APPENDIX E
SUMMARY OF LESIONS IN REGIMEN E MALE MICE IN THE 2-YEAR GAVAGE STUDY OF CHLORAL HYDRATE
(Single Dose on Postnatal Day 15)

TABLE E1

Summary of the Incidence of Neoplasms in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate[a]

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Disposition Summary				
Animals initially in study	48	48	48	48
Early deaths				
Moribund	1	1		3
Natural deaths	2	6	2	5
Survivors				
Died last week of study				1
Terminal sacrifice	45	41	46	39
Animals examined microscopically	48	48	48	48
Alimentary System				
Intestine large, cecum	(47)	(5)	(1)	(46)
Lymphoma malignant				2 (4%)
Intestine small, duodenum	(47)	(5)	(1)	(47)
Lymphoma malignant			1 (100%)	
Intestine small, ileum	(47)	(5)	(45)	
Lymphoma malignant	1 (2%)			
Intestine small, jejunum	(47)	(6)	(45)	
Adenocarcinoma		1 (17%)		
Lymphoma malignant				1 (2%)
Liver	(48)	(48)	(48)	(48)
Cholangiocarcinoma		1 (2%)		
Hemangiosarcoma	1 (2%)	1 (2%)	2 (4%)	
Hepatoblastoma	1 (2%)			
Hepatocellular adenoma	16 (33%)	6 (13%)	12 (25%)	8 (17%)
Hepatocellular adenoma, multiple	2 (4%)	2 (4%)		3 (6%)
Hepatocellular carcinoma	9 (19%)	10 (21%)	6 (13%)	11 (23%)
Hepatocellular carcinoma, multiple	1 (2%)			1 (2%)
Hepatocholangiocarcinoma	1 (2%)			
Histiocytic sarcoma	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Lymphoma malignant	4 (8%)	3 (6%)	1 (2%)	2 (4%)
Pancreas	(47)	(6)	(2)	(47)
Lymphoma malignant				1 (2%)
Salivary glands	(47)	(7)	(3)	(48)
Histiocytic sarcoma			1 (33%)	
Lymphoma malignant		1 (14%)		1 (2%)
Stomach, forestomach	(48)	(6)	(1)	(47)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant				1 (2%)
Cardiovascular System				
None				
Endocrine System				
Adrenal gland	(48)	(6)	(2)	(47)
Carcinoma, metastatic, lung				1 (2%)
Adrenal gland, cortex	(48)	(6)	(2)	(47)
Adenoma				1 (2%)
Lymphoma malignant		1 (17%)		1 (2%)
Islets, pancreatic	(47)	(6)	(3)	(47)
Adenoma			1 (33%)	

TABLE E1
Summary of the Incidence of Neoplasms in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Endocrine System (continued)				
Thyroid gland	(48)	(6)	(2)	(47)
Adenoma	2 (4%)			
General Body System				
Tissue NOS			(1)	
Lymphoma malignant, thoracic				1 (100%)
Genital System				
Coagulating gland	(48)	(7)	(1)	(46)
Lymphoma malignant				1 (2%)
Prostate	(48)	(6)	(2)	(47)
Lymphoma malignant	1 (2%)	1 (17%)		1 (2%)
Seminal vesicle	(48)	(8)	(1)	(46)
Lymphoma malignant				1 (2%)
Hematopoietic System				
Bone marrow	(48)	(7)	(2)	(48)
Hemangiosarcoma	1 (2%)			
Histiocytic sarcoma				1 (2%)
Lymphoma malignant		1 (14%)		
Lymph node	(48)	(11)	(4)	(47)
Fibrosarcoma, metastatic, axillary, skeletal muscle				1 (2%)
Fibrosarcoma, metastatic, thoracic, skeletal muscle				1 (2%)
Histiocytic sarcoma, lumbar	1 (2%)			
Histiocytic sarcoma, renal	1 (2%)	1 (9%)		
Lymphoma malignant		1 (9%)		
Lymphoma malignant, renal	1 (2%)			1 (2%)
Lymph node, mandibular	(48)	(7)	(2)	(46)
Fibrosarcoma, metastatic, skeletal muscle				1 (2%)
Histiocytic sarcoma	1 (2%)			1 (2%)
Lymphoma malignant	2 (4%)	1 (14%)		1 (2%)
Lymph node, mesenteric	(47)	(7)	(4)	(46)
Histiocytic sarcoma		1 (14%)	1 (25%)	1 (2%)
Lymphoma malignant	2 (4%)	1 (14%)		2 (4%)
Spleen	(46)	(11)	(4)	(47)
Hemangiosarcoma	1 (2%)	1 (9%)		2 (4%)
Histiocytic sarcoma		1 (9%)	1 (25%)	1 (2%)
Lymphoma malignant	4 (9%)	3 (27%)	1 (25%)	2 (4%)
Thymus	(36)	(5)	(1)	(35)
Lymphoma malignant		1 (20%)		2 (6%)
Integumentary System				
Mammary gland	(3)		(4)	
Histiocytic sarcoma				1 (25%)

