

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

Table 1. Neoplasms by Body System for Terminal Sacrifice Females Bisphenol-A Stop Dose Arm

<i>System and Neoplasm</i>		<i>Treatment (ug/kg)</i>					
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>2.5</i>	<i>25</i>	<i>250</i>	<i>2500</i>	<i>25000</i>
Endocrine System							
Pituitary Gland * Adenoma, Pars Distalis	Simple Incidence	23/49 (46.9%)	16/50 (32.0%)	14/48 (29.2%)	20/50 (40.0%)	20/50 (40.0%)	20/46 (43.5%)
	Poly-K Incidence	23/38.5 (59.8%)	16/36.3 (44.1%)	14/33.5 (41.8%)	20/39.4 (50.8%)	20/38.5 (51.9%)	20/35.5 (56.3%)
	Terminal Incidence	7/11 (63.6%)	5/12 (41.7%)	8/13 (61.5%)	6/13 (46.2%)	9/17 (52.9%)	6/13 (46.2%)
	Time-to-First	502	397	442	448	520	445
	Poly-K P-Value	0.470	0.112N	0.081N	0.271N	0.308N	0.469N
Genital System							
Uterus * Polyp Stromal	Simple Incidence	7/49 (14.3%)	4/49 (8.2%)	5/48 (10.4%)	6/49 (12.2%)	4/49 (8.2%)	1/46 (2.2%)
	Poly-K Incidence	7/33.0 (21.2%)	4/32.3 (12.4%)	5/32.5 (15.4%)	6/35.9 (16.7%)	4/35.8 (11.2%)	1/31.0 (3.2%)
	Terminal Incidence	2/11 (18.2%)	1/12 (8.3%)	1/13 (7.7%)	1/13 (7.7%)	1/17 (5.9%)	0/13 (0.0%)
	Time-to-First	467	446	461	497	539	706
	Poly-K P-Value	0.041N*	0.263N	0.384N	0.433N	0.207N	0.032N*
Integumentary System							
Mammary Gland * Adenocarcinoma	Simple Incidence	3/50 (6.0%)	11/50 (22.0%)	5/48 (10.4%)	7/49 (14.3%)	9/50 (18.0%)	5/46 (10.9%)
	Poly-K Incidence	3/32.3 (9.3%)	11/33.3 (33.0%)	5/32.1 (15.6%)	7/35.4 (19.8%)	9/36.6 (24.6%)	5/32.0 (15.6%)
	Terminal Incidence	1/11 (9.1%)	2/12 (16.7%)	2/13 (15.4%)	0/13 (0.0%)	5/17 (29.4%)	0/13 (0.0%)
	Time-to-First	681	573	458	450	488	615
	Poly-K P-Value	0.453	0.016 *	0.348	0.189	0.083	0.346
Mammary Gland * Adenocarcinoma or Adenoma	Simple Incidence	4/50 (8.0%)	12/50 (24.0%)	5/48 (10.4%)	9/49 (18.4%)	9/50 (18.0%)	6/46 (13.0%)
	Poly-K Incidence	4/33.0 (12.1%)	12/33.3 (36.0%)	5/32.1 (15.6%)	9/35.9 (25.0%)	9/36.6 (24.6%)	6/32.8 (18.3%)
	Terminal Incidence	1/11 (9.1%)	3/12 (25.0%)	2/13 (15.4%)	1/13 (7.7%)	5/17 (29.4%)	0/13 (0.0%)
	Time-to-First	514	573	458	450	488	463
	Poly-K P-Value	0.483	0.018 *	0.482	0.140	0.149	0.360
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	45/50 (90.0%)	46/50 (92.0%)	38/48 (79.2%)	43/49 (87.8%)	38/50 (76.0%)	38/46 (82.6%)
	Poly-K Incidence	45/47.8 (94.2%)	46/47.7 (96.5%)	38/42.8 (88.9%)	43/47.0 (91.5%)	38/46.3 (82.1%)	38/41.5 (91.6%)
	Terminal Incidence	9/11 (81.8%)	11/12 (91.7%)	11/13 (84.6%)	11/13 (84.6%)	12/17 (70.6%)	12/13 (92.3%)
	Time-to-First	385	400	339	448	390	383
	Poly-K P-Value	0.040N*	0.479	0.265N	0.451N	0.051N	0.468N
Mammary Gland * Fibroadenoma	Simple Incidence	43/50 (86.0%)	45/50 (90.0%)	37/48 (77.1%)	42/49 (85.7%)	36/50 (72.0%)	34/46 (73.9%)
	Poly-K Incidence	43/47.7 (90.2%)	45/47.5 (94.6%)	37/42.2 (87.8%)	42/46.2 (90.9%)	36/45.5 (79.1%)	34/40.6 (83.7%)
	Terminal Incidence	8/11 (72.7%)	11/12 (91.7%)	11/13 (84.6%)	11/13 (84.6%)	12/17 (70.6%)	12/13 (92.3%)
	Time-to-First	385	400	339	448	390	383
	Poly-K P-Value	0.021N*	0.319	0.489N	0.600	0.099N	0.257N

P-values for dose trend are presented in the "Control" column.

