

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	— ^f	757 (T)
Poly-3 test	P=0.4175	P=0.2089	P=0.2078	—	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
<i>3-Month interim evaluation</i>	8	8		
<i>6-Month interim evaluation</i>	8		8	
<i>12-Month interim evaluation</i>	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%)			