TABLE E1
Summary of the Incidence of Neoplasms in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Integumentary System (continued)				
Skin	(47)	(9)	(3)	(47)
Fibrosarcoma	1 (2%)		1 (33%)	
Hemangioma		1 (11%)		
Hemangiosarcoma	1 (2%)			
Lymphoma malignant	1 (2%)			1 (2%)
Papilloma		1 (11%)		
Sarcoma				1 (2%)
Schwannoma malignant		1 (11%)		
Musculoskeletal System				
Skeletal muscle	(48)	(8)	(2)	(48)
Fibrosarcoma, back				1 (2%)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant		1 (13%)		1 (2%)
Schwannoma malignant		2 (25%)		
Nervous System				
Brain, cerebrum	(47)	(7)	(2)	(48)
Lymphoma malignant		1 (14%)		
Spinal cord, thoracic	(47)	(7)	(2)	(48)
Lymphoma malignant		1 (14%)		
Respiratory System				
Lung	(48)	(8)	(4)	(47)
Alveolar/bronchiolar adenoma	4 (8%)			7 (15%)
Alveolar/bronchiolar carcinoma	4 (8%)		2 (50%)	3 (6%)
Alveolar/bronchiolar carcinoma, multiple				1 (2%)
Cholangiocarcinoma, metastatic, liver		1 (13%)		
Fibrosarcoma, metastatic, skeletal muscle				1 (2%)
Hepatocellular carcinoma, metastatic, liver	3 (6%)	3 (38%)	1 (25%)	2 (4%)
Histiocytic sarcoma	1 (2%)		1 (25%)	1 (2%)
Lymphoma malignant		1 (13%)		1 (2%)
Special Senses System				
Eye	(48)	(7)	(2)	(48)
Lymphoma malignant				1 (2%)
Harderian gland	(48)	(10)	(4)	(48)
Adenoma	4 (8%)	3 (30%)	2 (50%)	
Lymphoma malignant		1 (10%)		
Lacrimal gland	(48)	(7)	(1)	(47)
Lymphoma malignant		1 (14%)		1 (2%)
Urinary System				
Kidney	(48)	(8)	(2)	(47)
Carcinoma, metastatic, lung				1 (2%)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant	1 (2%)	1 (13%)		2 (4%)
Urinary bladder	(48)	(7)	(2)	(47)
Lymphoma malignant		1 (14%)		

TABLE E1
Summary of the Incidence of Neoplasms in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Neoplasm Summary				
Total animals with primary neoplasms[b]	36	26	23	32
Total primary neoplasms	75	56	35	75
Total animals with benign neoplasms	26	10	14	17
Total benign neoplasms	28	13	15	19
Total animals with malignant neoplasms	19	18	12	21
Total malignant neoplasms	47	43	20	56
Total animals with metastatic neoplasms	3	4	1	4
Total metastatic neoplasms	3	4	1	8

