

APPENDIX C
SUMMARY OF LESIONS IN REGIMEN C
FEMALE MICE IN THE 2-YEAR GAVAGE STUDY
OF CHLORAL HYDRATE
(Single Dose on Postnatal Day 28)

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TABLE C1

Summary of the Incidence of Neoplasms in Regimen C Female 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	3	4		2
Natural deaths	3	4	3	6
Survivors				
Terminal sacrifice	42	40	45	40
Animals examined microscopically	48	48	48	48
Alimentary System				
Esophagus	(45)	(7)	(2)	(46)
Lymphoma malignant		1 (14%)		
Gallbladder	(43)	(8)	(3)	(44)
Lymphoma malignant		2 (25%)	1 (33%)	
Intestine large, cecum	(46)	(6)	(1)	(43)
Lymphoma malignant	2 (4%)			1 (2%)
Intestine small, duodenum	(45)	(7)	(1)	(41)
Lymphoma malignant	1 (2%)	1 (14%)		1 (2%)
Intestine small, ileum	(42)	(6)	(1)	(43)
Lymphoma malignant	1 (2%)			2 (5%)
Intestine small, jejunum	(44)	(7)	(2)	(44)
Lymphoma malignant		1 (14%)	1 (50%)	
Liver	(48)	(48)	(48)	(48)
Hemangiosarcoma			1 (2%)	
Hepatocellular adenoma	3 (6%)	3 (6%)	1 (2%)	2 (4%)
Hepatocellular adenoma, multiple			1 (2%)	
Hepatocellular carcinoma	3 (6%)			
Histiocytic sarcoma	1 (2%)	1 (2%)		
Lymphoma malignant	5 (10%)	10 (21%)	4 (8%)	9 (19%)
Mesentery	(2)	(4)	(1)	
Hemangiosarcoma			1 (100%)	
Sarcoma		1 (25%)		
Pancreas	(46)	(8)	(2)	(46)
Lymphoma malignant	2 (4%)	2 (25%)	1 (50%)	2 (4%)
Salivary glands	(48)	(9)	(3)	(48)
Lymphoma malignant	1 (2%)	3 (33%)		2 (4%)
Stomach, forestomach	(47)	(7)	(2)	(44)
Lymphoma malignant		2 (29%)		
Squamous cell carcinoma	1 (2%)			
Stomach, glandular	(47)	(7)	(2)	(44)
Lymphoma malignant		2 (29%)	1 (50%)	
Cardiovascular System				
Heart	(48)	(8)	(3)	(48)
Lymphoma malignant		1 (13%)		
Endocrine System				
Adrenal gland	(46)	(9)	(2)	(46)
Fibrosarcoma, metastatic, skin		1 (11%)		
Adrenal gland, cortex	(46)	(8)	(2)	(46)
Histiocytic sarcoma		1 (13%)		
Lymphoma malignant	1 (2%)	3 (38%)		2 (4%)

TABLE C1

Summary of the Incidence of Neoplasms in Regimen C Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Endocrine System (continued)				
Islets, pancreatic	(46)	(7)	(3)	(45)
Adenoma			1 (33%)	
Lymphoma malignant		1 (14%)	1 (33%)	
Pituitary gland	(40)	(4)	(42)	
Adenoma, pars distalis	1 (3%)			1 (2%)
Thyroid gland	(48)	(8)	(2)	(48)
Lymphoma malignant		1 (13%)		
General Body System				
None				
Genital System				
Clitoral gland	(38)	(8)	(1)	(37)
Lymphoma malignant		1 (13%)		
Ovary	(47)	(28)	(28)	(45)
Cystadenoma		1 (4%)		1 (2%)
Granulosa cell tumor benign				1 (2%)
Hemangiosarcoma, periovarian tissue				1 (2%)
Histiocytic sarcoma	1 (2%)			
Luteoma				1 (2%)
Lymphoma malignant		2 (7%)	1 (4%)	1 (2%)
Lymphoma malignant, periovarian tissue	1 (2%)			
Sarcoma		1 (4%)		
Yolk sac carcinoma				1 (2%)
Uterus	(48)	(29)	(28)	(47)
Fibrosarcoma			1 (4%)	
Histiocytic sarcoma	1 (2%)			
Leiomyoma		1 (3%)		
Lymphoma malignant		1 (3%)		
Polyp	1 (2%)			
Vagina	(47)	(8)	(1)	(46)
Fibrosarcoma				1 (2%)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant		3 (38%)		
Hematopoietic System				
Bone marrow	(48)	(8)	(1)	(46)
Lymphoma malignant	3 (6%)	3 (38%)	1 (100%)	2 (4%)
Lymph node	(48)	(15)	(6)	(48)
Fibrosarcoma, metastatic, renal, uterus			1 (17%)	
Lymphoma malignant	1 (2%)			1 (2%)
Lymphoma malignant, axillary		1 (7%)		
Lymphoma malignant, inguinal		2 (13%)	1 (17%)	
Lymphoma malignant, lumbar	1 (2%)		1 (17%)	
Lymphoma malignant, mediastinal		1 (7%)		
Lymphoma malignant, renal		2 (13%)	1 (17%)	2 (4%)
Lymphoma malignant, thoracic				1 (2%)
Lymph node, mandibular	(48)	(9)	(4)	(47)
Lymphoma malignant	2 (4%)	4 (44%)	2 (50%)	7 (15%)
Lymph node, mesenteric	(47)	(11)	(4)	(43)
Lymphoma malignant	4 (9%)	6 (55%)	3 (75%)	6 (14%)
Sarcoma		1 (9%)		

