APPENDIX B
SUMMARY OF LESIONS IN REGIMEN B FEMALE MICE IN THE 2-YEAR GAVAGE STUDY OF CHLORAL HYDRATE

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TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate[a]

	Vehicle Control[b]	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
Disposition Summary				
Animals initially in study	72	48	48	48
3-Month interim evaluation	8	8		
6-Month interim evaluation	8		8	
12-Month interim evaluation	8			8
Early deaths				
Moribund	2	2	3	
Natural deaths	9	4	6	7
Survivors				
Terminal sacrifice	37	34	31	33
Animals examined microscopically	72	48	48	48

Systems Examined at 3 Months with No Neoplasms Observed

Alimentary System
Cardiovascular System
Endocrine System
General Body System
Genital System
Hematopoietic System
Integumentary System
Musculoskeletal System
Nervous System
Respiratory System
Special Senses System
Urinary System

6-Month Interim Evaluation

Respiratory System			
Lung	(8)		(8)
Alveolar/bronchiolar adenoma	1 (13%)		

Systems Examined with No Neoplasms Observed

Alimentary System
Cardiovascular System
Endocrine System
General Body System
Genital System
Hematopoietic System
Integumentary System
Musculoskeletal System
Nervous System
Special Senses System
Urinary System

TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
12-Month Interim Evaluation				
Alimentary System				
Mesentery	(1)			
Yolk sac carcinoma, metastatic, ovary	1 (100%)			
Genital System				
Ovary	(8)			(7)
Yolk sac carcinoma	1 (13%)			
Systems Examined with No Neoplasms Observed				
Cardiovascular System				
Endocrine System				
General Body System				
Hematopoietic System				
Integumentary System				
Musculoskeletal System				
Nervous System				
Respiratory System				
Special Senses System				
Urinary System				
2-Year Study				
Alimentary System				
Esophagus	(47)	(36)	(40)	(38)
Lymphoma malignant			1 (3%)	
Gallbladder	(46)	(37)	(36)	(36)
Lymphoma malignant		2 (5%)		
Intestine large, cecum	(42)	(37)	(37)	(32)
Lymphoma malignant	1 (2%)	2 (5%)		
Intestine large, colon	(46)	(37)	(37)	(34)
Lymphoma malignant	2 (4%)		1 (3%)	
Intestine small, jejunum	(41)	(37)	(37)	(32)
Lymphoma malignant	2 (5%)	1 (3%)	1 (3%)	
Liver	(48)	(40)	(40)	(40)
Fibrosarcoma, metastatic, skin			1 (3%)	
Hepatocellular adenoma	1 (2%)	1 (3%)	1 (3%)	2 (5%)
Hepatocellular carcinoma	1 (2%)		1 (3%)	2 (5%)
Histiocytic sarcoma	1 (2%)		1 (3%)	1 (3%)
Lymphoma malignant	6 (13%)	6 (15%)	7 (18%)	8 (20%)
Mesentery	(1)	(1)	(2)	
Fibrosarcoma, metastatic, skin			1 (50%)	
Lymphoma malignant	1 (100%)			
Pancreas	(48)	(40)	(39)	(37)
Fibrosarcoma	1 (2%)			
Fibrosarcoma, metastatic, skin			2 (5%)	
Lymphoma malignant	2 (4%)	2 (5%)	5 (13%)	1 (3%)

TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Alimentary System (continued)				
Salivary glands	(48)	(40)	(40)	(39)
Lymphoma malignant	3 (6%)	3 (8%)	3 (8%)	2 (5%)
Tongue	(48)	(39)	(39)	(40)
Lymphoma malignant			1 (3%)	
Papilloma squamous	1 (2%)			
Cardiovascular System				
Heart	(48)	(40)	(40)	(39)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant	1 (2%)		1 (3%)	
Endocrine System				
Adrenal gland, cortex	(46)	(40)	(37)	(37)
Adenoma, spindle cell		1 (3%)		
Lymphoma malignant	1 (2%)			1 (3%)
Adrenal gland, medulla	(46)	(40)	(37)	(37)
Lymphoma malignant	1 (2%)			1 (3%)
Pheochromocytoma malignant	1 (2%)			
Islets, pancreatic	(48)	(40)	(37)	(38)
Lymphoma malignant		1 (3%)	1 (3%)	
Parathyroid gland	(38)	(31)	(33)	(36)
Adenoma			1 (3%)	
Pituitary gland	(45)	(36)	(36)	(33)
Adenoma, pars distalis		3 (8%)	1 (3%)	1 (3%)
Adenoma, pars intermedia	2 (4%)			
Thyroid gland	(47)	(40)	(40)	(39)
Adenoma, follicular cell		1 (3%)	1 (3%)	
Lymphoma malignant		1 (3%)	1 (3%)	
General Body System				
Tissue NOS	(1)	(1)		
Fibrosarcoma, metastatic, skin			1 (100%)	
Lymphoma malignant, fat	1 (100%)			
Genital System				
Clitoral gland	(43)	(37)	(33)	(33)
Lymphoma malignant			1 (3%)	
Ovary	(48)	(40)	(39)	(38)
Cystadenoma	1 (2%)		2 (5%)	
Fibrosarcoma, metastatic, periovarian tissue, skin			1 (3%)	
Histiocytic sarcoma	1 (2%)			
Luteoma	1 (2%)			
Lymphoma malignant	2 (4%)	4 (10%)	2 (5%)	
Lymphoma malignant, periovarian tissue	1 (2%)		4 (10%)	3 (8%)
Teratoma benign		1 (3%)		1 (3%)

TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Genital System (continued)				
Uterus	(48)	(40)	(40)	(39)
Hemangiosarcoma	1 (2%)			
Histiocytic sarcoma	2 (4%)			1 (3%)
Lymphoma malignant			1 (3%)	1 (3%)
Polyp	1 (2%)	1 (3%)	1 (3%)	
Sarcoma stromal				1 (3%)
Vagina	(48)	(38)	(40)	(37)
Histiocytic sarcoma	2 (4%)	1 (3%)		2 (5%)
Lymphoma malignant	2 (4%)	1 (3%)	1 (3%)	
Hematopoietic System				
Bone marrow	(47)	(39)	(40)	(38)
Hemangiosarcoma	1 (2%)			
Lymphoma malignant	3 (6%)	3 (8%)	2 (5%)	
Lymph node	(48)	(40)	(40)	(40)
Histiocytic sarcoma, lumbar	1 (2%)			
Lymphoma malignant				1 (3%)
Lymphoma malignant, axillary		1 (3%)	1 (3%)	
Lymphoma malignant, lumbar	2 (4%)	1 (3%)	1 (3%)	
Lymphoma malignant, mediastinal	1 (2%)		1 (3%)	
Lymphoma malignant, renal	1 (2%)		3 (8%)	
Lymphoma malignant, thoracic			1 (3%)	1 (3%)
Squamous cell carcinoma, metastatic, lumbar, skin			1 (3%)	
Lymph node, mandibular	(47)	(40)	(39)	(39)
Lymphoma malignant	4 (9%)	4 (10%)	6 (15%)	7 (18%)
Lymph node, mesenteric	(46)	(40)	(38)	(39)
Fibrosarcoma, metastatic, skin			1 (3%)	
Histiocytic sarcoma	1 (2%)			1 (3%)
Lymphoma malignant	6 (13%)	6 (15%)	6 (16%)	8 (21%)
Spleen	(47)	(40)	(39)	(39)
Fibrosarcoma, metastatic, skin			1 (3%)	
Hemangiosarcoma	1 (2%)			1 (3%)
Histiocytic sarcoma				1 (3%)
Lymphoma malignant	8 (17%)	7 (18%)	11 (28%)	8 (21%)
Thymus	(41)	(33)	(31)	(30)
Fibrosarcoma, metastatic, skin			1 (3%)	
Lymphoma malignant	3 (7%)	4 (12%)	5 (16%)	5 (17%)
Integumentary System				
Mammary gland	(44)	(36)	(38)	(36)
Adenoacanthoma				1 (3%)
Adenocarcinoma		1 (3%)	1 (3%)	
Fibrosarcoma	1 (2%)			
Fibrosarcoma, metastatic, skin		1 (3%)		
Lymphoma malignant	1 (2%)		2 (5%)	

TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Integumentary System (continued)				
Skin	(45)	(39)	(39)	(38)
Fibrosarcoma		2 (5%)	2 (5%)	
Hemangiosarcoma	1 (2%)			
Lymphoma malignant	1 (2%)		2 (5%)	1 (3%)
Squamous cell carcinoma			1 (3%)	
Musculoskeletal System				
Skeletal muscle	(48)	(39)	(40)	(39)
Fibrosarcoma, metastatic, skin			1 (3%)	
Lymphoma malignant		1 (3%)	2 (5%)	
Nervous System				
Brain, cerebellum	(48)	(40)	(40)	(40)
Lymphoma malignant			2 (5%)	
Brain, cerebrum	(48)	(40)	(40)	(40)
Lymphoma malignant			1 (3%)	
Peripheral nerve	(48)	(38)	(39)	(38)
Lymphoma malignant		1 (3%)		
Respiratory System				
Lung	(48)	(40)	(40)	(40)
Adenoacanthoma, metastatic, mammary gland				1 (3%)
Adenocarcinoma, metastatic, mammary gland			1 (3%)	
Alveolar/bronchiolar adenoma	1 (2%)	2 (5%)	4 (10%)	7 (18%)
Alveolar/bronchiolar carcinoma		1 (3%)		
Fibrosarcoma, metastatic, skin			1 (3%)	
Histiocytic sarcoma	1 (2%)			1 (3%)
Lymphoma malignant	4 (8%)	3 (8%)	4 (10%)	8 (20%)
Squamous cell carcinoma, metastatic, skin			1 (3%)	
Nose	(47)	(40)	(40)	(40)
Fibrosarcoma, metastatic, skin		1 (3%)		
Special Senses System				
Eye	(41)	(38)	(34)	(35)
Histiocytic sarcoma, retrobulbar				1 (3%)
Harderian gland	(48)	(38)	(38)	(38)
Adenoma	2 (4%)	2 (5%)	2 (5%)	3 (8%)
Carcinoma	1 (2%)			
Lymphoma malignant	2 (4%)	2 (5%)	1 (3%)	
Lacrimal gland	(41)	(33)	(33)	(32)
Lymphoma malignant	1 (2%)	2 (6%)	2 (6%)	2 (6%)
Zymbal's gland	(43)	(38)	(36)	(36)
Fibrosarcoma, metastatic, skin		1 (3%)		
Lymphoma malignant			1 (3%)	

TABLE B1
Summary of the Incidence of Neoplasms in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Urinary System				
Kidney	(48)	(40)	(39)	(38)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant	6 (13%)	6 (15%)	7 (18%)	5 (13%)
Urinary bladder	(47)	(37)	(39) (36)	
Lymphoma malignant	3 (36%)	2 (5%)	2 (5%)	3 (8%)
Neoplasm Summary				
Total animals with primary neoplasms[c]				
6-Month interim evaluation	1			
2-Year study	21	19	25	28
Total primary neoplasms				
6-Month interim evaluation	1			
2-Year study	102	83	113	93
Total animals with benign neoplasms				
6-Month interim evaluation	1			
2-Year study	8	11	13	13
Total benign neoplasms				
6-Month interim evaluation	1			
2-Year study	10	12	13	14
Total animals with malignant neoplasms				
12-Month interim evaluation	1			
2-Year study	16	13	19	21
Total malignant neoplasms				
12-Month interim evaluation	1			
2-Year study	92	71	100	79
Total animals with metastatic neoplasms				
12-Month interim evaluation	1			
2-Year study		2	4	1
Total metastatic neoplasms				
12-Month interim evaluation	1			
2-Year study		3	14	1

