0099	0.0005	22	0.0100	0.0006	21	0.0112	0.0009	22	0.0098	0.0007	20	0.0099	0.0007	24	0.0104	0.0005
Spleen	21	0.286	0.011	22	0.307	0.013	21	0.304	0.008	22	0.288	0.009	20	0.314	0.010	24	0.307	0.011
Thymus	21	0.072	0.005	22	0.088	0.008	21	0.074	0.006	22	0.065	0.006	20	0.070	0.005	24	0.073	0.005
Thyroid Gland	21	0.0183	0.0008	22	0.0178	0.0008	21	0.0178	0.0007	22	0.0172	0.0006	20	0.0185	0.0010	24	0.0186	0.0007
Uterus	21	0.371	0.022	22	0.354	0.026	20	0.414	0.026	22	0.364	0.028	20	0.411	0.029	24	0.403	0.030

Table 19. Summary Statistics of Female Relative Organ to Receiving Weight (mg/g) Bisphenol-A Continuous Dose (μg/kg$_{BW}$/day)																		
	0.0			***2.5***			***25***			***250***			***2500***			***25000***		
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.1781	0.0087	22	0.1633	0.0061	21	0.1690	0.0066	22	0.1863	0.0125	20	0.1832	0.0088	24	0.1776	0.0090
Brain	21	5.156	0.226	22	4.601	0.193	21	4.816	0.155	22	5.182	0.170	20	4.926	0.133	24	5.044	0.182
Fat Pad Ov/Pm	21	32.34	1.75	22	36.28	1.67	21	32.18	1.24	22	34.76	1.25	20	34.69	1.62	24	33.15	1.34
Fat Pad Retro	21	32.37	2.73	22	40.04	2.81	21	35.04	2.12	22	33.47	1.71	20	32.92	2.46	24	33.70	1.62
Heart	21	3.156	0.081	22	3.059	0.077	21	3.214	0.095	22	3.176	0.087	20	3.130	0.081	24	3.296	0.077
Kidney	21	5.50	0.17	22	5.43	0.17	21	5.69	0.22	22	5.47	0.12	20	5.51	0.17	23	5.59	0.13
Liver	21	25.52	0.58	22	25.94	0.76	21	27.31	0.60	22	26.40	0.56	20	26.67	0.70	24	27.22	0.67
Ovary	20	0.334	0.018	22	0.316	0.018	17	0.327	0.013	21	0.342	0.013	18	0.334	0.013	21	0.339	0.019
Pituitary Gland	21	0.0506	0.0034	22	0.0455	0.0025	21	0.0537	0.0045	22	0.0502	0.0034	20	0.0492	0.0040	24	0.0526	0.0032
Spleen	21	1.443	0.050	22	1.373	0.044	21	1.453	0.046	22	1.477	0.046	20	1.535	0.051	24	1.524	0.049
Thymus	21	0.369	0.031	22	0.387	0.026	21	0.348	0.024	22	0.329	0.028	20	0.340	0.021	24	0.357	0.021
Thyroid Gland	21	0.0927	0.0038	22	0.0809	0.0044	21	0.0846	0.0035	22	0.0889	0.0039	20	0.0907	0.0047	24	0.0923	0.0036
Uterus	21	1.916	0.150	22	1.644	0.145	20	1.981	0.148	22	1.890	0.164	20	2.046	0.169	24	2.072	0.211

Table 20. Summary Statistics of Male Organ Weight (g) Bisphenol-A Continuous Dose (µg/kg·BW/day)																		
	0.0			***2.5***			***25***			***250***			***2500***			***25000***		
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0601	0.0028	22	0.0642	0.0028	18	0.0680	0.0024	24	0.0625	0.0021	18	0.0617	0.0026	21	0.0574	0.0017
Brain	18	2.303	0.024	22	2.310	0.027	18	2.296	0.036	24	2.245	0.026	18	2.281	0.030	21	2.240	0.021
Epididymis (Paired)	18	1.285	0.037	22	1.213	0.037	18	1.321	0.025	24	1.271	0.040	18	1.272	0.035	21	1.250	0.025
Fat Pad Epidid	18	12.980	0.663	22	14.458	0.831	18	13.577	0.595	24	14.083	0.847	18	14.274	1.159	21	14.201	0.999
Fat Pad Retro	18	22.15	1.82	22	22.75	1.58	18	24.47	2.51	24	22.94	1.87	18	21.84	2.69	21	23.64	2.42
Heart	18	2.042	0.061	22	2.137	0.050	18	2.261	0.084	24	2.206	0.073	18	2.188	0.070	21	1.990	0.037
Kidney	17	4.08	0.15	22	4.20	0.12	17	4.15	0.17	24	4.05	0.11	17	4.00	0.17	21	3.88	0.08
Liver	18	22.14	0.93	22	21.11	0.69	18	22.65	0.96	24	22.35	0.58	18	22.14	0.97	21	20.62	0.59
Pituitary Gland	18	0.0146	0.0007	22	0.0146	0.0006	18	0.0152	0.0006	24	0.0161	0.0012	18	0.0154	0.0008	21	0.0151	0.0006
Sem Ves	18	1.185	0.043	22	1.113	0.047	18	1.145	0.049	24	1.171	0.053	18	1.096	0.057	21	1.189	0.043
Spleen	18	0.924	0.030	22	0.957	0.033	18	0.973	0.036	24	0.961	0.027	18	0.955	0.042	21	0.871	0.034
Testes (Paired)	18	3.591	0.117	22	3.435	0.127	18	3.619	0.079	24	3.378	0.135	18	3.559	0.079	21	3.513	0.115
Thymus	18	0.150	0.011	22	0.138	0.009	18	0.125	0.012	24	0.158	0.010	18	0.140	0.010	21	0.150	0.011
Thyroid Gland	18	0.0435	0.0020	22	0.0427	0.0024	18	0.0440	0.0025	24	0.0422	0.0016	18	0.0409	0.0019	21	0.0445	0.0018
Receiving Weight	18	700.86	19.23	22	722.41	20.17	18	709.29	21.23	24	713.39	15.46	18	703.99	25.55	21	694.74	17.93

Table 21. Summary Statistics of Male Relative Organ to Brain Weight (g/g) Bisphenol-A Continuous Dose (μg/kg$_{BW}$/day)																	
	0.0			***2.5***			***25***			***250***			***2500***			***25000***	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0261	0.0012	22	0.0278	0.0011	18	0.0297	0.0011	24	0.0278	0.0008	18	0.0270	0.0010	21	0.0257	0.0008
Epididymis (Paired)	18	0.559	0.016	22	0.527	0.018	18	0.578	0.014	24	0.565	0.016	18	0.558	0.013	21	0.559	0.011
Fat Pad Epididymis	18	5.617	0.263	22	6.281	0.366	18	5.910	0.230	24	6.294	0.390	18	6.241	0.496	21	6.349	0.449
Fat Pad Retro	18	9.59	0.74	22	9.88	0.69	18	10.57	1.02	24	10.19	0.81	18	9.56	1.21	21	10.59	1.09
Heart	18	0.886	0.022	22	0.926	0.021	18	0.987	0.037	24	0.983	0.031	18	0.960	0.029	21	0.890	0.017
Kidney	17	1.77	0.05	22	1.82	0.05	17	1.80	0.06	24	1.80	0.04	17	1.75	0.07	21	1.73	0.04
Liver	18	9.58	0.34	22	9.15	0.29	18	9.84	0.34	24	9.97	0.26	18	9.71	0.43	21	9.21	0.26
Pituitary Gland	18	0.0063	0.0002	22	0.0063	0.0003	18	0.0067	0.0003	24	0.0071	0.0005	18	0.0067	0.0004	21	0.0067	0.0003
Seminal Vesicles	18	0.514	0.017	22	0.481	0.019	18	0.502	0.025	24	0.522	0.023	18	0.481	0.025	21	0.531	0.018
Spleen	18	0.401	0.012	22	0.415	0.014	18	0.425	0.016	24	0.428	0.011	18	0.419	0.018	21	0.389	0.014
Testes (Paired)	18	1.559	0.047	22	1.496	0.061	18	1.581	0.037	24	1.501	0.057	18	1.561	0.032	21	1.571	0.051
Thymus	18	0.065	0.005	22	0.060	0.004	18	0.054	0.005	24	0.071	0.004	18	0.062	0.005	21	0.067	0.005
Thyroid Gland	18	0.0188	0.0008	22	0.0185	0.0010	18	0.0191	0.0010	24	0.0188	0.0007	18	0.0178	0.0007	21	0.0199	0.0008