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm

[b] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE E2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Harderian Gland: Adenoma				
Overall rate[a]	4/48 (8%)	3/10 (30%)	2/4 (50%)	0/48 (0%)
Adjusted rate[b]	8.5%	46.2%	58.2%	0.0%
Terminal rate[c]	4/45 (9%)	3/3 (100%)	2/2 (100%)	0/40 (0%)
First incidence (days)	757	757 (T)	757 (T)	—[e]
Poly-3 test[d]	(NA)	—[f]	—	P=0.0623N
Liver: Hepatocellular Adenoma				
Overall rate	18/48 (38%)	8/48 (17%)	12/48 (25%)	11/48 (23%)
Adjusted rate	38.0%	18.0%	25.3%	23.5%
Terminal rate	17/45 (38%)	8/41 (20%)	12/46 (26%)	9/40 (23%)
First incidence (days)	709	757 (T)	757 (T)	710
Poly-3 test	P=0.1715N	P=0.0270N	P=0.1338N	P=0.0957N
Liver: Hepatocellular Carcinoma				
Overall rate	10/48 (21%)	10/48 (21%)	6/48 (13%)	12/48 (25%)
Adjusted rate	21.1%	22.2%	12.6%	25.3%
Terminal rate	9/45 (20%)	8/41 (20%)	5/46 (11%)	8/40 (20%)
First incidence (days)	721	634	718	622
Poly-3 test	P=0.4060	P=0.5496	P=0.2030N	P=0.4062
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	24/48 (50%)	17/48 (35%)	18/48 (38%)	21/48 (44%)
Adjusted rate	50.5%	37.8%	37.8%	44.2%
Terminal rate	22/45 (49%)	15/41 (37%)	17/46 (37%)	16/40 (40%)
First incidence (days)	709	634	718	622
Poly-3 test	P=0.4031N	P=0.1527N	P=0.1496N	P=0.3405N
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	10/48 (21%)	10/48 (21%)	6/48 (13%)	12/48 (25%)
Adjusted rate	21.1%	22.2%	12.6%	25.3%
Terminal rate	9/45 (20%)	8/41 (20%)	5/46 (11%)	8/40 (20%)
First incidence (days)	721	634	718	622
Poly-3 test	P=0.4060	P=0.5496	P=0.2030N	P=0.4062
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	24/48 (50%)	17/48 (35%)	18/48 (38%)	21/48 (44%)
Adjusted rate	50.5%	37.8%	37.8%	44.2%
Terminal rate	22/45 (49%)	15/41 (37%)	17/46 (37%)	16/40 (40%)
First incidence (days)	709	634	718	622
Poly-3 test	P=0.4031N	P=0.1527N	P=0.1496N	P=0.3405N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	4/48 (8%)	0/8 (0%)	0/4 (0%)	7/47 (15%)
Adjusted rate	8.5%	0.0%	0.0%	15.2%
Terminal rate	4/45 (9%)	0/1 (0%)	0/2 (0%)	5/39 (13%)
First incidence (days)	757 (T)	—	—	622
Poly-3 test	(NA)	—	—	P=0.2469

TABLE E2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	4/48 (8%)	0/8 (0%)	2/4 (50%)	4/47 (9%)
Adjusted rate	8.5%	0.0%	58.2%	8.8%
Terminal rate	4/45 (9%)	0/1 (0%)	2/2 (100%)	4/39 (10%)
First incidence (days)	757 (T)	—	757 (T)	757 (T)
Poly-3 test	(NA)	—	—	P=0.6228
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	8/48 (17%)	0/8 (0%)	2/4 (50%)	11/47 (23%)
Adjusted rate	16.9%	0.0%	58.2%	23.9%
Terminal rate	8/45 (18%)	0/1 (0%)	2/2 (100%)	9/39 (23%)
First incidence (days)	757 (T)	—	757 (T)	622
Poly-3 test	(NA)	—	—	P=0.2832
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	2/48 (4%)	3/48 (6%)	2/48 (4%)	2/48 (4%)
Adjusted rate	4.2%	6.7%	4.2%	4.2%
Terminal rate	2/45 (4%)	3/41 (7%)	2/46 (4%)	0/40 (0%)
First incidence (days)	757 (T)	757 (T)	757 (T)	622
Poly-3 test	P=0.5031N	P=0.4732	P=0.6917N	P=0.6926
All Organs: Malignant Lymphoma				
Overall rate	5/48 (10%)	3/48 (6%)	2/48 (4%)	2/48 (4%)
Adjusted rate	10.5%	6.7%	4.2%	4.3%
Terminal rate	4/45 (9%)	2/41 (5%)	2/46 (4%)	1/40 (2%)
First incidence (days)	607	741	757 (T)	736
Poly-3 test	P=0.1585N	P=0.3946N	P=0.2189N	P=0.2262N
All Organs: Benign Neoplasms				
Overall rate	26/48 (54%)	10/48 (21%)	14/48 (29%)	17/48 (35%)
Adjusted rate	54.9%	22.5%	29.5%	35.9%
Terminal rate	25/45 (56%)	10/41 (24%)	14/46 (30%)	13/40 (33%)
First incidence (days)	709	757 (T)	757 (T)	622
Poly-3 test	P=0.1451N	P=0.0009N	P=0.0093N	P=0.0479N
All Organs: Malignant Neoplasms				
Overall rate	19/48 (40%)	18/48 (38%)	12/48 (25%)	21/48 (44%)
Adjusted rate	39.6%	39.1%	25.0%	44.0%
Terminal rate	16/45 (36%)	13/41 (32%)	10/46 (22%)	14/40 (35%)
First incidence (days)	607	587	632	622
Poly-3 test	P=0.4207	P=0.5636N	P=0.0948N	P=0.4093