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

b Forty-eight mice served as vehicle controls for regimens A and B; the remaining 24 mice were designated for regimen B interim evaluations.

c Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE B2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control (Regimen A)	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)	2 Years (Regimen A)
Harderian Gland: Adenoma					
Overall rate[a]	2/48 (4%)	2/38 (5%)	2/38 (5%)	3/38 (8%)	2/47 (4%)
Adjusted rate[b]	4.7%	5.6%	5.8%	8.3%	4.8%
Terminal rate[c]	2/37 (5%)	2/33 (6%)	2/30 (7%)	3/33 (9%)	2/35 (6%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test[d]	P=0.5675	P=0.6275	P=0.6142	P=0.4216	P=0.6884
Harderian Gland: Adenoma or Carcinoma					
Overall rate	3/48 (6%)	2/38 (5%)	2/38 (5%)	3/38 (8%)	2/47 (4%)
Adjusted rate	7.0%	5.6%	5.8%	8.3%	4.8%
Terminal rate	3/37 (8%)	2/33 (6%)	2/30 (7%)	3/33 (9%)	2/35 (6%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.4707N	P=0.5829N	P=0.5984N	P=0.5814	P=0.5072N
Liver: Hepatocellular Adenoma					
Overall rate	1/48 (2%)	1/40 (3%)	1/40 (3%)	2/40 (5%)	2/48 (4%)
Adjusted rate	2.3%	2.7%	2.8%	5.3%	4.7%
Terminal rate	1/37 (3%)	1/34 (3%)	1/31 (3%)	2/33 (6%)	2/36 (6%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.3231	P=0.7287	P=0.7241	P=0.4553	P=0.5027
Liver: Hepatocellular Carcinoma					
Overall rate	1/48 (2%)	0/40 (0%)	1/40 (3%)	2/40 (5%)	1/48 (2%)
Adjusted rate	2.3%	0.0%	2.8%	5.3%	2.3%
Terminal rate	1/37 (3%)	0/34 (0%)	1/31 (3%)	2/33 (6%)	1/36 (3%)
First incidence (days)	757 (T)	—[e]	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.4537	P=0.5288N	P=0.7241	P=0.4553	P=0.7589N
Liver: Hepatocellular Adenoma or Carcinoma					
Overall rate	2/48 (4%)	1/40 (3%)	2/40 (5%)	4/40 (10%)	3/48 (6%)
Adjusted rate	4.7%	2.7%	5.5%	10.6%	7.0%
Terminal rate	2/37 (5%)	1/34 (3%)	2/31 (7%)	4/33 (12%)	3/36 (8%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.2637	P=0.5502N	P=0.6343	P=0.2787	P=0.5035
Lung: Alveolar/bronchiolar Adenoma					
Overall rate	1/48 (2%)	2/40 (5%)	4/40 (10%)	7/40 (18%)	4/48 (8%)
Adjusted rate	2.3%	5.4%	11.0%	18.6%	9.4%
Terminal rate	1/37 (3%)	2/34 (6%)	4/31 (13%)	7/33 (21%)	4/36 (11%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.1385	P=0.4497	P=0.1309	P=0.0173	P=0.1805
Lung: Alveolar/bronchiolar Adenoma or Carcinoma					
Overall rate	1/48 (2%)	3/40 (8%)	4/40 (10%)	7/40 (18%)	4/48 (8%)
Adjusted rate	2.3%	8.1%	11.0%	18.6%	9.4%
Terminal rate	1/37 (3%)	3/34 (9%)	4/31 (13%)	7/33 (21%)	4/36 (11%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.1887	P=0.2542	P=0.1309	P=0.0173	P=0.1805

TABLE B2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control (Regimen A)	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)	2 Years (Regimen A)
Pituitary Gland (Pars Distalis): Adenoma					
Overall rate	0/45 (0%)	3/36 (8%)	1/36 (3%)	1/33 (3%)	5/41 (12%)
Adjusted rate	0.0%	8.9%	3.0%	3.2%	13.3%
Terminal rate	0/36 (0%)	3/32 (9%)	0/29 (0%)	1/28 (4%)	5/32 (16%)
First incidence (days)	—	757 (T)	695	757 (T)	757 (T)
Poly-3 test	P=0.0278	P=0.0849	P=0.4620	P=0.4434	P=0.0237
Skin: Fibrosarcoma					
Overall rate	0/45 (0%)	2/39 (5%)	2/39 (5%)	0/38 (0%)	2/46 (4%)
Adjusted rate	0.0%	5.5%	5.5%	0.0%	4.8%
Terminal rate	0/37 (0%)	1/34 (3%)	0/31 (0%)	0/33 (0%)	2/36 (6%)
First incidence (days)	—	699	682	—	757 (T)
Poly-3 test	P=0.4175	P=0.2089	P=0.2078	—[f]	P=0.2419
Skin: Fibrosarcoma, Hemangiosarcoma, or Squamous Cell Carcinoma					
Overall rate	1/45 (2%)	2/39 (5%)	3/39 (8%)	0/38 (0%)	4/46 (9%)
Adjusted rate	2.4%	5.5%	8.2%	0.0%	9.6%
Terminal rate	1/37 (3%)	1/34 (3%)	0/31 (0%)	0/33 (0%)	3/36 (8%)
First incidence (days)	757 (T)	699	631	—	692
Poly-3 test	P=0.2155	P=0.4561	P=0.2627	P=0.5266N	P=0.1867
All Organs: Histiocytic Sarcoma					
Overall rate	3/48 (6%)	1/40 (3%)	1/40 (3%)	3/40 (8%)	5/48 (10%)
Adjusted rate	7.0%	2.7%	2.8%	7.9%	11.4%
Terminal rate	2/37 (5%)	1/34 (3%)	1/31 (3%)	1/33 (3%)	2/36 (6%)
First incidence (days)	681	757 (T)	757 (T)	699	567
Poly-3 test	P=0.1054	P=0.3601N	P=0.3677N	P=0.6044	P=0.3698
All Organs: Malignant Lymphoma					
Overall rate	9/48 (19%)	8/40 (20%)	13/40 (33%)	14/40 (35%)	15/48 (31%)
Adjusted rate	20.5%	21.6%	34.8%	37.0%	34.1%
Terminal rate	4/37 (11%)	7/34 (21%)	10/31 (32%)	13/33 (39%)	11/36 (31%)
First incidence (days)	605	747	471	694	555
Poly-3 test	P=0.0834	P=0.5614	P=0.1156	P=0.0780	P=0.1210
All Organs: Benign Neoplasms					
Overall rate	8/48 (17%)	11/40 (28%)	13/40 (33%)	13/40 (33%)	16/48 (33%)
Adjusted rate	18.3%	29.7%	35.6%	34.4%	37.5%
Terminal rate	6/37 (16%)	11/34 (32%)	12/31 (39%)	12/33 (36%)	15/36 (42%)
First incidence (days)	551	757 (T)	695	694	747
Poly-3 test	P=0.0672	P=0.1732	P=0.0646	P=0.0789	P=0.0404
All Organs: Malignant Neoplasms					
Overall rate	16/48 (33%)	13/40 (33%)	19/40 (48%)	21/40 (53%)	23/48 (48%)
Adjusted rate	36.0%	34.9%	49.3%	54.5%	50.9%
Terminal rate	9/37 (24%)	11/34 (32%)	12/31 (39%)	17/33 (52%)	15/36 (42%)
First incidence (days)	605	699	471	670	555
Poly-3 test	P=0.0631	P=0.5518N	P=0.1587	P=0.0681	P=0.1194