Table 22. Summary Statistics of Male Relative Organ to Receiving Weight (mg/g) Bisphenol-A Continuous Dose (μg/kg·BW/day)																		
	0.0			***2.5***			***25***			***250***			***2500***			***25000***		
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0862	0.0037	22	0.0896	0.0041	18	0.0967	0.0036	24	0.0881	0.0029	18	0.0884	0.0036	21	0.0831	0.0025
Brain	18	3.316	0.072	22	3.249	0.097	18	3.271	0.080	24	3.179	0.076	18	3.301	0.103	21	3.263	0.081
Epididymis (Paired)	18	1.849	0.061	22	1.705	0.069	18	1.889	0.061	24	1.793	0.063	18	1.831	0.058	21	1.821	0.055
Fat Pad Epididymis	18	18.463	0.780	22	19.759	0.707	18	19.186	0.703	24	19.489	0.999	18	19.984	1.124	21	20.225	1.152
Fat Pad Retro	18	31.27	1.98	22	30.94	1.49	18	33.70	2.63	24	31.46	2.26	18	29.69	2.72	21	33.25	2.87
Heart	18	2.925	0.074	22	2.995	0.094	18	3.204	0.103	24	3.106	0.095	18	3.140	0.094	21	2.882	0.049
Kidney	17	5.83	0.14	22	5.85	0.14	17	5.87	0.15	24	5.70	0.12	17	5.67	0.16	21	5.62	0.11
Liver	18	31.42	0.63	22	29.28	0.62	18	31.89	0.85	24	31.35	0.51	18	31.39	0.65	21	29.72	0.50
Pituitary Gland	18	0.0210	0.0009	22	0.0203	0.0007	18	0.0217	0.0010	24	0.0225	0.0016	18	0.0220	0.0010	21	0.0220	0.0011
Seminal Vesicles	18	1.701	0.060	22	1.559	0.071	18	1.638	0.088	24	1.660	0.085	18	1.585	0.097	21	1.734	0.076
Spleen	18	1.327	0.046	22	1.330	0.039	18	1.390	0.062	24	1.356	0.041	18	1.363	0.046	21	1.258	0.040
Testes (Paired)	18	5.162	0.181	22	4.823	0.208	18	5.178	0.187	24	4.769	0.209	18	5.118	0.132	21	5.135	0.223
Thymus	18	0.216	0.015	22	0.197	0.015	18	0.178	0.017	24	0.224	0.014	18	0.204	0.018	21	0.219	0.018
Thyroid Gland	18	0.0622	0.0024	22	0.0594	0.0029	18	0.0626	0.0036	24	0.0595	0.0022	18	0.0586	0.0027	21	0.0644	0.0027

Table 23. ANOVA Results for Organ Weight[1] for Bisphenol-A Continuous Dose (µg/kg'BW'/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Dose	5	124	0.226	0.950
	Brain	Dose	5	124	0.756	0.583
	Fat Pad Ov/Pm	Dose	5	124	1.499	0.195
	Fat Pad Retro	Dose	5	124	2.466	**0.036**
	Heart	Dose	5	124	2.131	0.066
	Kidney	Dose	5	123	2.868	**0.017**
	Liver	Dose	5	124	1.592	0.167
	Ovary	Dose	5	113	0.261	0.933
	Pituitary Gland	Dose	5	124	0.754	0.584
	Spleen	Dose	5	124	0.904	0.481
	Thymus	Dose	5	124	2.180	0.060
	Thyroid Gland	Dose	5	124	0.383	0.859
	Uterus	Dose	5	123	0.851	0.516
M	Adrenal Gland	Dose	5	115	2.180	0.061
	Brain	Dose	5	115	1.250	0.290
	Epididymis (Paired)	Dose	5	115	1.092	0.368
	Fat Pad Epididymis	Dose	5	115	0.370	0.868
	Fat Pad Retro	Dose	5	115	0.184	0.968
	Heart	Dose	5	115	2.546	**0.031**
	Kidney	Dose	5	112	0.768	0.574
	Liver	Dose	5	115	1.064	0.383
	Pituitary Gland	Dose	5	115	0.450	0.812
	Seminal Vesicles	Dose	5	115	0.603	0.697
	Spleen	Dose	5	115	1.282	0.276
	Testes (Paired)	Dose	5	115	0.678	0.640
	Thymus	Dose	5	115	1.247	0.291
	Thyroid Gland	Dose	5	115	0.407	0.843

[1] Analyses were conducted separately for females and males.

Table 24. Comparisons of Least Squares Mean Female Organ Weight for Bisphenol-A Continuous Dose (µg/kg^{1}$_{BW}$/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.072	0.004	0.846	0.076	0.003	105.5	0.884	0.075	0.004	103.5	0.980	0.075	0.003	104.1	0.960	0.076	0.004	105.7	0.880	0.073	0.003	101.3	0.999
Brain	2.086	0.026	0.213	2.112	0.025	101.3	0.912	2.102	0.026	100.8	0.988	2.083	0.025	99.9	0.999	2.048	0.026	98.2	0.753	2.076	0.024	99.5	0.998
Fat Pad Ov/Pm	14.056	0.957	0.438	17.117	0.935	121.8	0.092	14.411	0.957	102.5	0.999	14.428	0.935	102.6	0.998	14.837	0.981	105.6	0.969	14.205	0.896	101.1	0.999
Fat Pad Retro	14.094	1.451	0.184	19.778	1.418	140.3	**0.025**	16.060	1.451	114.0	0.798	14.123	1.418	100.2	0.999	14.135	1.487	100.3	0.999	14.700	1.357	104.3	0.998
Heart	1.308	0.043	0.690	1.435	0.042	109.7	0.133	1.415	0.043	108.1	0.270	1.289	0.042	98.5	0.997	1.313	0.044	100.3	0.999	1.379	0.040	105.4	0.620
Kidney	2.269	0.079	0.193	2.541	0.077	112.0	0.061	2.507	0.079	110.5	0.132	2.229	0.077	98.2	0.995	2.306	0.081	101.6	0.997	2.296	0.075	101.2	0.999
Liver	10.690	0.571	0.992	12.422	0.558	116.2	0.121	12.163	0.571	113.8	0.243	10.787	0.558	100.9	0.999	11.263	0.585	105.4	0.931	11.652	0.534	109.0	0.608
Ovary	0.140	0.006	0.618	0.147	0.006	104.7	0.906	0.142	0.007	101.0	0.999	0.138	0.006	98.3	0.999	0.140	0.007	99.5	0.999	0.140	0.006	100.0	1.000
Pituitary Gland	0.021	0.001	0.928	0.021	0.001	102.9	0.998	0.023	0.001	113.7	0.453	0.020	0.001	99.0	0.999	0.020	0.001	97.9	0.999	0.022	0.001	104.9	0.976
Spleen	0.598	0.024	0.453	0.648	0.023	108.3	0.419	0.638	0.024	106.6	0.638	0.600	0.023	100.3	0.999	0.642	0.024	107.4	0.554	0.638	0.022	106.7	0.605
Thymus	0.150	0.012	0.148	0.185	0.012	123.8	0.130	0.155	0.012	103.6	0.997	0.135	0.012	90.3	0.849	0.142	0.012	95.3	0.992	0.151	0.011	100.8	0.999
Thyroid Gland	0.038	0.002	0.910	0.037	0.002	97.7	0.994	0.037	0.002	97.4	0.989	0.036	0.002	93.7	0.717	0.038	0.002	98.9	0.999	0.039	0.002	100.8	0.999
Uterus	0.773	0.056	0.322	0.742	0.054	96.0	0.993	0.872	0.057	112.8	0.602	0.757	0.054	98.0	0.999	0.831	0.057	107.6	0.917	0.832	0.052	107.7	0.896