N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 2. Neoplasms by Body System for Terminal Sacrifice Males Bisphenol-A Stop Dose Arm</i>							
<i>System and Neoplasm</i>	<i>Treatment (ug/kg)</i>						
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>2.5</i>	<i>25</i>	<i>250</i>	<i>2500</i>	<i>25000</i>
Alimentary System							
Liver * Lymphoma Malignant	Simple Incidence	1/50 (2.0%)	0/48 (0.0%)	1/48 (2.1%)	3/50 (6.0%)	2/50 (4.0%)	5/46 (10.9%)
	Poly-K Incidence	1/37.5 (2.7%)	0/33.4 (0.0%)	1/35.6 (2.8%)	3/32.9 (9.1%)	2/37.4 (5.3%)	5/30.0 (16.7%)
	Terminal Incidence	0/17 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/13 (0.0%)	0/15 (0.0%)	0/9 (0.0%)
	Time-to-First	518	----	393	399	426	253
	Poly-K P-Value	0.008 **	0.523N	0.750	0.258	0.499	0.055
Endocrine System							
Adrenal Medulla * Pheochromocytoma Benign	Simple Incidence	4/47 (8.5%)	2/46 (4.3%)	5/48 (10.4%)	5/49 (10.2%)	0/50 (0.0%)	4/44 (9.1%)
	Poly-K Incidence	4/36.0 (11.1%)	2/32.5 (6.2%)	5/35.2 (14.2%)	5/30.6 (16.3%)	0/35.8 (0.0%)	4/26.3 (15.2%)
	Terminal Incidence	2/17 (11.8%)	1/16 (6.3%)	4/16 (25.0%)	4/13 (30.8%)	0/15 (0.0%)	3/9 (33.3%)
	Time-to-First	643	637	587	686	----	706
	Poly-K P-Value	0.437N	0.384N	0.487	0.397	0.059N	0.462
Islets, Pancreatic * Adenocarcinoma or Adenoma	Simple Incidence	4/48 (8.3%)	4/47 (8.5%)	2/48 (4.2%)	4/48 (8.3%)	1/50 (2.0%)	4/44 (9.1%)
	Poly-K Incidence	4/36.5 (10.9%)	4/33.0 (12.1%)	2/35.0 (5.7%)	4/30.8 (13.0%)	1/35.9 (2.8%)	4/28.2 (14.2%)
	Terminal Incidence	3/17 (17.6%)	2/16 (12.5%)	1/16 (6.3%)	2/13 (15.4%)	0/15 (0.0%)	1/9 (11.1%)
	Time-to-First	680	671	682	609	706	537
	Poly-K P-Value	0.405N	0.588	0.356N	0.547	0.181N	0.496
Islets, Pancreatic * Adenoma	Simple Incidence	4/48 (8.3%)	4/47 (8.5%)	2/48 (4.2%)	4/48 (8.3%)	1/50 (2.0%)	4/44 (9.1%)
	Poly-K Incidence	4/36.5 (10.9%)	4/33.0 (12.1%)	2/35.0 (5.7%)	4/30.8 (13.0%)	1/35.9 (2.8%)	4/28.2 (14.2%)
	Terminal Incidence	3/17 (17.6%)	2/16 (12.5%)	1/16 (6.3%)	2/13 (15.4%)	0/15 (0.0%)	1/9 (11.1%)
	Time-to-First	680	671	682	609	706	537
	Poly-K P-Value	0.405N	0.588	0.356N	0.547	0.181N	0.496
Pituitary Gland * Adenoma, Pars Distalis	Simple Incidence	29/46 (63.0%)	22/48 (45.8%)	19/48 (39.6%)	19/49 (38.8%)	19/50 (38.0%)	17/43 (39.5%)
	Poly-K Incidence	29/39.9 (72.7%)	22/38.4 (57.2%)	19/37.7 (50.4%)	19/34.3 (55.4%)	19/40.1 (47.4%)	17/30.8 (55.2%)
	Terminal Incidence	13/17 (76.5%)	8/16 (50.0%)	9/16 (56.3%)	9/13 (69.2%)	5/15 (33.3%)	5/9 (55.6%)
	Time-to-First	552	529	477	558	551	465
	Poly-K P-Value	0.023N*	0.098N	0.026N*	0.074N	0.012N*	0.082N
Genital System							
Prostate, Dorsal/Lateral Lobe * Lymphoma Malignant	Simple Incidence	0/46 (0.0%)	0/48 (0.0%)	0/48 (0.0%)	3/50 (6.0%)	2/49 (4.1%)	4/45 (8.9%)
	Poly-K Incidence	0/35.1 (0.0%)	0/33.4 (0.0%)	0/34.8 (0.0%)	3/32.9 (9.1%)	2/37.4 (5.3%)	4/29.1 (13.8%)
	Terminal Incidence	0/17 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/13 (0.0%)	0/15 (0.0%)	0/9 (0.0%)
	Time-to-First	----	----	----	399	426	253
	Poly-K P-Value	0.002 **	-----	-----	0.106	0.251	0.038 *