TABLE B2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control (Regimen A)	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)	2 Years (Regimen A)
All Organs: Benign or Malignant Neoplasms					
Overall rate	21/48 (44%)	19/40 (48%)	25/40 (63%)	28/40 (70%)	33/48 (69%)
Adjusted rate	46.6%	51.0%	64.8%	72.7%	73.0%
Terminal rate	13/37 (35%)	17/34 (50%)	18/31 (58%)	24/33 (73%)	25/36 (69%)
First incidence (days)	551	699	471	670	555
Poly-3 test	P=0.0037	P=0.4292	P=0.0719	P=0.0119	P=0.0093

(T)Terminal sacrifice

[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] Value of statistic cannot be computed.

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate[a]

	Vehicle Control[b]	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
Disposition Summary				
Animals initially in study	72	48	48	48
3-Month interim evaluation	8	8		
6-Month interim evaluation	8		8	
12-Month interim evaluation	8			8
Early deaths				
Moribund	2	2	3	
Natural deaths	9	4	6	7
Survivors				
Terminal sacrifice	37	34	31	33
Animals examined microscopically	72	48	48	48
3-Month Interim Evaluation				
Alimentary System				
Esophagus	(8)	(8)		
Inflammation, mediastinum	1 (13%)			
Liver	(8)	(8)		
Infiltration cellular, lymphocytic	1 (13%)	3 (38%)		
Necrosis	6 (75%)	5 (63%)		
Tension lipoidosis		4 (50%)		
Salivary glands	(8)	(8)		
Infiltration cellular, lymphocytic	5 (63%)			
Endocrine System				
Adrenal gland, cortex	(8)	(8)		
Hyperplasia, spindle cell	4 (50%)	3 (38%)		
Islets, pancreatic	(8)	(8)		
Hyperplasia		1 (13%)		
Thyroid gland	(7)	(8)		
Degeneration		1 (13%)		
Ultimobranchial cyst		1 (13%)		
Genital System				
Ovary	(8)	(8)		
Congestion	1 (13%)			
Hematopoietic System				
Bone marrow	(8)	(8)		
Hyperplasia	1 (13%)			
Lymph node, mandibular	(8)	(8)		
Hyperplasia, lymphoid	1 (13%)			
Lymph node, mesenteric	(7)	(8)		
Hemorrhage		1 (13%)		
Hyperplasia, lymphoid	1 (14%)			

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

[b] Forty-eight mice served as vehicle controls for regimens A and B; the remaining 24 mice were designated for regimen B interim evaluations.

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
3-Month Interim Evaluation (continued)				
Hematopoietic System (continued)				
Thymus	(8)	(8)		
Cyst	1 (13%)	1 (13%)		
Inflammation, mediastinum	1 (13%)			
Respiratory System				
Lung	(8)	(8)		
Congestion	1 (13%)			
Hemorrhage	1 (13%)			
Infiltration cellular, lymphocytic	1 (13%)	1 (13%)		
Inflammation		1 (13%)		
Nose	(8)	(8)		
Mineralization, nasolacrimal duct		1 (13%)		
Urinary System				
Urinary bladder	(8)	(8)		
Infiltration cellular, lymphocytic	1 (13%)			
Systems Examined with No Lesions Observed				
Cardiovascular System				
General Body System				
Integumentary System				
Musculoskeletal System				
Nervous System				
Special Senses System				
6-Month Interim Evaluation				
Alimentary System				
Liver	(8)		(8)	
Infiltration cellular, lymphocytic	3 (38%)		4 (50%)	
Necrosis	5 (63%)		6 (75%)	
Tension lipoidosis	1 (13%)		5 (63%)	
Vacuolization cytoplasmic	5 (63%)		7 (88%)	
Salivary glands	(8)		(8)	
Infiltration cellular, lymphocytic	4 (50%)		3 (38%)	
Stomach, forestomach	(8)		(8)	
Hyperkeratosis			1 (13%)	
Stomach, glandular	(8)		(8)	
Inflammation	1 (13%)			
Tongue	(8)		(8)	
Infiltration cellular, histiocytic	1 (13%)			