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 25. Comparisons of Least Squares Mean Male Organ Weight for Bisphenol-A Continuous Dose (µg/kg'BW/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.060	0.003	0.197	0.064	0.002	106.9	0.619	0.068	0.003	113.2	0.110	0.063	0.002	104.1	0.912	0.062	0.003	102.7	0.988	0.057	0.002	95.5	0.894
Brain	2.303	0.029	0.057	2.310	0.026	100.3	0.999	2.296	0.029	99.7	0.999	2.245	0.025	97.5	0.415	2.281	0.029	99.1	0.979	2.240	0.027	97.3	0.368
Epididymis (Paired)	1.285	0.036	0.875	1.213	0.033	94.3	0.424	1.321	0.036	102.8	0.930	1.271	0.032	98.9	0.998	1.272	0.036	99.0	0.999	1.250	0.034	97.3	0.925
Fat Pad Epidid	12.980	0.929	0.418	14.458	0.841	111.4	0.635	13.577	0.929	104.6	0.987	14.083	0.805	108.5	0.828	14.274	0.929	110.0	0.773	14.201	0.860	109.4	0.786
Fat Pad Retro	22.154	2.273	0.861	22.751	2.056	102.7	0.999	24.468	2.273	110.4	0.919	22.943	1.969	103.6	0.999	21.845	2.273	98.6	0.999	23.641	2.105	106.7	0.984
Heart	2.042	0.068	0.773	2.137	0.061	104.7	0.732	2.261	0.068	110.8	0.090	2.206	0.059	108.0	0.236	2.188	0.068	107.2	0.395	1.990	0.063	97.5	0.971
Kidney	4.078	0.140	0.138	4.201	0.123	103.0	0.940	4.146	0.140	101.7	0.996	4.053	0.118	99.4	0.999	4.004	0.140	98.2	0.994	3.882	0.126	95.2	0.736
Liver	22.135	0.819	0.465	21.114	0.740	95.4	0.811	22.652	0.819	102.3	0.988	22.351	0.709	101.0	0.999	22.140	0.819	100.0	1.000	20.617	0.758	93.1	0.506
Pituitary Gland	0.015	0.001	0.443	0.015	0.001	99.8	0.999	0.015	0.001	103.9	0.987	0.016	0.001	109.6	0.616	0.015	0.001	105.1	0.961	0.015	0.001	103.1	0.994
Sem Ves	1.185	0.052	0.991	1.113	0.047	93.9	0.747	1.145	0.052	96.6	0.974	1.171	0.045	98.8	0.999	1.096	0.052	92.5	0.616	1.189	0.048	100.3	0.999
Spleen	0.924	0.036	0.320	0.957	0.032	103.6	0.932	0.973	0.036	105.3	0.775	0.961	0.031	104.0	0.889	0.955	0.036	103.3	0.957	0.871	0.033	94.2	0.695
Testes (Paired)	3.591	0.123	0.792	3.435	0.111	95.6	0.798	3.619	0.123	100.8	0.999	3.378	0.106	94.1	0.536	3.559	0.123	99.1	0.999	3.513	0.113	97.8	0.986
Thymus	0.150	0.011	0.685	0.138	0.010	92.1	0.881	0.125	0.011	83.3	0.343	0.158	0.010	105.2	0.975	0.140	0.011	93.1	0.939	0.150	0.010	99.8	0.999
Thyroid Gland	0.044	0.002	0.898	0.043	0.002	98.2	0.998	0.044	0.002	101.1	0.999	0.042	0.002	96.9	0.984	0.041	0.002	94.0	0.849	0.045	0.002	102.3	0.996

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 26. ANOCOVA Results for Organ Weight with Covariate Brain Weight[1] for Bisphenol-A Continuous Dose (µg/kg'BW'/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Brain Weight	1	123	2.096	0.150
		Dose	5	123	0.240	0.944
	Fat Pad Ov/Pm	Brain Weight	1	123	10.117	**0.001**
		Dose	5	123	1.351	0.247
	Fat Pad Retro	Brain Weight	1	123	4.182	**0.042**
		Dose	5	123	2.142	0.064
	Heart	Brain Weight	1	123	8.708	**0.003**
		Dose	5	123	1.833	0.111
	Kidney	Brain Weight	1	122	5.851	**0.017**
		Dose	5	122	2.500	**0.034**
	Liver	Brain Weight	1	123	5.562	**0.019**
		Dose	5	123	1.409	0.225
	Ovary	Brain Weight	1	112	6.397	**0.012**
		Dose	5	112	0.166	0.974
	Pituitary Gland	Brain Weight	1	123	4.011	**0.047**
		Dose	5	123	0.649	0.663
	Spleen	Brain Weight	1	123	9.432	**0.002**
		Dose	5	123	0.992	0.425
	Thymus	Brain Weight	1	123	1.664	0.199
		Dose	5	123	1.965	0.088
	Thyroid Gland	Brain Weight	1	123	1.722	0.191
		Dose	5	123	0.425	0.830
	Uterus	Brain Weight	1	122	0.464	0.497
		Dose	5	122	0.808	0.546
M	Adrenal Gland	Brain Weight	1	114	10.377	**0.001**
		Dose	5	114	1.913	0.097
	Epididymis (Paired)	Brain Weight	1	114	6.705	**0.010**
		Dose	5	114	1.226	0.301
	Fat Pad Epididymis	Brain Weight	1	114	2.676	0.104
		Dose	5	114	0.458	0.806
	Fat Pad Retro	Brain Weight	1	114	4.321	**0.039**
		Dose	5	114	0.272	0.927
	Heart	Brain Weight	1	114	12.930	**<.001**
		Dose	5	114	2.703	**0.023**
	Kidney	Brain Weight	1	111	37.330	**<.001**
		Dose	5	111	0.430	0.826
	Liver	Brain Weight	1	114	18.544	**<.001**
		Dose	5	114	1.238	0.295
	Pituitary Gland	Brain Weight	1	114	3.876	0.051
		Dose	5	114	0.678	0.640
	Seminal Vesicles	Brain Weight	1	114	5.397	**0.021**
		Dose	5	114	0.866	0.506
	Spleen	Brain Weight	1	114	9.359	**0.002**
		Dose	5	114	1.128	0.349
	Testes (Paired)	Brain Weight	1	114	3.041	0.083
		Dose	5	114	0.596	0.703
	Thymus	Brain Weight	1	114	0.466	0.496
		Dose	5	114	1.317	0.261
	Thyroid Gland	Brain Weight	1	114	14.282	**<.001**
		Dose	5	114	0.643	0.667

[1] Analyses were conducted separately for females and males.

Table 27. Comparisons of Least Squares Mean Female Organ Weight with Covariate Brain Weight for Bisphenol-A Continuous Dose (µg/kg·BW/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.072	0.004	0.723	0.076	0.003	104.8	0.926	0.075	0.004	103.1	0.988	0.075	0.003	104.2	0.957	0.077	0.004	106.6	0.804	0.073	0.003	101.5	0.999
Fat Pad Ov/Pm	14.047	0.924	0.656	16.832	0.907	119.8	0.126	14.234	0.926	101.3	0.999	14.445	0.903	102.8	0.998	15.216	0.954	108.3	0.846	14.298	0.865	101.8	0.999
Fat Pad Retro	14.084	1.433	0.266	19.495	1.407	138.4	**0.033**	15.883	1.435	112.8	0.842	14.140	1.400	100.4	0.999	14.512	1.480	103.0	0.999	14.793	1.341	105.0	0.995
Heart	1.308	0.041	0.936	1.423	0.041	108.8	0.178	1.407	0.041	107.6	0.304	1.290	0.040	98.6	0.997	1.328	0.043	101.5	0.996	1.383	0.039	105.7	0.540
Kidney	2.268	0.077	0.314	2.521	0.076	111.2	0.082	2.494	0.078	110.0	0.150	2.229	0.076	98.3	0.996	2.329	0.080	102.7	0.973	2.306	0.074	101.7	0.996
Liver	10.686	0.561	0.800	12.294	0.551	115.0	0.157	12.083	0.562	113.1	0.274	10.795	0.548	101.0	0.999	11.433	0.579	107.0	0.819	11.694	0.525	109.4	0.550
Ovary	0.140	0.006	0.814	0.145	0.006	103.8	0.958	0.141	0.007	100.6	0.999	0.138	0.006	98.7	0.999	0.142	0.007	101.4	0.999	0.140	0.006	100.1	0.999
Pituitary Gland	0.021	0.001	0.894	0.021	0.001	101.6	0.999	0.023	0.001	112.9	0.498	0.020	0.001	99.2	0.999	0.021	0.001	99.7	0.999	0.022	0.001	105.4	0.964
Spleen	0.598	0.023	0.267	0.641	0.022	107.2	0.527	0.633	0.023	106.0	0.701	0.600	0.022	100.4	0.999	0.651	0.024	108.9	0.346	0.640	0.021	107.1	0.521
Thymus	0.149	0.012	0.193	0.184	0.012	122.8	0.156	0.154	0.012	103.0	0.998	0.135	0.012	90.4	0.853	0.144	0.012	96.6	0.998	0.151	0.011	101.2	0.999
Thyroid Gland	0.038	0.002	0.796	0.037	0.002	97.2	0.985	0.037	0.002	97.0	0.982	0.036	0.002	93.7	0.721	0.038	0.002	99.7	0.999	0.039	0.002	101.0	0.999
Uterus	0.773	0.056	0.363	0.746	0.055	96.5	0.996	0.873	0.057	113.0	0.592	0.757	0.055	98.0	0.999	0.827	0.058	106.9	0.943	0.831	0.052	107.5	0.905