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Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 2. Neoplasms by Body System for Terminal Sacrifice Males Bisphenol-A Stop Dose Arm</i>							
<i>System and Neoplasm</i>		<i>Treatment (ug/kg)</i>					
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>2.5</i>	<i>25</i>	<i>250</i>	<i>2500</i>	<i>25000</i>
Prostate, Ventral Lobe * Adenocarcinoma or Adenoma	Simple Incidence	4/48 (8.3%)	4/47 (8.5%)	4/47 (8.5%)	2/50 (4.0%)	4/49 (8.2%)	6/45 (13.3%)
	Poly-K Incidence	4/35.7 (11.2%)	4/33.0 (12.1%)	4/34.1 (11.7%)	2/30.8 (6.5%)	4/36.5 (11.0%)	6/28.7 (20.9%)
	Terminal Incidence	2/17 (11.8%)	2/16 (12.5%)	4/16 (25.0%)	2/13 (15.4%)	1/15 (6.7%)	1/9 (11.1%)
	Time-to-First	675	679	724 (T)	724 (T)	593	530
	Poly-K P-Value	0.273	0.601	0.619	0.407N	0.635N	0.233
Prostate, Ventral Lobe * Adenoma	Simple Incidence	4/48 (8.3%)	4/47 (8.5%)	4/47 (8.5%)	2/50 (4.0%)	4/49 (8.2%)	6/45 (13.3%)
	Poly-K Incidence	4/35.7 (11.2%)	4/33.0 (12.1%)	4/34.1 (11.7%)	2/30.8 (6.5%)	4/36.5 (11.0%)	6/28.7 (20.9%)
	Terminal Incidence	2/17 (11.8%)	2/16 (12.5%)	4/16 (25.0%)	2/13 (15.4%)	1/15 (6.7%)	1/9 (11.1%)
	Time-to-First	675	679	724 (T)	724 (T)	593	530
	Poly-K P-Value	0.273	0.601	0.619	0.407N	0.635N	0.233
Hematopoietic System							
Bone Marrow * Lymphoma Malignant	Simple Incidence	1/47 (2.1%)	0/47 (0.0%)	0/46 (0.0%)	3/50 (6.0%)	2/49 (4.1%)	5/45 (11.1%)
	Poly-K Incidence	1/36.1 (2.8%)	0/32.6 (0.0%)	0/34.3 (0.0%)	3/32.9 (9.1%)	2/37.4 (5.3%)	5/29.7 (16.8%)
	Terminal Incidence	0/17 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/13 (0.0%)	0/15 (0.0%)	0/9 (0.0%)
	Time-to-First	518	----	----	399	426	253
	Poly-K P-Value	0.005 **	0.520N	0.510N	0.271	0.512	0.059
Spleen * Lymphoma Malignant	Simple Incidence	1/47 (2.1%)	0/47 (0.0%)	1/47 (2.1%)	3/49 (6.1%)	2/49 (4.1%)	5/45 (11.1%)
	Poly-K Incidence	1/36.1 (2.8%)	0/32.6 (0.0%)	1/35.4 (2.8%)	3/32.5 (9.2%)	2/37.4 (5.3%)	5/29.7 (16.8%)
	Terminal Incidence	0/17 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/13 (0.0%)	0/15 (0.0%)	0/9 (0.0%)
	Time-to-First	518	----	393	399	426	253
	Poly-K P-Value	0.009 **	0.520N	0.757	0.267	0.512	0.059
Urinary System							
Kidney * Lymphoma Malignant	Simple Incidence	1/50 (2.0%)	0/48 (0.0%)	1/48 (2.1%)	3/50 (6.0%)	2/50 (4.0%)	5/45 (11.1%)
	Poly-K Incidence	1/37.5 (2.7%)	0/33.4 (0.0%)	1/35.6 (2.8%)	3/32.9 (9.1%)	2/37.4 (5.3%)	5/29.7 (16.8%)
	Terminal Incidence	0/17 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/13 (0.0%)	0/15 (0.0%)	0/9 (0.0%)
	Time-to-First	518	----	393	399	426	253
	Poly-K P-Value	0.007 **	0.523N	0.750	0.258	0.499	0.053