TABLE E2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
All Organs: Benign or Malignant Neoplasms				
Overall rate	36/48 (75%)	26/48 (54%)	23/48 (48%)	32/48 (67%)
Adjusted rate	75.0%	56.5%	47.9%	67.1%
Terminal rate	33/45 (73%)	21/41 (51%)	21/46 (46%)	25/40 (63%)
First incidence (days)	607	587	632	622
Poly-3 test	P=0.3460N	P=0.0452N	P=0.0048N	P=0.2647N

(T)Terminal sacrifice
(NA)Not applicable

[a] Number of neoplasm-bearing animals/number of animals with tissue examined microscopically

[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality

[c] Observed incidence at terminal kill

[d] Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in a dose group is indicated by **N**.

[e] Not applicable; no neoplasms in animal group

[f] Tissue was examined microscopically only when it was observed to be abnormal at necropsy; thus, statistical comparisons with the vehicle controls are not appropriate.

TABLE E3
Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate[a]

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Disposition Summary				
Animals initially in study	48	48	48	48
Early deaths				
Moribund	1	1		3
Natural deaths	2	6	2	5
Survivors				
Died last week of study				1
Terminal sacrifice	45	41	46	39
Animals examined microscopically	48	48	48	48
Alimentary System				
Esophagus	(48)	(7)	(2)	(47)
Inflammation				1 (2%)
Gallbladder	(47)	(6)	(1)	(43)
Calculus microscopic observation only	1 (2%)			
Ectasia				2 (5%)
Infiltration cellular, lymphocytic	6 (13%)			2 (5%)
Inflammation	1 (2%)			1 (2%)
Intestine large, cecum	(47)	(5)	(1)	(46)
Hyperplasia, lymphoid	2 (4%)	1 (20%)		3 (7%)
Hyperplasia, lymphoid tissue	1 (2%)			1 (2%)
Intestine large, colon	(47)	(5)	(1)	(46)
Hyperplasia, lymphoid	1 (2%)			1 (2%)
Intestine large, rectum	(45)	(5)	(1)	(45)
Hyperplasia, lymphoid				1 (2%)
Intestine small, ileum	(47)	(5)		(45)
Hyperplasia, lymphoid	3 (6%)			2 (4%)
Intestine small, jejunum	(47)	(6)		(45)
Hyperplasia, lymphoid	1 (2%)			1 (2%)
Liver	(48)	(48)	(48)	(48)
Angiectasis	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Basophilic focus	10 (21%)	2 (4%)	9 (19%)	11 (23%)
Congestion	1 (2%)	1 (2%)		
Cyst, bile duct	1 (2%)	4 (8%)	3 (6%)	1 (2%)
Degeneration				2 (4%)
Eosinophilic focus	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)		1 (2%)
Hyperplasia, ito cell			1 (2%)	
Infarct			2 (4%)	1 (2%)
Infiltration cellular, lymphocytic	11 (23%)	17 (35%)	15 (31%)	3 (6%)
Necrosis	3 (6%)		3 (6%)	6 (13%)
Regeneration	1 (2%)	1 (2%)		1 (2%)
Tension lipoidosis	16 (33%)	13 (27%)	9 (19%)	10 (21%)
Thrombus	1 (2%)	1 (2%)		
Vacuolization cytoplasmic	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Mesentery	(1)			
Infarct	1 (100%)			

[a] Number of animals examined microscopically at the site and the number of animals with lesion

