

RR-9: CLARITY-BPA Core Study
Data from 33 – Appendix XXXIII Interim Sacrifice Lesion Incidence Statistical Report - Neoplastic

<i>Table 1. Neoplasms by Body System for Interim Sacrifice Females 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>
Integumentary System							
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	4/20 (20.0%)	1/22 (4.5%)	1/20 (5.0%)	1/22 (4.5%)	1/20 (5.0%)	2/22 (9.1%)
	Terminal Incidence	4/20 (20.0%)	1/22 (4.5%)	1/20 (5.0%)	1/22 (4.5%)	1/20 (5.0%)	2/20 (10.0%)
	Time-to-First	363 (T)	365 (T)	365 (T)	363 (T)	364 (T)	363 (T)
	CAFE P-Value	0.184N	0.144N	0.171N	0.144N	0.171N	0.286N
Mammary Gland * Fibroadenoma							
Mammary Gland * Fibroadenoma	Simple Incidence	4/20 (20.0%)	1/22 (4.5%)	1/20 (5.0%)	1/22 (4.5%)	1/20 (5.0%)	2/22 (9.1%)
	Terminal Incidence	4/20 (20.0%)	1/22 (4.5%)	1/20 (5.0%)	1/22 (4.5%)	1/20 (5.0%)	2/20 (10.0%)
	Time-to-First	363 (T)	365 (T)	365 (T)	363 (T)	364 (T)	363 (T)
	CAFE P-Value	0.184N	0.144N	0.171N	0.144N	0.171N	0.286N

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.

<i>Table 2. Neoplasms by Body System for Interim 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>
none							

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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<i>Table 3. Neoplasms by Body System for Interim 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>
Genital System							
Uterus * Polyp Stromal	Simple Incidence	1/23 (4.3%)	0/22 (0.0%)	1/21 (4.8%)	0/24 (0.0%)	3/20 (15.0%)	3/24 (12.5%)
	Terminal Incidence	1/21 (4.8%)	0/22 (0.0%)	1/21 (4.8%)	0/22 (0.0%)	3/20 (15.0%)	3/24 (12.5%)
	Time-to-First	362 (T)	----	360 (T)	----	362 (T)	362 (T)
	CAFE P-Value	0.037 *	0.511N	0.733	0.489N	0.252	0.321
Integumentary System							
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	2/23 (8.7%)	4/22 (18.2%)	4/22 (18.2%)	1/24 (4.2%)	2/20 (10.0%)	6/24 (25.0%)
	Terminal Incidence	2/21 (9.5%)	4/22 (18.2%)	3/21 (14.3%)	0/22 (0.0%)	2/20 (10.0%)	6/24 (25.0%)
	Time-to-First	361 (T)	356 (T)	311	256	362 (T)	362 (T)
	CAFE P-Value	0.241	0.311	0.311	0.484N	0.641	0.136
Mammary Gland * Fibroadenoma	Simple Incidence	2/23 (8.7%)	3/22 (13.6%)	3/22 (13.6%)	1/24 (4.2%)	2/20 (10.0%)	6/24 (25.0%)
	Terminal Incidence	2/21 (9.5%)	3/22 (13.6%)	2/21 (9.5%)	0/22 (0.0%)	2/20 (10.0%)	6/24 (25.0%)
	Time-to-First	361 (T)	356 (T)	311	256	362 (T)	362 (T)
	CAFE P-Value	0.150	0.478	0.478	0.484N	0.641	0.136

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

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<i>Table 4. Neoplasms by Body System for Interim 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>
Alimentary System							
Liver * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.282N	0.244N
Pancreas * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.282N	0.244N
Cardiovascular System							
Heart * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/20 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.268N	0.244N
Endocrine System							
Adrenal Cortex * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/20 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.268N	0.244N
Parathyroid Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/21 (0.0%)	0/19 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/21 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/21 (0.0%)	0/17 (0.0%)	0/24 (0.0%)	0/17 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.029N*	0.256N	0.282N	0.223N	0.282N	0.256N
Pituitary Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/20 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.268N	0.244N
Genital System							
Prostate, Dorsal/Lateral Lobe * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/20 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)

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<i>Table 4. Neoplasms by Body System for Interim 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>
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.268N	0.244N
Hematopoietic System							
Bone Marrow * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.296N	0.244N
Spleen * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.296N	0.244N
Integumentary System							
Mammary Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/21 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/21 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/17 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.256N	0.268N	0.223N	0.282N	0.244N
Urinary System							
Kidney * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/22 (0.0%)	0/20 (0.0%)	0/24 (0.0%)	0/19 (0.0%)	0/22 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/18 (0.0%)	0/24 (0.0%)	0/18 (0.0%)	0/21 (0.0%)
	Time-to-First	282	----	----	----	----	----
	CAFE P-Value	0.028N*	0.244N	0.268N	0.223N	0.282N	0.244N

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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<i>Table 5. Neoplasms by Body System for Interim Sacrifice Females 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>
Integumentary System				
Mammary Gland * Adenocarcinoma	Simple Incidence	0/23 (0.0%)	2/26 (7.7%)	0/26 (0.0%)
	Terminal Incidence	0/21 (0.0%)	1/24 (4.2%)	0/26 (0.0%)
	Time-to-First	----	257	----
	CAFE P-Value	0.639N	0.276	
Mammary Gland * Adenocarcinoma or Fibroadenoma	Simple Incidence	2/23 (8.7%)	4/26 (15.4%)	4/26 (15.4%)
	Terminal Incidence	2/21 (9.5%)	3/24 (12.5%)	4/26 (15.4%)
	Time-to-First	361 (T)	257	360 (T)
	CAFE P-Value	0.325	0.395	0.395
Mammary Gland * Fibroadenoma	Simple Incidence	2/23 (8.7%)	2/26 (7.7%)	4/26 (15.4%)
	Terminal Incidence	2/21 (9.5%)	2/24 (8.3%)	4/26 (15.4%)
	Time-to-First	361 (T)	361 (T)	360 (T)
	CAFE P-Value	0.297	0.647N	0.395

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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Table 6. Neoplasms by Body System for Interim 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	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Pancreas * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/25 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.088N	0.205N	0.214N
Cardiovascular System				
Heart * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Endocrine System				
Adrenal Cortex * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Parathyroid Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Pituitary Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Genital System				
Prostate, Dorsal/Lateral Lobe * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)

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<i>Table 6. Neoplasms by Body System for Interim 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>
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Hematopoietic System				
Bone Marrow * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/26 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.086N	0.205N	0.205N
Spleen * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/25 (0.0%)	0/25 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.090N	0.214N	0.214N
Integumentary System				
Mammary Gland * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/25 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/22 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.088N	0.205N	0.214N
Urinary System				
Kidney * Lymphoma Malignant	Simple Incidence	2/22 (9.1%)	0/26 (0.0%)	0/25 (0.0%)
	Terminal Incidence	0/18 (0.0%)	0/22 (0.0%)	0/23 (0.0%)
	Time-to-First	282	----	----
	CAFE P-Value	0.088N	0.205N	0.214N

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.