P-values for dose trend are presented in the "Control" column.

N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 3. Neoplasms by Body System for Terminal Sacrifice Females Bisphenol-A Continuous Dose Arm</i>							
<i>System and Neoplasm</i>	<i>Treatment (ug/kg)</i>						
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>2.5</i>	<i>25</i>	<i>250</i>	<i>2500</i>	<i>25000</i>
Endocrine System							
Pituitary Gland * Adenoma, Pars Distalis	Simple Incidence	21/50 (42.0%)	22/48 (45.8%)	12/46 (26.1%)	20/49 (40.8%)	19/49 (38.8%)	21/46 (45.7%)
	Poly-K Incidence	21/39.9 (52.7%)	22/37.1 (59.2%)	12/31.4 (38.2%)	20/36.6 (54.7%)	19/34.1 (55.8%)	21/35.4 (59.3%)
	Terminal Incidence	7/16 (43.8%)	12/19 (63.2%)	4/14 (28.6%)	8/13 (61.5%)	5/10 (50.0%)	4/8 (50.0%)
	Time-to-First	477	497	434	561	456	510
	Poly-K P-Value	0.313	0.356	0.153N	0.523	0.487	0.356
Genital System							
Uterus * Polyp Stromal	Simple Incidence	5/50 (10.0%)	3/48 (6.3%)	7/45 (15.6%)	2/49 (4.1%)	4/48 (8.3%)	3/46 (6.5%)
	Poly-K Incidence	5/36.4 (13.7%)	3/34.6 (8.7%)	7/29.5 (23.7%)	2/33.5 (6.0%)	4/29.2 (13.7%)	3/32.2 (9.3%)
	Terminal Incidence	1/16 (6.3%)	0/19 (0.0%)	4/14 (28.6%)	0/13 (0.0%)	0/10 (0.0%)	0/8 (0.0%)
	Time-to-First	506	321	441	542	673	569
	Poly-K P-Value	0.333N	0.383N	0.231	0.247N	0.638N	0.424N
Integumentary System							
Mammary Gland * Adenocarcinoma	Simple Incidence	4/50 (8.0%)	6/48 (12.5%)	6/46 (13.0%)	5/49 (10.2%)	9/50 (18.0%)	3/46 (6.5%)
	Poly-K Incidence	4/34.4 (11.6%)	6/32.9 (18.2%)	6/30.4 (19.8%)	5/34.6 (14.5%)	9/31.3 (28.8%)	3/31.2 (9.6%)
	Terminal Incidence	3/16 (18.8%)	6/19 (31.6%)	1/14 (7.1%)	0/13 (0.0%)	3/10 (30.0%)	0/8 (0.0%)
	Time-to-First	673	719 (T)	434	377	561	685
	Poly-K P-Value	0.412	0.336	0.286	0.504	0.071	0.555N
Mammary Gland * Adenocarcinoma or Adenoma	Simple Incidence	6/50 (12.0%)	7/48 (14.6%)	8/46 (17.4%)	6/49 (12.2%)	10/50 (20.0%)	4/46 (8.7%)
	Poly-K Incidence	6/34.9 (17.2%)	7/32.9 (21.3%)	8/30.4 (26.4%)	6/34.8 (17.2%)	10/31.3 (31.9%)	4/31.8 (12.6%)
	Terminal Incidence	4/16 (25.0%)	7/19 (36.8%)	3/14 (21.4%)	0/13 (0.0%)	4/10 (40.0%)	0/8 (0.0%)
	Time-to-First	564	719 (T)	434	377	561	542
	Poly-K P-Value	0.513N	0.452	0.271	0.624	0.126	0.428N
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	41/50 (82.0%)	40/48 (83.3%)	34/46 (73.9%)	41/49 (83.7%)	35/50 (70.0%)	38/46 (82.6%)
	Poly-K Incidence	41/47.0 (87.2%)	40/43.7 (91.5%)	34/38.7 (87.8%)	41/46.5 (88.2%)	35/42.3 (82.7%)	38/42.2 (90.1%)
	Terminal Incidence	13/16 (81.3%)	17/19 (89.5%)	12/14 (85.7%)	10/13 (76.9%)	7/10 (70.0%)	7/8 (87.5%)
	Time-to-First	431	321	434	261	419	467
	Poly-K P-Value	0.421N	0.366	0.608	0.573	0.366N	0.457
Mammary Gland * Fibroadenoma	Simple Incidence	41/50 (82.0%)	40/48 (83.3%)	33/46 (71.7%)	39/49 (79.6%)	35/50 (70.0%)	38/46 (82.6%)
	Poly-K Incidence	41/47.0 (87.2%)	40/43.7 (91.5%)	33/38.4 (86.0%)	39/45.3 (86.1%)	35/42.3 (82.7%)	38/42.2 (90.1%)
	Terminal Incidence	13/16 (81.3%)	17/19 (89.5%)	12/14 (85.7%)	10/13 (76.9%)	7/10 (70.0%)	7/8 (87.5%)
	Time-to-First	431	321	434	261	419	467
	Poly-K P-Value	0.410N	0.366	0.567N	0.565N	0.366N	0.457