TABLE E3
Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Alimentary System (continued)				
Pancreas	(47)	(6)	(2)	(47)
Atrophy	2 (4%)			1 (2%)
Basophilic focus				1 (2%)
Focal cellular change	2 (4%)			5 (11%)
Hyperplasia	1 (2%)			
Infiltration cellular, lymphocytic	6 (13%)			6 (13%)
Inflammation	1 (2%)		1 (50%)	1 (2%)
Salivary glands	(47)	(7)	(3)	(48)
Atrophy				1 (2%)
Focal cellular change	1 (2%)			
Infiltration cellular, lymphocytic	43 (91%)	3 (43%)		42 (88%)
Mineralization		1 (14%)		
Stomach, glandular	(47)	(6)	(1)	(47)
Hyperplasia				1 (2%)
Infiltration cellular, lymphocytic	2 (4%)			2 (4%)
Inflammation				2 (4%)
Mineralization				1 (2%)
Tongue	(48)	(7)	(2)	(48)
Infiltration cellular, lymphocytic	1 (2%)			
Cardiovascular System				
Heart	(48)	(7)	(2)	(48)
Atrophy	1 (2%)			
Degeneration	1 (2%)			
Fibrosis		1 (14%)		
Infiltration cellular, lymphocytic	2 (4%)			
Necrosis		1 (14%)		
Pigmentation, valve		1 (14%)		
Endocrine System				
Adrenal gland, cortex	(48)	(6)	(2)	(47)
Atrophy	1 (2%)			
Clear cell focus	3 (6%)			4 (9%)
Congestion	1 (2%)			
Focal cellular change	1 (2%)			2 (4%)
Hyperplasia	11 (23%)			10 (21%)
Hyperplasia, spindle cell	43 (90%)	5 (83%)		42 (89%)
Necrosis				1 (2%)
Vacuolization cytoplasmic		1 (17%)		
Adrenal gland, medulla	(47)	(6)	(2)	(46)
Fibrosis				2 (4%)
Hyperplasia	7 (15%)			13 (28%)
Necrosis				1 (2%)
Parathyroid gland	(43)	(6)	(2)	(46)
Cyst				2 (4%)
Ectopic thymus				1 (2%)
Pituitary gland	(44)	(5)	(1)	(36)
Cyst	1 (2%)			
Hyperplasia, pars distalis	3 (7%)			2 (6%)
Thyroid gland	(48)	(6)	(2)	(47)
Hypertrophy, follicle		1 (17%)		
Ultimobranchial cyst	1 (2%)	1 (17%)		

TABLE E3
Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
General Body System				
None				
Genital System				
Coagulating gland	(48)	(7)	(1)	(46)
Atrophy				1 (2%)
Infiltration cellular, lymphocytic	3 (6%)			
Epididymis	(48)	(6)	(2)	(48)
Granuloma sperm	1 (2%)			
Infiltration cellular, lymphocytic	2 (4%)	1 (17%)		1 (2%)
Inflammation		1 (17%)		
Mineralization	1 (2%)			
Penis		(1)		
Cyst		1 (100%)		
Preputial gland	(47)	(10)	(6)	(46)
Atrophy	2 (4%)			1 (2%)
Cyst	4 (9%)	5 (50%)	4 (67%)	5 (11%)
Cyst, multiple		1 (10%)		
Ectasia	30 (64%)	4 (40%)	2 (33%)	26 (57%)
Infiltration cellular, lymphocytic	1 (2%)		1 (17%)	4 (9%)
Inflammation	1 (2%)		1 (17%)	2 (4%)
Necrosis, fat			1 (17%)	
Prostate	(48)	(6)	(2)	(47)
Fibrosis				1 (2%)
Infiltration cellular, lymphocytic	16 (33%)			10 (21%)
Inflammation				1 (2%)
Seminal vesicle	(48)	(8)	(1)	(46)
Atrophy				1 (2%)
Ectasia		1 (13%)		
Testes	(48)	(7)	(2)	(48)
Degeneration		1 (14%)		1 (2%)
Infiltration cellular, lymphocytic				1 (2%)
Mineralization				2 (4%)
Hematopoietic System				
Bone marrow	(48)	(7)	(2)	(48)
Atrophy	1 (2%)			
Congestion				1 (2%)
Hyperplasia	4 (8%)			4 (8%)
Pigmentation	1 (2%)	2 (29%)		3 (6%)
Lymph node, mandibular	(48)	(7)	(2)	(46)
Hematopoietic cell proliferation				1 (2%)
Hyperplasia, lymphoid				2 (4%)
Infiltration cellular, lymphocytic	4 (8%)			
Lymph node, mesenteric	(47)	(7)	(4)	(46)
Angiectasis		1 (14%)		
Congestion	4 (9%)		1 (25%)	2 (4%)
Hematopoietic cell proliferation	3 (6%)			1 (2%)
Hemorrhage	10 (21%)	4 (57%)	1 (25%)	20 (43%)
Hyperplasia, lymphoid			1 (25%)	1 (2%)
Infiltration cellular, lymphocytic	2 (4%)			
Inflammation				2 (4%)