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
6-Month Interim Evaluation (continued)				
Endocrine System				
Adrenal gland, cortex	(8)		(8)	
Degeneration, fatty			1 (13%)	
Hyperplasia, spindle cell	4 (50%)		7 (88%)	
Parathyroid gland	(4)		(6)	
Ectopic thymus	1 (25%)			
Genital System				
Ovary	(8)		(8)	
Cyst	1 (13%)			
Hematocyst	1 (13%)			
Uterus	(8)		(8)	
Infiltration cellular, lymphocytic			1 (13%)	
Vagina	(7)		(8)	
Infiltration cellular, lymphocytic	1 (14%)			
Hematopoietic System				
Bone marrow	(8)		(8)	
Hyperplasia	1 (13%)		1 (13%)	
Lymph node, mandibular	(8)		(8)	
Fibrosis	1 (13%)			
Hyperplasia, lymphoid	2 (25%)		2 (25%)	
Spleen	(8)		(8)	
Congestion	1 (13%)			
Hematopoietic cell proliferation	1 (13%)		1 (13%)	
Hyperplasia, lymphoid	1 (13%)			
Thymus	(7)		(7)	
Atrophy, cortex	2 (29%)			
Hemorrhage			1 (14%)	
Hyperplasia, lymphoid, medulla			1 (14%)	
Integumentary System				
Skin	(8)		(8)	
Hyperplasia	1 (13%)			
Respiratory System				
Lung	(8)		(8)	
Infiltration cellular, lymphocytic	5 (63%)		3 (38%)	
Special Senses System				
Lacrimal gland	(6)		(7)	
Infiltration cellular, lymphocytic	2 (33%)		3 (43%)	

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
6-Month Interim Evaluation (continued)				
Urinary System				
Kidney	(8)		(8)	
Infiltration cellular, lymphocytic	2 (25%)		4 (50%)	
Urinary bladder			(8)	
Infiltration cellular, lymphocytic			1 (13%)	
Systems Examined with No Lesions Observed				
Cardiovascular System				
General Body System				
Musculoskeletal System				
Nervous System				
12-Month Interim Evaluation				
Alimentary System				
Esophagus	(8)			(8)
Hyperkeratosis	1 (13%)			
Gallbladder	(8)			(6)
Infiltration cellular, lymphocytic	1 (13%)			
Intestine large, cecum	(8)			(8)
Hyperplasia, lymphoid				1 (13%)
Intestine large, rectum	(8)			(6)
Cyst	1 (13%)			
Liver	(8)			(8)
Infiltration cellular, lymphocytic	5 (63%)			6 (75%)
Necrosis				3 (38%)
Tension lipoidosis	2 (25%)			1 (13%)
Vacuolization cytoplasmic	5 (63%)			3 (38%)
Pancreas	(8)			(8)
Infiltration cellular, lymphocytic	2 (25%)			2 (25%)
Salivary glands	(8)			(8)
Atrophy				1 (13%)
Infiltration cellular, lymphocytic	7 (88%)			7 (88%)
Stomach, forestomach	(8)			(8)
Hyperkeratosis				1 (13%)
Cardiovascular System				
Heart	(8)			(8)
Cardiomyopathy	1 (13%)			
Endocrine System				
Adrenal gland, cortex	(7)			(8)
Congestion				1 (13%)
Hyperplasia, spindle cell	6 (86%)			6 (75%)
Vacuolization cytoplasmic				2 (25%)

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
12-Month Interim Evaluation (continued)				
Endocrine System (continued)				
Pituitary gland	(5)			(5)
Cyst				1 (20%)
Thyroid gland	(6)			(6)
Ultimobranchial cyst				1 (17%)
Genital System				
Clitoral gland	(6)			(6)
Atrophy	5 (83%)			3 (50%)
Ovary	(8)			(7)
Atrophy	2 (25%)			1 (14%)
Cyst, periovarian tissue				2 (29%)
Hematocyst				1 (14%)
Infiltration cellular, lymphocytic				1 (14%)
Uterus	(8)			(8)
Hyperplasia, cystic, endometrium	2 (25%)			3 (38%)
Infiltration cellular, lymphocytic	1 (13%)			
Vagina	(8)			(8)
Infiltration cellular, lymphocytic	3 (38%)			
Hematopoietic System				
Bone marrow	(8)			(8)
Hyperplasia	1 (13%)			
Lymph node, mandibular	(8)			(8)
Hemorrhage				2 (25%)
Hyperplasia, lymphoid	3 (38%)			1 (13%)
Lymph node, mesenteric	(8)			(8)
Atrophy				4 (50%)
Hyperplasia, lymphoid				1 (13%)
Spleen	(8)			(8)
Hyperplasia, lymphoid	1 (13%)			
Infiltration cellular, lymphocytic				1 (13%)
Thymus	(7)			(8)
Atrophy, cortex	3 (43%)			
Cyst				1 (13%)
Hemorrhage				1 (13%)
Hyperplasia, lymphoid, medulla				6 (75%)
Musculoskeletal System				
Bone, femur	(8)			(8)
Fibrous osteodystrophy				2 (25%)
Nervous System				
Brain, cerebrum	(8)			(8)
Mineralization, multifocal, thalamus	1 (13%)			2 (25%)