P-values for dose trend are presented in the "Control" column.

N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.

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Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 4. Neoplasms by Body System for Terminal Sacrifice Males Bisphenol-A Continuous Dose Arm</i>							
<i>System and Neoplasm</i>	<i>Treatment (ug/kg)</i>						
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>2.5</i>	<i>25</i>	<i>250</i>	<i>2500</i>	<i>25000</i>
Endocrine System							
Islets, Pancreatic * Adenocarcinoma or Adenoma	Simple Incidence	2/50 (4.0%)	3/46 (6.5%)	7/48 (14.6%)	1/48 (2.1%)	4/49 (8.2%)	5/45 (11.1%)
	Poly-K Incidence	2/33.7 (5.9%)	3/33.4 (9.0%)	7/32.9 (21.3%)	1/32.3 (3.1%)	4/33.4 (12.0%)	5/28.8 (17.4%)
	Terminal Incidence	2/15 (13.3%)	2/16 (12.5%)	4/17 (23.5%)	1/14 (7.1%)	2/16 (12.5%)	3/11 (27.3%)
	Time-to-First	726 (T)	674	617	726 (T)	694	650
	Poly-K P-Value	0.181	0.496	0.066	0.515N	0.330	0.150
Islets, Pancreatic * Adenoma	Simple Incidence	2/50 (4.0%)	3/46 (6.5%)	7/48 (14.6%)	1/48 (2.1%)	4/49 (8.2%)	5/45 (11.1%)
	Poly-K Incidence	2/33.7 (5.9%)	3/33.4 (9.0%)	7/32.9 (21.3%)	1/32.3 (3.1%)	4/33.4 (12.0%)	5/28.8 (17.4%)
	Terminal Incidence	2/15 (13.3%)	2/16 (12.5%)	4/17 (23.5%)	1/14 (7.1%)	2/16 (12.5%)	3/11 (27.3%)
	Time-to-First	726 (T)	674	617	726 (T)	694	650
	Poly-K P-Value	0.181	0.496	0.066	0.515N	0.330	0.150
Pituitary Gland * Adenoma, Pars Distalis	Simple Incidence	21/48 (43.8%)	25/48 (52.1%)	23/48 (47.9%)	21/50 (42.0%)	21/50 (42.0%)	17/45 (37.8%)
	Poly-K Incidence	21/36.9 (56.9%)	25/37.6 (66.6%)	23/38.4 (59.8%)	21/38.4 (54.7%)	21/38.0 (55.2%)	17/33.7 (50.5%)
	Terminal Incidence	7/14 (50.0%)	10/16 (62.5%)	8/17 (47.1%)	9/14 (64.3%)	8/16 (50.0%)	4/11 (36.4%)
	Time-to-First	494	613	412	460	546	386
	Poly-K P-Value	0.147N	0.254	0.490	0.515N	0.535N	0.374N
Genital System							
Prostate, Ventral Lobe * Adenocarcinoma or Adenoma	Simple Incidence	6/50 (12.0%)	7/48 (14.6%)	2/48 (4.2%)	4/49 (8.2%)	2/49 (4.1%)	6/46 (13.0%)
	Poly-K Incidence	6/34.4 (17.4%)	7/34.4 (20.3%)	2/32.3 (6.2%)	4/32.9 (12.1%)	2/33.1 (6.0%)	6/29.4 (20.4%)
	Terminal Incidence	3/15 (20.0%)	4/16 (25.0%)	2/17 (11.8%)	2/14 (14.3%)	2/16 (12.5%)	3/11 (27.3%)
	Time-to-First	603	683	726 (T)	713	726 (T)	613
	Poly-K P-Value	0.287N	0.499	0.148N	0.394N	0.139N	0.506
Prostate, Ventral Lobe * Adenoma	Simple Incidence	6/50 (12.0%)	7/48 (14.6%)	2/48 (4.2%)	4/49 (8.2%)	2/49 (4.1%)	6/46 (13.0%)
	Poly-K Incidence	6/34.4 (17.4%)	7/34.4 (20.3%)	2/32.3 (6.2%)	4/32.9 (12.1%)	2/33.1 (6.0%)	6/29.4 (20.4%)
	Terminal Incidence	3/15 (20.0%)	4/16 (25.0%)	2/17 (11.8%)	2/14 (14.3%)	2/16 (12.5%)	3/11 (27.3%)
	Time-to-First	603	683	726 (T)	713	726 (T)	613
	Poly-K P-Value	0.287N	0.499	0.148N	0.394N	0.139N	0.506
Nervous System							
Brain, Cerebrum * Granular Cell Tumor Benign	Simple Incidence	0/50 (0.0%)	0/48 (0.0%)	0/48 (0.0%)	4/49 (8.2%)	1/49 (2.0%)	0/46 (0.0%)
	Poly-K Incidence	0/33.7 (0.0%)	0/34.0 (0.0%)	0/32.3 (0.0%)	4/33.9 (11.8%)	1/33.3 (3.0%)	0/28.5 (0.0%)
	Terminal Incidence	0/15 (0.0%)	0/16 (0.0%)	0/17 (0.0%)	1/14 (7.1%)	0/16 (0.0%)	0/11 (0.0%)
	Time-to-First	----	----	----	600	676	----
	Poly-K P-Value	0.162	-----	-----	0.058	0.498	-----