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 28. Comparisons of Least Squares Mean Male Organ Weight with Covariate Brain Weight for Bisphenol-A Continuous Dose (µg/kg'BW/day)

	0.0			2.5				25				250				2500				25000			
Organ	**Mean**	**SE**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**
Adrenal Gland	0.059	0.002	0.449	0.063	0.002	106.6	0.625	0.068	0.002	113.6	0.080	0.063	0.002	106.6	0.617	0.062	0.002	103.6	0.955	0.058	0.002	98.1	0.997
Epididymis (Paired)	1.278	0.036	0.766	1.203	0.032	94.1	0.375	1.316	0.036	102.9	0.907	1.280	0.031	100.2	0.999	1.271	0.036	99.5	0.999	1.261	0.033	98.7	0.996
Fat Pad Epidid	12.858	0.926	0.276	14.301	0.840	111.2	0.650	13.489	0.924	104.9	0.983	14.241	0.805	110.8	0.677	14.254	0.923	110.9	0.715	14.381	0.861	111.8	0.622
Fat Pad Retro	21.779	2.248	0.590	22.268	2.040	102.2	0.999	24.196	2.245	111.1	0.900	23.428	1.955	107.6	0.971	21.785	2.241	100.0	1.000	24.198	2.092	111.1	0.890
Heart	2.023	0.065	0.739	2.113	0.059	104.4	0.739	2.248	0.065	111.1	0.060	2.230	0.056	110.2	0.069	2.185	0.064	108.0	0.261	2.018	0.060	99.8	0.999
Kidney	4.031	0.122	0.460	4.126	0.108	102.4	0.963	4.103	0.122	101.8	0.991	4.129	0.103	102.5	0.955	3.976	0.122	98.7	0.997	3.970	0.111	98.5	0.995
Liver	21.871	0.765	0.987	20.774	0.694	95.0	0.717	22.461	0.764	102.7	0.972	22.693	0.665	103.8	0.879	22.098	0.763	101.0	0.999	21.010	0.712	96.1	0.872
Pituitary Gland	0.015	0.001	0.268	0.014	0.001	99.5	0.999	0.015	0.001	104.2	0.982	0.016	0.001	111.9	0.425	0.015	0.001	105.9	0.928	0.015	0.001	105.5	0.940
Sem Ves	1.175	0.051	0.691	1.101	0.047	93.7	0.706	1.138	0.051	96.8	0.979	1.183	0.045	100.7	0.999	1.095	0.051	93.1	0.682	1.203	0.048	102.4	0.993
Spleen	0.915	0.034	0.632	0.946	0.031	103.3	0.942	0.967	0.034	105.6	0.718	0.972	0.030	106.2	0.599	0.953	0.034	104.1	0.894	0.883	0.032	96.5	0.935
Testes (Paired)	3.574	0.122	0.964	3.413	0.111	95.5	0.774	3.606	0.122	100.9	0.999	3.400	0.106	95.1	0.711	3.556	0.121	99.5	0.999	3.538	0.113	99.0	0.999
Thymus	0.150	0.011	0.605	0.138	0.010	91.9	0.877	0.125	0.011	83.3	0.352	0.159	0.010	106.1	0.954	0.140	0.011	93.4	0.951	0.151	0.010	100.8	0.999
Thyroid Gland	0.043	0.002	0.595	0.042	0.002	97.7	0.995	0.044	0.002	101.5	0.999	0.043	0.002	100.1	0.999	0.041	0.002	95.1	0.916	0.045	0.002	106.0	0.821

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 29. ANOCOVA Results for Organ Weight with Covariate Receiving Weight[1] for Bisphenol-A Continuous Dose (µg/kg·BW/day)

Sex	Organ	Effect	NumDF	DenDF	Fvalue	P value
F	Adrenal Gland	Receiving Weight	1	123	12.973	**<.001**
		Dose	5	123	0.261	0.933
	Fat Pad Ov/Pm	Receiving Weight	1	123	138.773	**<.001**
		Dose	5	123	0.790	0.558
	Fat Pad Retro	Receiving Weight	1	123	254.121	**<.001**
		Dose	5	123	0.679	0.640
	Heart	Receiving Weight	1	123	134.178	**<.001**
		Dose	5	123	1.144	0.341
	Kidney	Receiving Weight	1	122	85.752	**<.001**
		Dose	5	122	1.168	0.328
	Liver	Receiving Weight	1	123	317.401	**<.001**
		Dose	5	123	1.301	0.267
	Ovary	Receiving Weight	1	112	10.566	**0.001**
		Dose	5	112	0.014	0.999
	Pituitary Gland	Receiving Weight	1	123	2.317	0.130
		Dose	5	123	0.661	0.653
	Spleen	Receiving Weight	1	123	78.918	**<.001**
		Dose	5	123	0.957	0.447
	Thymus	Receiving Weight	1	123	22.100	**<.001**
		Dose	5	123	0.996	0.423
	Thyroid Gland	Receiving Weight	1	123	16.097	**<.001**
		Dose	5	123	0.639	0.670
	Uterus	Receiving Weight	1	122	3.354	0.069
		Dose	5	122	0.862	0.509
M	Adrenal Gland	Receiving Weight	1	114	20.032	**<.001**
		Dose	5	114	2.113	0.068
	Epididymis (Paired)	Receiving Weight	1	114	7.748	**0.006**
		Dose	5	114	1.276	0.279
	Fat Pad Epididymis	Receiving Weight	1	114	110.607	**<.001**
		Dose	5	114	0.655	0.658
	Fat Pad Retro	Receiving Weight	1	114	149.524	**<.001**
		Dose	5	114	0.786	0.561
	Heart	Receiving Weight	1	114	40.517	**<.001**
		Dose	5	114	2.846	**0.018**
	Kidney	Receiving Weight	1	111	115.172	**<.001**
		Dose	5	111	0.819	0.538
	Liver	Receiving Weight	1	114	234.755	**<.001**
		Dose	5	114	3.317	**0.007**
	Pituitary Gland	Receiving Weight	1	114	10.883	**0.001**
		Dose	5	114	0.509	0.768
	Seminal Vesicles	Receiving Weight	1	114	1.556	0.214
		Dose	5	114	0.656	0.657
	Spleen	Receiving Weight	1	114	30.880	**<.001**
		Dose	5	114	1.173	0.326
	Testes (Paired)	Receiving Weight	1	114	3.886	0.051
		Dose	5	114	0.787	0.561
	Thymus	Receiving Weight	1	114	0.089	0.765
		Dose	5	114	1.230	0.299
	Thyroid Gland	Receiving Weight	1	114	16.636	**<.001**
		Dose	5	114	0.601	0.699

[1] Analyses were conducted separately for females and males.

Table 30. Comparisons of Least Squares Mean Female Organ Weight with Covariate Receiving Weight for Bisphenol-A Continuous Dose (µg/kg$_{BW}$/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.073	0.003	0.545	0.074	0.003	100.6	0.999	0.074	0.003	101.4	0.999	0.077	0.003	104.9	0.906	0.077	0.003	105.5	0.870	0.074	0.003	100.9	0.999
Fat Pad Ov/Pm	14.577	0.660	0.839	15.370	0.661	105.4	0.867	13.936	0.660	95.6	0.937	15.323	0.648	105.1	0.884	15.301	0.676	105.0	0.904	14.560	0.617	99.9	0.999
Fat Pad Retro	14.982	0.834	0.603	16.793	0.834	112.1	0.407	15.248	0.834	101.8	0.999	15.653	0.819	104.5	0.968	14.927	0.854	99.6	0.999	15.307	0.779	102.2	0.998
Heart	1.331	0.030	0.466	1.358	0.030	102.0	0.956	1.394	0.030	104.7	0.429	1.329	0.029	99.8	0.999	1.333	0.030	100.1	0.999	1.395	0.028	104.8	0.380
Kidney	2.303	0.061	0.725	2.406	0.061	104.4	0.647	2.467	0.061	107.1	0.214	2.291	0.060	99.5	0.999	2.335	0.062	101.4	0.995	2.345	0.058	101.8	0.983
Liver	11.052	0.304	**0.049**	11.207	0.304	101.4	0.996	11.832	0.304	107.1	0.249	11.410	0.298	103.2	0.866	11.585	0.311	104.8	0.610	11.899	0.284	107.7	0.159
Ovary	0.141	0.006	0.913	0.142	0.006	101.1	0.999	0.141	0.007	100.4	0.999	0.140	0.006	99.7	0.999	0.141	0.006	100.1	0.999	0.141	0.006	100.0	1.000
Pituitary Gland	0.021	0.001	0.935	0.021	0.001	99.9	1.000	0.023	0.001	112.3	0.549	0.021	0.001	99.5	0.999	0.020	0.001	97.9	0.999	0.022	0.001	104.7	0.980
Spleen	0.609	0.019	0.053	0.611	0.019	100.3	0.999	0.628	0.019	103.1	0.928	0.619	0.018	101.6	0.994	0.652	0.019	107.1	0.349	0.645	0.017	106.0	0.464
Thymus	0.153	0.011	0.302	0.173	0.011	113.4	0.559	0.152	0.011	99.2	0.999	0.141	0.011	92.1	0.897	0.146	0.011	95.1	0.986	0.153	0.010	100.1	1.000
Thyroid Gland	0.039	0.002	0.570	0.036	0.002	93.1	0.614	0.037	0.002	95.4	0.873	0.037	0.001	94.5	0.770	0.038	0.002	98.8	0.999	0.039	0.001	100.4	0.999
Uterus	0.766	0.055	0.433	0.765	0.055	99.8	0.999	0.880	0.057	114.9	0.466	0.745	0.054	97.4	0.999	0.825	0.057	107.8	0.911	0.828	0.052	108.1	0.880