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
12-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(8)			(8)
Infiltration cellular, lymphocytic	7 (88%)			7 (88%)
Inflammation				1 (13%)
Special Senses System				
Harderian gland	(8)			(8)
Infiltration cellular, lymphocytic	1 (13%)			
Lacrimal gland	(7)			(8)
Infiltration cellular, lymphocytic	3 (43%)			5 (63%)
Urinary System				
Kidney	(8)			(8)
Cyst, renal tubule				1 (13%)
Infiltration cellular, lymphocytic	7 (88%)			6 (75%)
Nephropathy	1 (13%)			
Urinary bladder	(8)			(8)
Infiltration cellular, lymphocytic	6 (75%)			6 (75%)
Systems Examined with No Lesions Observed				
General Body System				
Integumentary System				
2-Year Study				
Alimentary System				
Esophagus	(47)	(36)	(40)	(38)
Dilatation			1 (3%)	
Hyperkeratosis	1 (2%)			
Infiltration cellular, lymphocytic			1 (3%)	
Ulcer	1 (2%)			
Gallbladder	(46)	(37)	(36)	(36)
Infiltration cellular, lymphocytic	4 (9%)	2 (5%)	4 (11%)	6 (17%)
Inflammation			1 (3%)	
Intestine large, cecum	(42)	(37)	(37)	(32)
Hyperplasia, lymphoid	5 (12%)		2 (5%)	4 (13%)
Intestine large, colon	(46)	(37)	(37)	(34)
Hyperplasia, goblet cell				1 (3%)
Hyperplasia, lymphoid				1 (3%)
Intestine large, rectum	(44)	(37)	(37)	(32)
Erosion	2 (5%)			
Inflammation		1 (3%)		
Intestine small, duodenum	(40)	(37)	(37)	(33)
Hyperplasia, lymphoid			1 (3%)	
Infiltration cellular, lymphocytic				1 (3%)
Intestine small, ileum	(40)	(35)	(37)	(31)
Hyperplasia, lymphoid	2 (5%)	2 (6%)	3 (8%)	2 (6%)

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Alimentary System (continued)				
Intestine small, jejunum	(41)	(37)	(37)	(32)
Hyperplasia, goblet cell			1 (3%)	
Hyperplasia, lymphoid		2 (5%)	2 (5%)	
Liver	(48)	(40)	(40)	(40)
Apoptosis		1 (3%)		
Atrophy		1 (3%)		
Basophilic focus	1 (2%)		3 (8%)	2 (5%)
Clear cell focus				2 (5%)
Degeneration, centrilobular			1 (3%)	
Degeneration, cystic				1 (3%)
Degeneration, fatty				1 (3%)
Eosinophilic focus		1 (3%)	2 (5%)	3 (8%)
Hematopoietic cell proliferation	3 (6%)	3 (8%)	5 (13%)	1 (3%)
Hyperplasia, Kupffer cell				1 (3%)
Infiltration cellular, lymphocytic	33 (69%)	27 (68%)	29 (73%)	27 (68%)
Infiltration cellular, plasma cell		1 (3%)		
Inflammation	2 (4%)			
Leukocytosis		1 (3%)		
Mixed cell focus				1 (3%)
Necrosis	32 (67%)	24 (60%)	21 (53%)	20 (50%)
Necrosis, coagulative	1 (2%)		3 (8%)	1 (3%)
Tension lipoidosis	17 (35%)	10 (25%)	10 (25%)	8 (20%)
Vacuolization cytoplasmic	26 (54%)	29 (73%)	28 (70%)	24 (60%)
Mesentery	(1)	(1)	(2)	
Infiltration cellular, lymphocytic		1 (100%)		
Necrosis, fat			1 (50%)	
Pancreas	(48)	(40)	(39)	(37)
Atrophy	1 (2%)	1 (3%)	1 (3%)	
Ectasia, duct		1 (3%)		
Focal cellular change	2 (4%)	2 (5%)	2 (5%)	2 (5%)
Infiltration cellular, lymphocytic	26 (54%)	21 (53%)	16 (41%)	16 (43%)
Inflammation		1 (3%)		
Salivary glands	(48)	(40)	(40)	(39)
Atrophy			3 (8%)	3 (8%)
Hyperplasia, duct	1 (2%)			
Infiltration cellular, lymphocytic	38 (79%)	33 (83%)	35 (88%)	31 (79%)
Inflammation		1 (3%)		
Mineralization		1 (3%)		1 (3%)
Stomach, forestomach	(47)	(37)	(38)	(35)
Hyperkeratosis			1 (3%)	2 (6%)
Hyperplasia				1 (3%)
Ulcer				1 (3%)
Stomach, glandular	(47)	(37)	(38)	(36)
Crystals	1 (2%)			
Cyst	2 (4%)	1 (3%)	3 (8%)	2 (6%)
Degeneration, hyaline	1 (2%)			
Hyperplasia				1 (3%)
Inflammation			1 (3%)	
Tongue	(48)	(39)	(39)	(40)
Infiltration cellular, mast cell	2 (4%)	2 (5%)		
Polyarteritis	1 (2%)			