P-values for dose trend are presented in the “Control” column.
N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

Table 5. Neoplasms by Body System for Terminal Sacrifice Females EE2 Continuous Dose Arm				
System and Neoplasm	Treatment (ug/kg)			
Lesion	Statistic	Control	0.05	0.50
Endocrine System				
Adrenal Medulla * Pheochromocytoma Benign	Simple Incidence	0/50 (0.0%)	1/26 (3.8%)	2/26 (7.7%)
	Poly-K Incidence	0/34.2 (0.0%)	1/15.9 (6.3%)	2/15.7 (12.7%)
	Terminal Incidence	0/16 (0.0%)	1/7 (14.3%)	1/4 (25.0%)
	Time-to-First	----	728 (T)	527
	Poly-K P-Value	0.048 *	0.349	0.088
Pituitary Gland * Adenoma,Pars Distalis	Simple Incidence	21/50 (42.0%)	10/26 (38.5%)	17/26 (65.4%)
	Poly-K Incidence	21/39.9 (52.7%)	10/18.3 (54.6%)	17/23.2 (73.3%)
	Terminal Incidence	7/16 (43.8%)	4/7 (57.1%)	2/4 (50.0%)
	Time-to-First	477	484	360
	Poly-K P-Value	0.055	0.561	0.068
Pituitary Gland * Carcinoma,Pars Distalis	Simple Incidence	1/50 (2.0%)	0/26 (0.0%)	3/26 (11.5%)
	Poly-K Incidence	1/34.6 (2.9%)	0/15.9 (0.0%)	3/16.1 (18.7%)
	Terminal Incidence	0/16 (0.0%)	0/7 (0.0%)	0/4 (0.0%)
	Time-to-First	615	----	610
	Poly-K P-Value	0.053	0.652N	0.084
Thyroid Gland * Adenoma,C-Cell	Simple Incidence	0/50 (0.0%)	0/26 (0.0%)	2/25 (8.0%)
	Poly-K Incidence	0/34.2 (0.0%)	0/15.9 (0.0%)	2/15.2 (13.2%)
	Terminal Incidence	0/16 (0.0%)	0/7 (0.0%)	0/4 (0.0%)
	Time-to-First	----	----	610
	Poly-K P-Value	0.036 *	-----	0.083
Genital System				
Uterus * Polyp Stromal	Simple Incidence	5/50 (10.0%)	3/26 (11.5%)	1/26 (3.8%)
	Poly-K Incidence	5/36.4 (13.7%)	3/17.4 (17.2%)	1/15.7 (6.4%)
	Terminal Incidence	1/16 (6.3%)	0/7 (0.0%)	0/4 (0.0%)
	Time-to-First	506	485	527
	Poly-K P-Value	0.383N	0.529	0.389N