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

Table 31. Comparisons of Least Squares Mean Male Organ Weight with Covariate Receiving Weight for Bisphenol-A Continuous Dose (µg/kg$^{'BW}$/day)

	0.0			***2.5***				***25***				***250***				***2500***				***25000***			
Organ	***Mean***	***SE***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.060	0.002	0.234	0.064	0.002	105.1	0.778	0.068	0.002	112.5	0.097	0.062	0.002	103.1	0.958	0.062	0.002	102.4	0.989	0.058	0.002	96.0	0.907
Epididymis (Paired)	1.288	0.035	0.972	1.206	0.032	93.6	0.288	1.320	0.035	102.5	0.949	1.268	0.031	98.4	0.990	1.274	0.035	98.9	0.998	1.256	0.033	97.5	0.938
Fat Pad Epidid	13.200	0.665	0.110	14.006	0.603	106.1	0.829	13.535	0.665	102.5	0.995	13.913	0.576	105.4	0.877	14.396	0.665	109.1	0.569	14.612	0.617	110.7	0.378
Fat Pad Retro	22.733	1.502	0.414	21.565	1.362	94.9	0.966	24.356	1.502	107.1	0.900	22.496	1.301	99.0	0.999	22.166	1.502	97.5	0.998	24.720	1.393	108.7	0.782
Heart	2.053	0.058	0.963	2.113	0.053	102.9	0.904	2.259	0.058	110.0	0.057	2.197	0.051	107.0	0.227	2.195	0.058	106.9	0.294	2.012	0.054	98.0	0.979
Kidney	4.114	0.099	0.083	4.135	0.087	100.5	0.999	4.154	0.099	101.0	0.998	4.029	0.083	97.9	0.939	4.005	0.099	97.3	0.888	3.944	0.089	95.9	0.557
Liver	22.362	0.470	0.563	20.649	0.426	92.3	**0.033**	22.608	0.470	101.1	0.995	22.175	0.407	99.2	0.998	22.266	0.470	99.6	0.999	21.040	0.436	94.1	0.149
Pituitary Gland	0.015	0.001	0.344	0.014	0.001	97.9	0.998	0.015	0.001	103.2	0.993	0.016	0.001	108.5	0.681	0.015	0.001	104.8	0.963	0.015	0.001	103.6	0.987
Sem Ves	1.187	0.052	0.963	1.109	0.047	93.4	0.685	1.145	0.052	96.4	0.966	1.169	0.045	98.5	0.999	1.097	0.052	92.4	0.605	1.193	0.048	100.5	0.999
Spleen	0.929	0.032	0.387	0.946	0.029	101.7	0.994	0.972	0.032	104.6	0.793	0.957	0.027	102.9	0.945	0.958	0.032	103.0	0.951	0.881	0.029	94.8	0.678
Testes (Paired)	3.599	0.121	0.859	3.419	0.110	95.0	0.696	3.617	0.121	100.5	0.999	3.372	0.105	93.7	0.468	3.563	0.121	99.0	0.999	3.527	0.112	98.0	0.990
Thymus	0.150	0.011	0.697	0.139	0.010	92.3	0.894	0.125	0.011	83.3	0.352	0.158	0.010	105.3	0.973	0.140	0.011	93.1	0.941	0.150	0.010	99.7	0.999
Thyroid Gland	0.044	0.002	0.961	0.042	0.002	96.4	0.964	0.044	0.002	100.3	0.999	0.042	0.002	95.8	0.934	0.041	0.002	93.8	0.790	0.045	0.002	102.8	0.988

1. All p-values and % are relative to the control group, except p-values for the linear trend are presented under the control group.

c) EE_2 Treatments Continuous Dose

Table 32. Summary Statistics of Female Organ Weight (g)
Ethinyl Estradiol Dose (µg/kg·BW/day)

	0.0			0.05			0.5	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.0724	0.0020	24	0.0753	0.0042	26	0.0922	0.0038
Brain	21	2.086	0.017	24	2.094	0.017	26	2.068	0.018
Fat Pad Ov/Pm	21	14.06	1.16	24	15.53	0.76	26	11.41	0.65
Fat Pad Retro	21	14.09	1.51	24	15.56	1.25	26	12.97	0.94
Heart	21	1.308	0.048	24	1.404	0.035	26	1.415	0.038
Kidney	21	2.27	0.07	23	2.42	0.08	26	2.61	0.08
Liver	21	10.69	0.52	24	12.09	0.45	26	12.77	0.47
Ovary	20	0.140	0.008	23	0.143	0.004	23	0.115	0.008
Pituitary Gland	21	0.0206	0.0011	24	0.0227	0.0017	26	0.0269	0.0012
Spleen	21	0.598	0.025	24	0.645	0.021	26	0.646	0.025
Thymus	21	0.150	0.011	24	0.137	0.010	26	0.137	0.009
Thyroid Gland	21	0.0382	0.0017	24	0.0390	0.0018	26	0.0365	0.0012
Uterus	21	0.773	0.045	24	0.777	0.038	26	0.827	0.037
Receiving Weight	21	420.41	18.98	24	453.14	13.31	26	422.72	11.99

Table 33. Summary Statistics of Female Relative Organ to Brain Weight (g/g)
Ethinyl Estradiol Dose (µg/kg$_{BW}$/day)

	0.0			0.05			0.5	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.0348	0.0010	24	0.0360	0.0019	26	0.0447	0.0019
Fat Pad Ov/Pm	21	6.72	0.54	24	7.42	0.35	26	5.50	0.30
Fat Pad Retro	21	6.72	0.70	24	7.41	0.58	26	6.26	0.44
Heart	21	0.628	0.023	24	0.670	0.015	26	0.684	0.016
Kidney	21	1.09	0.03	23	1.15	0.04	26	1.26	0.04
Liver	21	5.12	0.24	24	5.77	0.20	26	6.17	0.21
Ovary	20	0.067	0.003	23	0.068	0.002	23	0.056	0.004
Pituitary Gland	21	0.0099	0.0005	24	0.0108	0.0008	26	0.0131	0.0006
Spleen	21	0.286	0.011	24	0.308	0.010	26	0.311	0.011
Thymus	21	0.072	0.005	24	0.065	0.005	26	0.066	0.004
Thyroid Gland	21	0.0183	0.0008	24	0.0186	0.0008	26	0.0177	0.0006
Uterus	21	0.371	0.022	24	0.372	0.019	26	0.399	0.016

Table 34. Summary Statistics of Female Relative Organ to Receiving Weight (mg/g)
Ethinyl Estradiol Dose (µg/kg$_{BW}$/day)