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Cardiovascular System				
Heart	(48)	(40)	(40)	(39)
Cardiomyopathy			1 (3%)	
Congestion				1 (3%)
Degeneration	1 (2%)			
Dilatation				1 (3%)
Hemorrhage, valve				1 (3%)
Infiltration cellular, lymphocytic		1 (3%)		
Inflammation	1 (2%)	1 (3%)	1 (3%)	
Polyarteritis	1 (2%)			
Thrombus	1 (2%)			
Endocrine System				
Adrenal gland	(46)	(40)	(37)	(37)
Accessory adrenal cortical nodule	1 (2%)			
Inflammation, extra adrenal tissue		1 (3%)		
Adrenal gland, cortex	(46)	(40)	(37)	(37)
Congestion				1 (3%)
Degeneration, fatty			1 (3%)	1 (3%)
Ectopic tissue	1 (2%)		1 (3%)	
Focal cellular change			2 (5%)	
Hyperplasia, spindle cell	43 (93%)	37 (93%)	34 (92%)	32 (86%)
Thrombus	1 (2%)			
Vacuolization cytoplasmic	2 (4%)	1 (3%)		1 (3%)
Adrenal gland, medulla	(46)	(40)	(37)	(37)
Congestion		1 (3%)		1 (3%)
Cytoplasmic alteration			1 (3%)	
Vacuolization cytoplasmic	1 (2%)	1 (3%)		
Islets, pancreatic	(48)	(40)	(37)	(38)
Hyperplasia				1 (3%)
Infiltration cellular, lymphocytic				1 (3%)
Parathyroid gland	(38)	(31)	(33)	(36)
Ectopic thymus	1 (3%)		1 (3%)	1 (3%)
Infiltration cellular, lymphocytic	1 (3%)			
Vacuolization cytoplasmic	1 (3%)			
Pituitary gland	(45)	(36)	(36)	(33)
Angiectasis		1 (3%)		
Cyst		1 (3%)		1 (3%)
Hyperplasia, pars distalis	4 (9%)	3 (8%)	1 (3%)	1 (3%)
Thyroid gland	(47)	(40)	(40)	(39)
Cyst, follicle		1 (3%)		3 (8%)
Degeneration	1 (2%)		1 (3%)	1 (3%)
Ectopic thymus				1 (3%)
Goiter adenomatous			1 (3%)	
Hyperplasia, follicular cell		1 (3%)	1 (3%)	1 (3%)
Hypertrophy, follicular cell				1 (3%)
Infiltration cellular, lymphocytic	4 (9%)	2 (5%)	2 (5%)	2 (5%)
Inflammation		1 (3%)		
Ultimobranchial cyst	11 (23%)	9 (23%)	8 (20%)	7 (18%)

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
General Body System				
None				
Genital System				
Clitoral gland	(43)	(37)	(33)	(33)
Atrophy	40 (93%)	35 (95%)	29 (88%)	31 (94%)
Infiltration cellular, lymphocytic				1 (3%)
Inflammation		1 (3%)	2 (6%)	
Ovary	(48)	(40)	(39)	(38)
Angiectasis				1 (3%)
Atrophy	39 (81%)	33 (83%)	34 (87%)	32 (84%)
Congestion	1 (2%)			
Cyst	10 (21%)	6 (15%)	6 (15%)	9 (24%)
Cyst, periovarian tissue	16 (33%)	12 (30%)	6 (15%)	8 (21%)
Hematocyst	7 (15%)	2 (5%)	5 (13%)	4 (11%)
Hyperplasia, adenomatous	2 (4%)	3 (8%)		
Infiltration cellular, lymphocytic	5 (10%)	3 (8%)	1 (3%)	1 (3%)
Mineralization				1 (3%)
Ovotestis			1 (3%)	
Uterus	(48)	(40)	(40)	(39)
Angiectasis	1 (2%)			
Atrophy	2 (4%)	2 (5%)	2 (5%)	1 (3%)
Dilatation	2 (4%)	1 (3%)	3 (8%)	1 (3%)
Ectasia, vein				1 (3%)
Fibrosis	1 (2%)	1 (3%)	1 (3%)	
Hyperplasia, cystic, endometrium	37 (77%)	32 (80%)	26 (65%)	29 (74%)
Infiltration cellular, lymphocytic				1 (3%)
Inflammation				1 (3%)
Prolapse	1 (2%)			
Thrombus		1 (3%)		
Vagina	(48)	(38)	(40)	(37)
Atrophy	2 (4%)	2 (5%)	2 (5%)	
Dysplasia	1 (2%)	1 (3%)		
Infiltration cellular, lymphocytic	3 (6%)	2 (5%)		
Inflammation		2 (5%)		
Metaplasia				1 (3%)
Hematopoietic System				
Bone marrow	(47)	(39)	(40)	(38)
Depletion			1 (3%)	
Hyperplasia	3 (6%)	6 (15%)	4 (10%)	3 (8%)
Hypoplasia		1 (3%)		
Pigmentation		1 (3%)	1 (3%)	
Lymph node	(48)	(40)	(40)	(40)
Hyperplasia, plasma cell			1 (3%)	
Hyperplasia, plasma cell, mediastinal		1 (3%)		
Inflammation			1 (3%)	

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node, mandibular	(47)	(40)	(39)	(39)
Atrophy		1 (3%)	1 (3%)	
Hematopoietic cell proliferation		1 (3%)		
Hemorrhage	3 (6%)	1 (3%)	1 (3%)	
Hyperplasia, lymphoid	7 (15%)	5 (13%)	10 (26%)	4 (10%)
Hyperplasia, plasma cell		1 (3%)		
Inflammation		1 (3%)		
Lymph node, mesenteric	(46)	(40)	(38)	(39)
Angiectasis			1 (3%)	
Atrophy	2 (4%)	2 (5%)		1 (3%)
Congestion, sinus				1 (3%)
Fibrosis		1 (3%)		
Hemorrhage	4 (9%)	1 (3%)	1 (3%)	1 (3%)
Hyperplasia, lymphoid	2 (4%)	2 (5%)	4 (11%)	4 (10%)
Hyperplasia, plasma cell		1 (3%)	1 (3%)	
Hyperplasia, reticulum cell			1 (3%)	
Inflammation			1 (3%)	
Spleen	(47)	(40)	(39)	(39)
Amyloid deposition			1 (3%)	
Atrophy	2 (4%)	2 (5%)		1 (3%)
Congestion				3 (8%)
Erythrophagocytosis				1 (3%)
Hematopoietic cell proliferation	4 (9%)	4 (10%)	7 (18%)	4 (10%)
Hyperplasia, lymphoid	13 (28%)	10 (25%)	11 (28%)	12 (31%)
Hyperplasia, plasma cell, red pulp		1 (3%)		
Thymus	(41)	(33)	(31)	(30)
Atrophy, cortex	30 (73%)	24 (73%)	20 (65%)	25 (83%)
Congestion	1 (2%)			1 (3%)
Cyst			1 (3%)	
Ectopic parathyroid gland	1 (2%)		1 (3%)	1 (3%)
Hyperplasia, lymphoid, medulla	14 (34%)	13 (39%)	12 (39%)	6 (20%)
Integumentary System				
Mammary gland	(44)	(36)	(38)	(36)
Galactocele		1 (3%)		
Hyperplasia	1 (2%)		1 (3%)	3 (8%)
Infiltration cellular, lymphocytic			1 (3%)	
Inflammation	1 (2%)			
Lactation	4 (9%)	1 (3%)	1 (3%)	
Metaplasia, squamous			1 (3%)	
Skin	(45)	(39)	(39)	(38)
Alopecia				1 (3%)
Infiltration cellular, lymphocytic		1 (3%)	1 (3%)	