TABLE E3
Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Hematopoietic System (continued)				
Spleen	(46)	(11)	(4)	(47)
Angiectasis				1 (2%)
Atrophy	1 (2%)			2 (4%)
Congestion	2 (4%)			1 (2%)
Cyst	1 (2%)			
Hematopoietic cell proliferation	8 (17%)	5 (45%)	1 (25%)	10 (21%)
Hyperplasia, lymphoid	5 (11%)		1 (25%)	6 (13%)
Infarct				2 (4%)
Thymus	(36)	(5)	(1)	(35)
Atrophy, cortex			1 (100%)	1 (3%)
Cyst	1 (3%)			1 (3%)
Hyperplasia, lymphoid, medulla				1 (3%)
Infiltration cellular, histiocytic				1 (3%)
Necrosis		1 (20%)		
Pigmentation		1 (20%)		
Integumentary System				
Skin	(47)	(9)	(3)	(47)
Atrophy, subcutaneous tissue		1 (11%)	1 (33%)	
Musculoskeletal System				
Bone, femur	(48)	(7)	(2)	(48)
Infiltration cellular, lymphocytic	1 (2%)			
Bone, sternum	(48)	(7)	(2)	(48)
Fibrous osteodystrophy, multifocal	1 (2%)	1 (14%)		
Skeletal muscle	(48)	(8)	(2)	(48)
Infiltration cellular, lymphocytic	2 (4%)			1 (2%)
Nervous System				
Brain, cerebrum	(47)	(7)	(2)	(48)
Hemorrhage		1 (14%)		
Infiltration cellular, lymphocytic				1 (2%)
Mineralization, multifocal, thalamus	25 (53%)	3 (43%)	1 (50%)	13 (27%)
Peripheral nerve	(47)	(7)	(2)	(48)
Infiltration cellular, lymphocytic	1 (2%)			
Spinal cord, thoracic	(47)	(7)	(2)	(48)
Cyst, meninges	1 (2%)			
Respiratory System				
Lung	(48)	(8)	(4)	(47)
Congestion	3 (6%)			1 (2%)
Cyst	1 (2%)			
Hemorrhage	1 (2%)	1 (13%)		
Hyperplasia, alveolar epithelium	11 (23%)			7 (15%)
Infiltration cellular, histiocytic	1 (2%)	1 (13%)		3 (6%)
Infiltration cellular, lymphocytic	42 (88%)	3 (38%)		37 (79%)
Inflammation	3 (6%)	1 (13%)		
Mineralization	1 (2%)			

TABLE E3
Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Respiratory System (continued)				
Nose	(48)	(7)	(2)	(48)
Infiltration cellular, lymphocytic				1 (2%)
Inflammation				2 (4%)
Special Senses System				
Eye	(48)	(7)	(2)	(48)
Inflammation, cornea		1 (14%)		
Harderian gland	(48)	(10)	(4)	(48)
Degeneration	1 (2%)			
Hyperplasia	1 (2%)			
Infiltration cellular, lymphocytic	25 (52%)	3 (30%)	2 (50%)	29 (60%)
Inflammation				1 (2%)
Lacrimal gland	(48)	(7)	(1)	(47)
Atrophy	6 (13%)			2 (4%)
Focal cellular change	1 (2%)			
Infiltration cellular, lymphocytic	18 (38%)	1 (14%)		8 (17%)
Vacuolization cytoplasmic				1 (2%)
Zymbal's gland	(44)	(4)	(2)	(45)
Infiltration cellular, lymphocytic	3 (7%)			
Inflammation				1 (2%)
Urinary System				
Kidney	(48)	(8)	(2)	(47)
Congestion		1 (13%)		2 (4%)
Cyst, renal tubule	1 (2%)			
Focal cellular change				1 (2%)
Infarct				1 (2%)
Infiltration cellular, lymphocytic	45 (94%)	4 (50%)	1 (50%)	42 (89%)
Infiltration cellular, plasma cell				1 (2%)
Inflammation		1 (13%)		1 (2%)
Mineralization	2 (4%)			1 (2%)
Nephropathy	6 (13%)		2 (100%)	4 (10%)
Pigmentation, renal tubule				1 (2%)
Vacuolization cytoplasmic	1 (2%)			
Urinary bladder	(48)	(7)	(2)	(47)
Ectasia		1 (14%)		
Infiltration cellular, lymphocytic	28 (58%)	1 (14%)		22 (47%)
Inflammation		1 (14%)		1 (2%)