	0.0			0.05			0.5	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	21	0.1781	0.0087	24	0.1691	0.0098	26	0.2184	0.0071
Brain	21	5.156	0.226	24	4.709	0.137	26	4.979	0.132
Fat Pad Ov/Pm	21	32.34	1.75	24	34.06	0.98	26	26.69	1.04
Fat Pad Retro	21	32.37	2.73	24	33.72	1.95	26	30.02	1.53
Heart	21	3.156	0.081	24	3.133	0.086	26	3.360	0.041
Kidney	21	5.50	0.17	23	5.34	0.10	26	6.19	0.10
Liver	21	25.52	0.58	24	26.73	0.68	26	30.12	0.53
Ovary	20	0.334	0.018	23	0.323	0.014	23	0.280	0.021
Pituitary Gland	21	0.0506	0.0034	24	0.0504	0.0036	26	0.0645	0.0029
Spleen	21	1.443	0.050	24	1.434	0.039	26	1.525	0.039
Thymus	21	0.369	0.031	24	0.302	0.020	26	0.324	0.018
Thyroid Gland	21	0.0927	0.0038	24	0.0860	0.0026	26	0.0877	0.0032
Uterus	21	1.916	0.150	24	1.760	0.114	26	1.971	0.088

Table 35. Summary Statistics of Male Organ Weight (g)
Ethinyl Estradiol Dose (µg/kg'BW'/day)

	0.0			*0.05*			*0.5*	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0601	0.0028	21	0.0626	0.0022	23	0.0629	0.0018
Brain	18	2.303	0.024	22	2.290	0.016	23	2.318	0.021
Epididymis (Paired)	18	1.285	0.037	22	1.243	0.034	23	1.335	0.031
Fat Pad Epidid	18	12.980	0.663	22	14.180	0.768	23	12.838	0.779
Fat Pad Retro	18	22.15	1.82	22	22.65	2.34	23	20.95	2.30
Heart	18	2.042	0.061	22	2.106	0.056	23	2.116	0.048
Kidney	17	4.08	0.15	21	4.01	0.13	23	4.17	0.12
Liver	18	22.14	0.93	22	22.16	0.74	23	23.06	0.64
Pituitary Gland	18	0.0146	0.0007	22	0.0156	0.0006	23	0.0160	0.0005
Sem Ves	18	1.185	0.043	22	1.270	0.059	23	1.124	0.042
Spleen	18	0.924	0.030	22	0.936	0.035	23	1.010	0.050
Testes (Paired)	18	3.591	0.117	22	3.478	0.093	23	3.564	0.090
Thymus	18	0.150	0.011	22	0.124	0.011	23	0.154	0.010
Thyroid Gland	18	0.0435	0.0020	22	0.0436	0.0020	23	0.0437	0.0015
Receiving Weight	18	700.86	19.23	22	712.31	21.34	23	704.45	15.59

Table 36. Summary Statistics of Male Relative Organ to Brain Weight (g/g)
Ethinyl Estradiol Dose (µg/kg'BW'/day)

	0.0			0.05			0.5	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0261	0.0012	21	0.0274	0.0009	23	0.0271	0.0007
Epididymis (Paired)	18	0.559	0.016	22	0.543	0.014	23	0.576	0.013
Fat Pad Epididymis	18	5.617	0.263	22	6.181	0.320	23	5.540	0.333
Fat Pad Retro	18	9.59	0.74	22	9.79	0.97	23	9.04	1.01
Heart	18	0.886	0.022	22	0.919	0.021	23	0.913	0.020
Kidney	17	1.77	0.05	21	1.75	0.05	23	1.80	0.05
Liver	18	9.58	0.34	22	9.66	0.29	23	9.96	0.29
Pituitary Gland	18	0.0063	0.0002	22	0.0068	0.0003	23	0.0069	0.0002
Seminal Vesicles	18	0.514	0.017	22	0.555	0.026	23	0.486	0.019
Spleen	18	0.401	0.012	22	0.408	0.015	23	0.436	0.021
Testes (Paired)	18	1.559	0.047	22	1.519	0.040	23	1.538	0.037
Thymus	18	0.065	0.005	22	0.054	0.005	23	0.067	0.004
Thyroid Gland	18	0.0188	0.0008	22	0.0190	0.0009	23	0.0189	0.0006

Table 37. Summary Statistics of Male Relative Organ to Receiving Weight (mg/g)
Ethinyl Estradiol Dose (µg/kg'BW'/day)

	0.0			0.05			0.5	
Organ	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***	***N***	***Mean***	***SE***
Adrenal Gland	18	0.0862	0.0037	21	0.0893	0.0032	23	0.0898	0.0027
Brain	18	3.316	0.072	22	3.266	0.086	23	3.323	0.072
Epididymis (Paired)	18	1.849	0.061	22	1.765	0.055	23	1.903	0.041
Fat Pad Epidid	18	18.463	0.780	22	19.759	0.723	23	17.991	0.771
Fat Pad Retro	18	31.27	1.98	22	30.88	2.47	23	28.95	2.72
Heart	18	2.925	0.074	22	2.986	0.085	23	3.023	0.075
Kidney	17	5.83	0.14	21	5.63	0.10	23	5.91	0.09
Liver	18	31.42	0.63	22	31.11	0.47	23	32.69	0.44
Pituitary Gland	18	0.0210	0.0009	22	0.0221	0.0008	23	0.0230	0.0009
Seminal Vesicles	18	1.701	0.060	22	1.815	0.100	23	1.601	0.054
Spleen	18	1.327	0.046	22	1.320	0.043	23	1.438	0.072
Testes (Paired)	18	5.162	0.181	22	4.957	0.181	23	5.086	0.129
Thymus	18	0.216	0.015	22	0.173	0.013	23	0.218	0.012
Thyroid Gland	18	0.0622	0.0024	22	0.0616	0.0026	23	0.0623	0.0021

Table 38. ANOVA Results for Organ Weight[1] for Ethinyl Estradiol Dose (µg/kg·BW/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Dose	2	68	9.275	**<.001**
	Brain	Dose	2	68	0.578	0.563
	Fat Pad Ov/Pm	Dose	2	68	6.431	**0.002**
	Fat Pad Retro	Dose	2	68	1.187	0.311
	Heart	Dose	2	68	2.027	0.139
	Kidney	Dose	2	67	5.064	**0.008**
	Liver	Dose	2	68	4.744	**0.011**
	Ovary	Dose	2	63	5.639	**0.005**
	Pituitary Gland	Dose	2	68	5.675	**0.005**
	Spleen	Dose	2	68	1.237	0.296
	Thymus	Dose	2	68	0.465	0.630
	Thyroid Gland	Dose	2	68	0.696	0.502
	Uterus	Dose	2	68	0.612	0.545
M	Adrenal Gland	Dose	2	59	0.444	0.643
	Brain	Dose	2	60	0.506	0.605
	Epididymis (Paired)	Dose	2	60	1.989	0.145
	Fat Pad Epididymis	Dose	2	60	0.995	0.375
	Fat Pad Retro	Dose	2	60	0.165	0.848
	Heart	Dose	2	60	0.503	0.607
	Kidney	Dose	2	58	0.403	0.670
	Liver	Dose	2	60	0.501	0.608
	Pituitary Gland	Dose	2	60	1.411	0.251
	Seminal Vesicles	Dose	2	60	2.383	0.100
	Spleen	Dose	2	60	1.320	0.274
	Testes (Paired)	Dose	2	60	0.356	0.701
	Thymus	Dose	2	60	2.524	0.088
	Thyroid Gland	Dose	2	60	0.004	0.995

[1] Analyses were conducted separately for females and males.

Table 39. Comparisons of Least Squares Mean Female Organ Weight for Ethinyl Estradiol Dose (µg/kg^{1}BW/day)

	0.0		*0.05*				*0.5*			
Organ	***Mean***	***SE***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.072	0.004	0.075	0.004	104.0	0.792	0.092	0.003	127.4	**<.001**
Brain	2.086	0.019	2.094	0.018	100.4	0.926	2.068	0.017	99.2	0.709
Fat Pad Ov/Pm	14.056	0.900	15.530	0.842	110.5	0.380	11.407	0.809	81.2	0.057
Fat Pad Retro	14.094	1.294	15.556	1.210	110.4	0.615	12.974	1.163	92.1	0.739
Heart	1.308	0.042	1.404	0.040	107.3	0.181	1.415	0.038	108.2	0.115
Kidney	2.269	0.082	2.415	0.078	106.5	0.327	2.615	0.073	115.2	**0.004**
Liver	10.690	0.508	12.093	0.475	113.1	0.085	12.775	0.457	119.5	**0.006**
Ovary	0.140	0.007	0.143	0.007	102.0	0.938	0.115	0.007	81.8	**0.017**
Pituitary Gland	0.021	0.001	0.023	0.001	110.1	0.463	0.027	0.001	130.6	**0.003**
Spleen	0.598	0.025	0.645	0.024	107.9	0.293	0.646	0.023	108.0	0.276
Thymus	0.150	0.011	0.137	0.010	91.8	0.607	0.137	0.010	91.8	0.594
Thyroid Gland	0.038	0.002	0.039	0.002	102.0	0.917	0.037	0.001	95.6	0.657
Uterus	0.773	0.042	0.777	0.039	100.5	0.996	0.827	0.038	107.1	0.523