TABLE C1

Summary of the Incidence of Neoplasms in Regimen C Female 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	(47)	(20)	(15)	(46)
Hemangiosarcoma		1 (5%)	2 (13%)	1 (2%)
Lymphoma malignant	7 (15%)	13 (65%)	5 (33%)	14 (30%)
Thymus	(38)	(6)	(4)	(37)
Lymphoma malignant	2 (5%)	2 (33%)	3 (75%)	2 (5%)
Sarcoma, metastatic, skin		1 (17%)		
Integumentary System				
Mammary gland	(46)	(6)	(2)	(47)
Adenocarcinoma		1 (17%)		1 (2%)
Adenoma				1 (2%)
Fibrous histiocytoma		1 (17%)		
Lymphoma malignant		1 (17%)		
Skin	(48)	(8)	(6)	(48)
Fibrosarcoma	1 (2%)	1 (13%)	1 (17%)	1 (2%)
Hemangiosarcoma			2 (33%)	
Hemangiosarcoma, metastatic, uncertain primary site		1 (13%)		
Lymphoma malignant		1 (13%)		
Sarcoma		1 (13%)		
Musculoskeletal System				
Bone, femur	(48)	(8)	(2)	(47)
Lymphoma malignant		1 (13%)		
Bone, sternum	(48)	(8)	(3)	(47)
Lymphoma malignant		1 (13%)		
Skeletal muscle	(48)	(8)	(3)	(48)
Fibrosarcoma				1 (2%)
Lymphoma malignant	1 (2%)	2 (25%)		
Nervous System				
Brain, cerebellum	(48)	(8)	(3)	(48)
Lymphoma malignant		1 (13%)		
Brain, cerebrum	(48)	(8)	(3)	(48)
Lymphoma malignant		2 (25%)		
Peripheral nerve	(48)	(8)	(3)	(48)
Lymphoma malignant		1 (13%)		
Spinal cord, thoracic	(48)	(8)	(3)	(48)
Lymphoma malignant		1 (13%)		
Respiratory System				
Lung	(48)	(8)	(4)	(48)
Alveolar/bronchiolar adenoma	3 (6%)			5 (10%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)			
Alveolar/bronchiolar carcinoma			1 (25%)	
Carcinoma, metastatic, harderian gland	1 (2%)			
Fibrous histiocytoma		1 (13%)		
Hemangiosarcoma				1 (2%)
Lymphoma malignant	3 (6%)	4 (50%)	1 (25%)	4 (8%)
Sarcoma, metastatic, skin		1 (13%)		
Yolk sac carcinoma, metastatic, ovary				1 (2%)