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

Table 5. Neoplasms by Body System for Terminal Sacrifice Females EE2 Continuous Dose Arm				
System and Neoplasm	Treatment (ug/kg)			
Lesion	Statistic	Control	0.05	0.50
Integumentary System				
Mammary Gland * Adenocarcinoma	Simple Incidence	4/50 (8.0%)	2/26 (7.7%)	10/26 (38.5%)
	Poly-K Incidence	4/34.4 (11.6%)	2/16.8 (11.9%)	10/17.6 (56.9%)
	Terminal Incidence	3/16 (18.8%)	0/7 (0.0%)	3/4 (75.0%)
	Time-to-First	673	490	488
	Poly-K P-Value	<.001 ***	0.667	<.001 ***
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	41/50 (82.0%)	19/26 (73.1%)	18/26 (69.2%)
	Poly-K Incidence	41/47.0 (87.2%)	19/23.0 (82.7%)	18/21.7 (82.9%)
	Terminal Incidence	13/16 (81.3%)	5/7 (71.4%)	3/4 (75.0%)
	Time-to-First	431	460	360
	Poly-K P-Value	0.347N	0.438N	0.453N
Mammary Gland * Fibroadenoma	Simple Incidence	41/50 (82.0%)	18/26 (69.2%)	14/26 (53.8%)
	Poly-K Incidence	41/47.0 (87.2%)	18/22.3 (80.8%)	14/20.2 (69.2%)
	Terminal Incidence	13/16 (81.3%)	5/7 (71.4%)	2/4 (50.0%)
	Time-to-First	431	460	360
	Poly-K P-Value	0.041N*	0.354N	0.056N
Nervous System				
Brain, Brain Stem * Carcinoma,Deep Invasion	Simple Incidence	1/50 (2.0%)	0/26 (0.0%)	3/26 (11.5%)
	Poly-K Incidence	1/34.6 (2.9%)	0/15.9 (0.0%)	3/16.1 (18.7%)
	Terminal Incidence	0/16 (0.0%)	0/7 (0.0%)	0/4 (0.0%)
	Time-to-First	615	---	610
	Poly-K P-Value	0.053	0.652N	0.084

P-values for dose trend are presented in the "Control" column.

N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.

RR9: CLARITY-BPA Core Study
Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

Table 6. Neoplasms by Body System for Terminal Sacrifice Males EE2 Continuous Dose Arm				
System and Neoplasm	Treatment (ug/kg)			
Lesion	Statistic	Control	0.05	0.50
Alimentary System				
Liver * Lymphoma Malignant	Simple Incidence	2/50 (4.0%)	2/26 (7.7%)	1/25 (4.0%)
	Poly-K Incidence	2/35.1 (5.7%)	2/19.3 (10.4%)	1/20.0 (5.0%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.610N	0.465	0.695N
Pancreas * Lymphoma Malignant	Simple Incidence	2/50 (4.0%)	2/26 (7.7%)	1/25 (4.0%)
	Poly-K Incidence	2/35.1 (5.7%)	2/19.3 (10.4%)	1/20.0 (5.0%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.610N	0.465	0.695N
Endocrine System				
Adrenal Cortex * Lymphoma Malignant	Simple Incidence	1/50 (2.0%)	2/26 (7.7%)	1/26 (3.8%)
	Poly-K Incidence	1/34.4 (2.9%)	2/19.3 (10.4%)	1/20.3 (4.9%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	494	369	473
	Poly-K P-Value	0.458	0.299	0.642
Pituitary Gland * Adenoma,Pars Distalis	Simple Incidence	21/48 (43.8%)	12/26 (46.2%)	6/26 (23.1%)
	Poly-K Incidence	21/36.9 (56.9%)	12/19.9 (60.2%)	6/20.8 (28.9%)
	Terminal Incidence	7/14 (50.0%)	6/9 (66.7%)	3/12 (25.0%)
	Time-to-First	494	543	518
	Poly-K P-Value	0.030N*	0.517	0.029N*
Pituitary Gland * Lymphoma Malignant	Simple Incidence	2/48 (4.2%)	2/26 (7.7%)	1/26 (3.8%)
	Poly-K Incidence	2/33.7 (5.9%)	2/19.3 (10.4%)	1/20.3 (4.9%)
	Terminal Incidence	0/14 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.588N	0.482	0.676N
Genital System				
Prostate, Ventral Lobe * Adenoma	Simple Incidence	6/50 (12.0%)	2/26 (7.7%)	2/26 (7.7%)
	Poly-K Incidence	6/34.4 (17.4%)	2/17.6 (11.4%)	2/20.7 (9.7%)
	Terminal Incidence	3/15 (20.0%)	2/9 (22.2%)	0/12 (0.0%)
	Time-to-First	603	725 (T)	462
	Poly-K P-Value	0.264N	0.433N	0.344N