1. All p-values and % are relative to the control group.

Table 40. Comparisons of Least Squares Mean Male Organ Weight for Ethinyl Estradiol Dose (µg/kg^{1}BW/day)

	0.0		*0.05*				*0.5*			
Organ	***Mean***	***SE***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.060	0.002	0.063	0.002	104.2	0.654	0.063	0.002	104.7	0.578
Brain	2.303	0.022	2.290	0.020	99.5	0.876	2.318	0.020	100.7	0.813
Epididymis (Paired)	1.285	0.036	1.243	0.033	96.7	0.589	1.335	0.032	103.8	0.486
Fat Pad Epidid	12.980	0.813	14.180	0.735	109.2	0.438	12.838	0.719	98.9	0.987
Fat Pad Retro	22.154	2.400	22.651	2.171	102.2	0.982	20.953	2.123	94.6	0.899
Heart	2.042	0.059	2.106	0.053	103.2	0.621	2.116	0.052	103.6	0.537
Kidney	4.078	0.145	4.014	0.130	98.4	0.922	4.175	0.125	102.4	0.824
Liver	22.135	0.822	22.156	0.743	100.1	0.999	23.059	0.727	104.2	0.602
Pituitary Gland	0.015	0.001	0.016	0.001	106.7	0.408	0.016	0.001	109.6	0.175
Sem Ves	1.185	0.053	1.270	0.048	107.2	0.380	1.124	0.047	94.9	0.593
Spleen	0.924	0.044	0.936	0.040	101.3	0.971	1.010	0.039	109.3	0.254
Testes (Paired)	3.591	0.106	3.478	0.096	96.8	0.638	3.564	0.094	99.2	0.972
Thymus	0.150	0.011	0.124	0.010	82.5	0.161	0.154	0.010	102.8	0.944
Thyroid Gland	0.044	0.002	0.044	0.002	100.2	0.999	0.044	0.002	100.5	0.994

1. All p-values and % are relative to the control group.

Table 41. ANOCOVA Results for Organ Weight with Covariate Brain Weight[1] for Ethinyl Estradiol Dose (µg/kg·BW/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Brain Weight	1	67	0.746	0.390
		Dose	2	67	9.551	**<.001**
	Fat Pad Ov/Pm	Brain Weight	1	67	4.956	**0.029**
		Dose	2	67	5.680	**0.005**
	Fat Pad Retro	Brain Weight	1	67	6.270	**0.014**
		Dose	2	67	0.816	0.446
	Heart	Brain Weight	1	67	9.624	**0.002**
		Dose	2	67	2.627	0.079
	Kidney	Brain Weight	1	66	3.707	0.058
		Dose	2	66	5.860	**0.004**
	Liver	Brain Weight	1	67	8.376	**0.005**
		Dose	2	67	5.939	**0.004**
	Ovary	Brain Weight	1	62	0.169	0.682
		Dose	2	62	5.188	**0.008**
	Pituitary Gland	Brain Weight	1	67	0.948	0.333
		Dose	2	67	5.958	**0.004**
	Spleen	Brain Weight	1	67	14.924	**<.001**
		Dose	2	67	1.802	0.172
	Thymus	Brain Weight	1	67	6.868	**0.010**
		Dose	2	67	0.489	0.615
	Thyroid Gland	Brain Weight	1	67	0.728	0.396
		Dose	2	67	0.559	0.574
	Uterus	Brain Weight	1	67	1.216	0.274
		Dose	2	67	0.762	0.470
M	Adrenal Gland	Brain Weight	1	58	0.899	0.347
		Dose	2	58	0.436	0.648
	Epididymis (Paired)	Brain Weight	1	59	5.148	**0.026**
		Dose	2	59	1.537	0.223
	Fat Pad Epididymis	Brain Weight	1	59	5.776	**0.019**
		Dose	2	59	1.511	0.229
	Fat Pad Retro	Brain Weight	1	59	6.709	**0.012**
		Dose	2	59	0.430	0.652
	Heart	Brain Weight	1	59	18.141	**<.001**
		Dose	2	59	0.678	0.511
	Kidney	Brain Weight	1	57	16.439	**<.001**
		Dose	2	57	0.093	0.911
	Liver	Brain Weight	1	59	12.112	**<.001**
		Dose	2	59	0.250	0.779
	Pituitary Gland	Brain Weight	1	59	5.810	**0.019**
		Dose	2	59	1.364	0.263
	Seminal Vesicles	Brain Weight	1	59	0.772	0.383
		Dose	2	59	2.583	0.084
	Spleen	Brain Weight	1	59	3.739	0.057
		Dose	2	59	1.045	0.358
	Testes (Paired)	Brain Weight	1	59	5.808	**0.019**
		Dose	2	59	0.238	0.789
	Thymus	Brain Weight	1	59	2.274	0.136
		Dose	2	59	2.163	0.123
	Thyroid Gland	Brain Weight	1	59	9.282	**0.003**
		Dose	2	59	0.054	0.947

[1] Analyses were conducted separately for females and males.

Table 42. Comparisons of Least Squares Mean Female Organ Weight with Covariate Brain Weight for Ethinyl Estradiol Dose (µg/kg$_{BW}$/day)

	0.0		*0.05*				*0.5*			
Organ	***Mean***	***SE***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.072	0.004	0.075	0.004	103.8	0.814	0.093	0.003	128.0	**<.001**
Fat Pad Ov/Pm	14.011	0.875	15.382	0.821	109.8	0.411	11.581	0.790	82.7	0.077
Fat Pad Retro	14.021	1.247	15.318	1.170	109.3	0.661	13.252	1.126	94.5	0.856
Heart	1.306	0.040	1.394	0.038	106.8	0.189	1.426	0.036	109.3	0.051
Kidney	2.266	0.080	2.402	0.077	106.0	0.363	2.629	0.072	116.0	**0.002**
Liver	10.658	0.483	11.987	0.453	112.5	0.086	12.899	0.436	121.0	**0.001**
Ovary	0.140	0.007	0.143	0.007	101.9	0.945	0.115	0.007	82.2	**0.022**
Pituitary Gland	0.021	0.001	0.023	0.001	109.8	0.488	0.027	0.001	131.4	**0.002**
Spleen	0.596	0.023	0.639	0.022	107.2	0.302	0.654	0.021	109.7	0.120
Thymus	0.149	0.010	0.135	0.010	90.8	0.517	0.140	0.009	93.8	0.721
Thyroid Gland	0.038	0.002	0.039	0.002	101.8	0.933	0.037	0.001	96.0	0.709
Uterus	0.772	0.042	0.773	0.040	100.2	0.999	0.832	0.038	107.8	0.466

1. All p-values and % are relative to the control group.

Table 43. Comparisons of Least Squares Mean Male Organ Weight with Covariate Brain Weight for Ethinyl Estradiol Dose (µg/kg$_{BW}$/day)

	0.0		*0.05*				*0.5*			
Organ	***Mean***	***SE***	***Mean***	***SE***	***Pct***	***P***	***Mean***	***SE***	***Pct***	***P***
Adrenal Gland	0.060	0.002	0.063	0.002	104.5	0.613	0.063	0.002	104.3	0.625
Epididymis (Paired)	1.286	0.035	1.250	0.032	97.2	0.655	1.328	0.031	103.3	0.567
Fat Pad Epidid	12.994	0.782	14.332	0.711	110.3	0.342	12.681	0.695	97.6	0.934
Fat Pad Retro	22.200	2.293	23.130	2.083	104.2	0.934	20.458	2.038	92.2	0.788
Heart	2.043	0.052	2.124	0.047	104.0	0.405	2.097	0.046	102.6	0.651
Kidney	4.091	0.129	4.057	0.116	99.2	0.970	4.126	0.111	100.9	0.967
Liver	22.156	0.755	22.368	0.685	101.0	0.967	22.841	0.671	103.1	0.715
Pituitary Gland	0.015	0.001	0.016	0.001	107.4	0.315	0.016	0.001	108.7	0.211
Sem Ves	1.185	0.053	1.274	0.048	107.5	0.357	1.120	0.047	94.5	0.556
Spleen	0.925	0.043	0.942	0.039	101.9	0.933	1.003	0.039	108.5	0.301
Testes (Paired)	3.593	0.102	3.498	0.093	97.3	0.708	3.544	0.091	98.6	0.906
Thymus	0.150	0.011	0.125	0.010	83.3	0.183	0.153	0.010	101.8	0.977
Thyroid Gland	0.044	0.002	0.044	0.002	101.1	0.971	0.043	0.002	99.3	0.989