TABLE C1

Summary of the Incidence of Neoplasms in Regimen C Female 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)	(8)	(3)	(47)
Carcinoma, metastatic, harderian gland	1 (2%)			
Lymphoma malignant		1 (13%)		
Trachea	(48)	(8)	(2)	(48)
Lymphoma malignant		1 (13%)		
Special Senses System				
Harderian gland	(48)	(10)	(5)	(47)
Adenoma	1 (2%)	2 (20%)	1 (20%)	1 (2%)
Carcinoma	1 (2%)			
Lymphoma malignant	1 (2%)	2 (20%)		
Lacrimal gland	(41)	(5)	(2)	(43)
Lymphoma malignant	1 (2%)	1 (20%)		1 (2%)
Zymbal's gland	(48)	(6)	(1)	(45)
Lymphoma malignant		1 (17%)		
Urinary System				
Kidney	(48)	(9)	(3)	(48)
Lymphoma malignant	2 (4%)	5 (56%)	1 (33%)	2 (4%)
Ureter	(1)			
Lymphoma malignant		1 (100%)		
Urinary bladder	(47)	(8)	(2)	(45)
Histiocytic sarcoma	1 (2%)			
Lymphoma malignant	1 (2%)	3 (38%)	1	(2%)
Neoplasm Summary				
Total animals with primary neoplasms ^b	23	25	14	28
Total primary neoplasms	64	119	42	83
Total animals with benign neoplasms	9	7	4	12
Total benign neoplasms	10	7	4	13
Total animals with malignant neoplasms	15	22	12	21
Total malignant neoplasms	54	112	38	70
Total animals with metastatic neoplasms	1	3	1	1
Total metastatic neoplasms	2	4	1	

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 C2
Statistical Analysis of Primary Neoplasms at 2 Years in Regimen C Female Mice
in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Liver: Hepatocellular Adenoma				
Overall rate ^a	3/48 (6%)	3/48 (6%)	2/48 (4%)	2/48 (4%)
Adjusted rate ^b	6.5%	6.5%	4.2%	4.5%
Terminal rate ^c	3/42 (7%)	3/40 (8%)	2/45 (4%)	2/40 (5%)
First incidence (days)	757 (T)	757 (T)	757 (T)	757 (T)
Poly-3 test ^d	P=0.3727N	P=0.6619N	P=0.4849N	P=0.5115N
Liver: Hepatocellular Carcinoma				
Overall rate	3/48 (6%)	0/48 (0%)	0/48 (0%)	0/48 (0%)
Adjusted rate	6.5%	0.0%	0.0%	0.0%
Terminal rate	2/42 (5%)	0/40 (0%)	0/45 (0%)	0/40 (0%)
First incidence (days)	682	— ^e	—	—
Poly-3 test	P=0.0528N	P=0.1197N	P=0.1140N	P=0.1244N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	6/48 (13%)	3/48 (6%)	2/48 (4%)	2/48 (4%)
Adjusted rate	13.0%	6.5%	4.2%	4.5%
Terminal rate	5/42 (12%)	3/40 (8%)	2/45 (4%)	2/40 (5%)
First incidence (days)	682	757 (T)	757 (T)	757 (T)
Poly-3 test	P=0.1037N	P=0.2447N	P=0.1246N	P=0.1432N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	4/48 (8%)	0/8 (0%)	0/4 (0%)	5/48 (10%)
Adjusted rate	8.7%	0.0%	0.0%	11.1%
Terminal rate	4/42 (10%)	0/0	0/1 (0%)	4/40 (10%)
First incidence (days)	757 (T)	—	—	707
Poly-3 test	(NA)	— ^f	—	P=0.4867
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	4/48 (8%)	0/8 (0%)	1/4 (25%)	5/48 (10%)
Adjusted rate	8.7%	0.0%	29.6%	11.1%
Terminal rate	4/42 (10%)	0/0	1/1 (100%)	4/40 (10%)
First incidence (days)	757 (T)	—	757 (T)	707
Poly-3 test	(NA)	—	—	P=0.4867
All Organs: Hemangiosarcoma				
Overall rate	0/48 (0%)	1/48 (2%)	3/48 (6%)	2/48 (4%)
Adjusted rate	0.0%	2.2%	6.3%	4.5%
Terminal rate	0/42 (0%)	0/40 (0%)	2/45 (4%)	1/40 (3%)
First incidence (days)	—	738	653	741
Poly-3 test	P=0.1518	P=0.5004	P=0.1264	P=0.2319
All Organs: Malignant Lymphoma				
Overall rate	8/48 (17%)	16/48 (33%)	6/48 (13%)	16/48 (33%)
Adjusted rate	17.2%	34.1%	12.6%	35.1%
Terminal rate	6/42 (14%)	12/40 (30%)	5/45 (11%)	13/40 (33%)
First incidence (days)	562	604	718	543
Poly-3 test	P=0.1250	P=0.0488	P=0.3714N	P=0.0404

TABLE C2

**Statistical Analysis of Primary Neoplasms at 2 Years in Regimen C Female Mice
in the 2-Year Gavage Study of Chloral Hydrate**