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Musculoskeletal System				
Bone, femur	(47)	(40)	(40)	(40)
Degeneration, cartilage				1 (3%)
Fibrous osteodystrophy	18 (38%)	9 (23%)	5 (13%)	9 (23%)
Bone, sternum	(47)	(40)	(40)	(40)
Fibrous osteodystrophy, multifocal	36 (77%)	28 (70%)	25 (63%)	29 (73%)
Skeletal muscle	(48)	(39)	(40)	(39)
Infiltration cellular, lymphocytic	2 (4%)	2 (5%)		1 (3%)
Polyarteritis	1 (2%)			
Nervous System				
Brain, cerebellum	(48)	(40)	(40)	(40)
Degeneration	1 (2%)			
Thrombus	1 (2%)			
Brain, cerebrum	(48)	(40)	(40)	(40)
Degeneration	1 (2%)			
Infiltration cellular, lymphocytic		2 (5%)		
Mineralization, multifocal, thalamus	28 (58%)	21 (53%)	23 (58%)	24 (60%)
Thrombus	1 (2%)			
Peripheral nerve	(48)	(38)	(39)	(38)
Infiltration cellular, lymphocytic		1 (3%)		
Inflammation			1 (3%)	
Spinal cord, thoracic	(48)	(40)	(40)	(39)
Degeneration	1 (2%)			
Infiltration cellular, lymphocytic		1 (3%)		
Thrombus	1 (2%)			
Respiratory System				
Larynx	(44)	(40)	(34)	(34)
Concretion				1 (3%)
Crystals				1 (3%)
Infiltration cellular, lymphocytic	1 (2%)			
Lung	(48)	(40)	(40)	(40)
Congestion		1 (3%)		1 (3%)
Foreign body	1 (2%)			
Giant cell				1 (3%)
Hemorrhage	2 (4%)	1 (3%)	1 (3%)	2 (5%)
Hyperplasia, alveolar epithelium		2 (5%)	1 (3%)	2 (5%)
Infiltration cellular, histiocytic		1 (3%)	2 (5%)	2 (5%)
Infiltration cellular, lymphocytic	37 (77%)	30 (75%)	29 (73%)	27 (68%)
Inflammation	4 (8%)	4 (10%)	2 (5%)	3 (8%)
Thrombus	1 (2%)			
Thrombus, capillary				1 (3%)
Nose	(47)	(40)	(40)	(40)
Cyst, nasolacrimal duct	1 (2%)			
Dilatation, glands			1 (3%)	
Inflammation	1 (2%)			

TABLE B3
Summary of the Incidence of Nonneoplastic Lesions in Regimen B 100 mg/kg Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	3 Months (Stop-Exposure)	6 Months (Stop-Exposure)	12 Months (Stop-Exposure)
2-Year Study (continued)				
Respiratory System (continued)				
Trachea	(47)	(40)	(39)	(39)
Cyst				1 (3%)
Foreign body				1 (3%)
Infiltration cellular, lymphocytic			1 (3%)	
Inflammation	1 (2%)			
Special Senses System				
Eye	(41)	(38)	(34)	(35)
Degeneration, retina	1 (2%)			
Inflammation		1 (3%)		
Thrombus	1 (2%)			
Harderian gland	(48)	(38)	(38)	(38)
Atrophy		1 (3%)		
Hyperplasia		2 (5%)		
Infiltration cellular, lymphocytic	18 (38%)	13 (34%)	16 (42%)	8 (21%)
Inflammation				1 (3%)
Thrombus	1 (2%)			
Lacrimal gland	(41)	(33)	(33)	(32)
Apoptosis		1 (3%)		
Atrophy	1 (2%)	1 (3%)		2 (6%)
Cytomegaly				1 (3%)
Ectasia, duct				1 (3%)
Infiltration cellular, lymphocytic	25 (61%)	21 (64%)	17 (52%)	13 (41%)
Necrosis		1 (3%)		
Zymbal's gland	(43)	(38)	(36)	(36)
Infiltration cellular, lymphocytic			1 (3%)	
Inflammation	1 (2%)			
Urinary System				
Kidney	(48)	(40)	(39)	(38)
Amyloid deposition, glomerulus	2 (4%)	1 (3%)	1 (3%)	2 (5%)
Congestion	1 (2%)			
Cyst, renal tubule	14 (29%)	9 (23%)	9 (23%)	8 (21%)
Glomerulosclerosis				1 (3%)
Hydronephrosis				1 (3%)
Hydronephrosis, bilateral	1 (2%)			
Infarct		1 (3%)		
Infiltration cellular, lymphocytic	39 (81%)	31 (78%)	31 (79%)	32 (84%)
Infiltration cellular, plasma cell		1 (3%)		
Inflammation	1 (2%)			
Inflammation, adventitia		1 (3%)		
Necrosis, coagulative			1 (3%)	
Nephropathy	3 (6%)		2 (5%)	4 (11%)
Pigmentation, renal tubule				1 (3%)
Polyarteritis	1 (2%)			
Urinary bladder	(47)	(37)	(39)	(36)
Infiltration cellular, lymphocytic	38 (81%)	31 (84%)	33 (85%)	28 (78%)
Polyarteritis	1 (2%)			