1. All p-values and % are relative to the control group.

Table 44. ANOCOVA Results for Organ Weight with Covariate Receiving Weight[1] for Ethinyl Estradiol Dose (µg/kg·BW/day)

Sex	*Organ*	*Effect*	*NumDF*	*DenDF*	*Fvalue*	*P value*
F	Adrenal Gland	Receiving Weight	1	67	7.424	**0.008**
		Dose	2	67	11.188	**<.001**
	Fat Pad Ov/Pm	Receiving Weight	1	67	189.877	**<.001**
		Dose	2	67	13.043	**<.001**
	Fat Pad Retro	Receiving Weight	1	67	91.001	**<.001**
		Dose	2	67	0.619	0.541
	Heart	Receiving Weight	1	67	90.028	**<.001**
		Dose	2	67	4.094	**0.021**
	Kidney	Receiving Weight	1	66	115.696	**<.001**
		Dose	2	66	17.260	**<.001**
	Liver	Receiving Weight	1	67	143.118	**<.001**
		Dose	2	67	15.122	**<.001**
	Ovary	Receiving Weight	1	62	0.734	0.394
		Dose	2	62	4.985	**0.009**
	Pituitary Gland	Receiving Weight	1	67	4.643	**0.034**
		Dose	2	67	6.364	**0.002**
	Spleen	Receiving Weight	1	67	59.158	**<.001**
		Dose	2	67	1.843	0.166
	Thymus	Receiving Weight	1	67	7.477	**0.007**
		Dose	2	67	0.959	0.388
	Thyroid Gland	Receiving Weight	1	67	25.133	**<.001**
		Dose	2	67	0.459	0.633
	Uterus	Receiving Weight	1	67	0.651	0.422
		Dose	2	67	0.698	0.501
M	Adrenal Gland	Receiving Weight	1	58	8.296	**0.005**
		Dose	2	58	0.428	0.653
	Epididymis (Paired)	Receiving Weight	1	59	15.433	**<.001**
		Dose	2	59	2.813	0.068
	Fat Pad Epididymis	Receiving Weight	1	59	76.254	**<.001**
		Dose	2	59	1.404	0.253
	Fat Pad Retro	Receiving Weight	1	59	66.767	**<.001**
		Dose	2	59	0.252	0.778
	Heart	Receiving Weight	1	59	23.478	**<.001**
		Dose	2	59	0.530	0.591
	Kidney	Receiving Weight	1	57	126.613	**<.001**
		Dose	2	57	2.409	0.099
	Liver	Receiving Weight	1	59	220.484	**<.001**
		Dose	2	59	3.141	0.050
	Pituitary Gland	Receiving Weight	1	59	4.510	**0.037**
		Dose	2	59	1.407	0.252
	Seminal Vesicles	Receiving Weight	1	59	2.162	0.146
		Dose	2	59	2.291	0.110
	Spleen	Receiving Weight	1	59	11.982	**0.001**
		Dose	2	59	1.635	0.203
	Testes (Paired)	Receiving Weight	1	59	7.307	**0.008**
		Dose	2	59	0.538	0.586
	Thymus	Receiving Weight	1	59	9.675	**0.002**
		Dose	2	59	3.276	**0.044**
	Thyroid Gland	Receiving Weight	1	59	14.716	**<.001**
		Dose	2	59	0.027	0.973

[1] Analyses were conducted separately for females and males.

Table 45. Comparisons of Least Squares Mean Female Organ Weight with Covariate Receiving Weight for Ethinyl Estradiol Dose (µg/kg'BW'/day)

	0.0		0.05				0.5			
Organ	**Mean**	**SE**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**
Adrenal Gland	0.073	0.004	0.074	0.003	100.5	0.995	0.093	0.003	126.9	**<.001**
Fat Pad Ov/Pm	14.651	0.465	14.490	0.440	98.9	0.954	11.887	0.418	81.1	**<.001**
Fat Pad Retro	14.848	0.852	14.236	0.806	95.9	0.821	13.582	0.765	91.5	0.432
Heart	1.333	0.028	1.361	0.027	102.1	0.701	1.435	0.025	107.7	**0.015**
Kidney	2.318	0.050	2.326	0.048	100.3	0.990	2.654	0.045	114.5	**<.001**
Liver	11.013	0.290	11.529	0.275	104.7	0.334	13.035	0.261	118.4	**<.001**
Ovary	0.140	0.007	0.142	0.007	101.2	0.979	0.116	0.007	82.2	**0.021**
Pituitary Gland	0.021	0.001	0.022	0.001	106.3	0.722	0.027	0.001	129.9	**0.002**
Spleen	0.611	0.019	0.622	0.018	101.7	0.882	0.657	0.017	107.4	0.132
Thymus	0.152	0.010	0.133	0.010	87.3	0.294	0.139	0.009	91.6	0.544
Thyroid Gland	0.039	0.001	0.038	0.001	97.3	0.810	0.037	0.001	95.3	0.527
Uterus	0.776	0.042	0.771	0.040	99.4	0.994	0.830	0.038	107.0	0.533

1. All p-values and % are relative to the control group.

Table 46. Comparisons of Least Squares Mean Male Organ Weight with Covariate Receiving Weight for Ethinyl Estradiol Dose (µg/kg'BW'/day)

	0.0		0.05				0.5			
Organ	**Mean**	**SE**	**Mean**	**SE**	**Pct**	**P**	**Mean**	**SE**	**Pct**	**P**
Adrenal Gland	0.060	0.002	0.062	0.002	103.7	0.687	0.063	0.002	104.4	0.576
Epididymis (Paired)	1.290	0.033	1.238	0.030	96.0	0.394	1.336	0.029	103.6	0.456
Fat Pad Epidid	13.139	0.542	13.996	0.490	106.5	0.393	12.889	0.479	98.1	0.913
Fat Pad Retro	22.611	1.659	22.122	1.501	97.8	0.964	21.100	1.467	93.3	0.711
Heart	2.050	0.050	2.097	0.046	102.3	0.705	2.118	0.045	103.3	0.486
Kidney	4.116	0.082	3.968	0.073	96.4	0.301	4.189	0.070	101.8	0.716
Liver	22.326	0.381	21.936	0.345	98.3	0.659	23.121	0.337	103.6	0.208
Pituitary Gland	0.015	0.001	0.016	0.001	106.0	0.458	0.016	0.001	109.4	0.171
Sem Ves	1.188	0.053	1.267	0.048	106.7	0.420	1.125	0.047	94.7	0.571
Spleen	0.929	0.041	0.930	0.037	100.1	0.999	1.011	0.036	108.9	0.226
Testes (Paired)	3.600	0.101	3.467	0.092	96.3	0.514	3.567	0.090	99.1	0.955
Thymus	0.151	0.011	0.123	0.010	81.0	0.091	0.155	0.009	102.3	0.956
Thyroid Gland	0.044	0.002	0.043	0.002	99.0	0.976	0.044	0.002	100.2	0.999

1. All p-values and % are relative to the control group.

B. Data

Organ weight data were extracted from the Genesis database using SAS Proc SQL, utilizing the Vortex ODBC driver.

Quality Control

1. Data Verification

The extraction of the data into SAS was verified by the statistical reviewer by review of the SAS code used to extract and verify the data.

2. Computer Program Verification

SAS programs were used to extract the data, explore the distributional properties of the data, and perform the statistical analysis.

The SAS programs were verified by detailed review of the program code, the program log, and the program output.

3. Statistical Report Review

3.1 Statistical Report Text

The statistical report was reviewed for logic, internal completeness, technical appropriateness, technical accuracy, and grammar. Technical appropriateness was reviewed based on statistical expertise.

Comments and questions were provided from the reviewer to the statistician. The statistician made appropriate changes and returned the report to the reviewer for final verification.

The text of the final statistical report was considered by the reviewer to be logical, internally complete, and technically appropriate and accurate. The statistical results stated in the text accurately presented those in the tables.

3.2 Table Verification

Analysis results were output from SAS to .rtf files using PROC REPORT, which were then copied into the statistical report.

Statistical report tables were verified by checking the procedure used to create the tables and, additionally, by checking numbers sufficiently to conclude that the tables are correct.

4. Conclusions

The final statistical report has been fully reviewed and is considered by the reviewer to be logical, internally complete, and technically appropriate and accurate.