RR9: CLARITY-BPA Core Study

Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

Table 6. Neoplasms by Body System for Terminal Sacrifice Males EE2 Continuous Dose Arm				
System and Neoplasm	Treatment (ug/kg)			
Lesion	Statistic	Control	0.05	0.50
Prostate, Ventral Lobe * Adenoma or Adenocarcinoma	Simple Incidence	6/50 (12.0%)	2/26 (7.7%)	2/26 (7.7%)
	Poly-K Incidence	6/34.4 (17.4%)	2/17.6 (11.4%)	2/20.7 (9.7%)
	Terminal Incidence	3/15 (20.0%)	2/9 (22.2%)	0/12 (0.0%)
	Time-to-First	603	725 (T)	462
	Poly-K P-Value	0.264N	0.433N	0.344N
Hematopoietic System				
Bone Marrow * Lymphoma Malignant	Simple Incidence	2/48 (4.2%)	2/26 (7.7%)	1/25 (4.0%)
	Poly-K Incidence	2/34.3 (5.8%)	2/19.3 (10.4%)	1/20.0 (5.0%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.601N	0.474	0.687N
Spleen * Lymphoma Malignant	Simple Incidence	2/49 (4.1%)	2/26 (7.7%)	1/25 (4.0%)
	Poly-K Incidence	2/34.3 (5.8%)	2/19.3 (10.4%)	1/20.0 (5.0%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.601N	0.474	0.688N
Spleen * Sarcoma	Simple Incidence	0/49 (0.0%)	2/26 (7.7%)	0/25 (0.0%)
	Poly-K Incidence	0/32.9 (0.0%)	2/18.8 (10.6%)	0/19.3 (0.0%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	----	459	----
	Poly-K P-Value	0.588	0.117	-----
Thymus * Lymphoma Malignant	Simple Incidence	2/50 (4.0%)	2/24 (8.3%)	1/25 (4.0%)
	Poly-K Incidence	2/35.1 (5.7%)	2/17.6 (11.4%)	1/19.3 (5.2%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/11 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.602	0.428	0.706N
Integumentary System				
Mammary Gland * Fibroma	Simple Incidence	2/50 (4.0%)	0/25 (0.0%)	2/25 (8.0%)
	Poly-K Incidence	2/34.1 (5.9%)	0/16.6 (0.0%)	2/19.3 (10.4%)
	Terminal Incidence	1/15 (6.7%)	0/8 (0.0%)	2/12 (16.7%)
	Time-to-First	622	----	726 (T)
	Poly-K P-Value	0.407	0.406N	0.477

RR9: CLARITY-BPA Core Study
 Data from 34-Appendix XXXIV Terminal Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 6. Neoplasms by Body System for Terminal Sacrifice Males EE2 Continuous Dose Arm</i>				
<i>System and Neoplasm</i>	<i>Treatment (ug/kg)</i>			
<i>Lesion</i>	<i>Statistic</i>	<i>Control</i>	<i>0.05</i>	<i>0.50</i>
Urinary System				
Kidney * Lymphoma Malignant	Simple Incidence	2/50 (4.0%)	2/26 (7.7%)	1/26 (3.8%)
	Poly-K Incidence	2/35.1 (5.7%)	2/19.3 (10.4%)	1/20.3 (4.9%)
	Terminal Incidence	0/15 (0.0%)	0/9 (0.0%)	0/12 (0.0%)
	Time-to-First	486	369	473
	Poly-K P-Value	0.605N	0.465	0.690N

P-values for dose trend are presented in the "Control" column.
 N indicates a negative trend or negative treatment comparison to control with corresponding lower-tail p-values.