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
All Organs: Benign Neoplasms				
Overall rate	9/48 (19%)	7/48 (15%)	4/48 (8%)	<u>13</u> /48 (27%)
Adjusted rate	19.6%	15.3%	8.4%	28.4%
Terminal rate	9/42 (21%)	7/40 (18%)	4/45 (9%)	11/40 (28%)
First incidence (days)	757 (T)	757 (T)	757 (T)	349
Poly-3 test	P=0.1399	P=0.3917N	P=0.1029N	P=0.2308
All Organs: Malignant Neoplasms				
Overall rate	15/48 (31%)	22/48 (46%)	12/48 (25%)	21/48 (44%)
Adjusted rate	31.5%	45.8%	25.1%	45.6%
Terminal rate	10/42 (24%)	14/40 (35%)	10/45 (22%)	16/40 (40%)
First incidence (days)	562	583	653	543
Poly-3 test	P=0.2432	P=0.1087	P=0.3209N	P=0.1151
All Organs: Benign or Malignant Neoplasms				
Overall rate	23/48 (48%)	25/48 (52%)	14/48 (29%)	28/48 (58%)
Adjusted rate	48.3%	52.1%	29.2%	59.7%
Terminal rate	18/42 (43%)	17/40 (43%)	12/45 (27%)	22/40 (55%)
First incidence (days)	562	583	653	349
Poly-3 test	P=0.2537	P=0.4331	P=0.0432N	P=0.1817

(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 C3
Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female 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	3	4		2
Natural deaths	3	4	3	6
Survivors				
Terminal sacrifice	42	40	45	40
Animals examined microscopically	48	48	48	48
Alimentary System				
Esophagus	(45)	(7)	(2)	(46)
Hyperkeratosis		1 (14%)		1 (2%)
Gallbladder	(43)	(8)	(3)	(44)
Accumulation hyaline droplet				1 (2%)
Infiltration cellular, lymphocytic	3 (7%)			2 (5%)
Intestine large, cecum	(46)	(6)	(1)	(43)
Hyperplasia, lymphoid	6 (13%)	1 (17%)		1 (2%)
Intestine large, colon	(46)	(7)	(2)	(43)
Hyperplasia, goblet cell	1 (2%)			1 (2%)
Intestine large, rectum	(46)	(7)	(2)	(43)
Fibrosis	1 (2%)			
Intestine small, ileum	(42)	(6)	(1)	(43)
Atrophy	1 (2%)			
Hyperplasia, lymphoid		1 (17%)		4 (9%)
Intestine small, jejunum	(44)	(7)	(2)	(44)
Hyperplasia, lymphoid	1 (2%)	1 (14%)		
Liver	(48)	(48)	(48)	(48)
Angiectasis			1 (2%)	
Basophilic focus	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Cyst, bile duct		1 (2%)		
Degeneration		1 (2%)	1 (2%)	1 (2%)
Degeneration, fatty		1 (2%)		
Eosinophilic focus		2 (4%)	1 (2%)	
Hematopoietic cell proliferation	5 (10%)	13 (27%)	13 (27%)	11 (23%)
Hyperplasia, Kupffer cell		2 (4%)		1 (2%)
Hyperplasia, oval cell			1 (2%)	
Infiltration cellular, lymphocytic	42 (88%)	35 (73%)	36 (75%)	33 (69%)
Infiltration cellular, plasma cell		1 (2%)	1 (2%)	
Inflammation	1 (2%)			1 (2%)
Necrosis	27 (56%)	33 (69%)	40 (83%)	34 (71%)
Necrosis, coagulative	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Regeneration		1 (2%)	1 (2%)	
Tension lipoidosis	19 (40%)	14 (29%)	20 (42%)	16 (33%)
Thrombus			1 (2%)	1 (2%)
Vacuolization cytoplasmic	31 (65%)	36 (75%)	42 (88%)	34 (71%)
Mesentery	(2)	(4)	(1)	
Necrosis, fat	2 (100%)	3 (75%)		

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

TABLE C3
Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female 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	(46)	(8)	(2)	(46)
Accumulation hyaline droplet, duct				1 (2%)
Atrophy	2 (4%)			
Cyst, duct		1 (13%)		
Degeneration	1 (2%)			1 (2%)
Focal cellular change				2 (4%)
Infiltration cellular, lymphocytic	24 (52%)	5 (63%)	1 (50%)	21 (46%)
Inflammation	1 (2%)			
Necrosis				1 (2%)
Salivary glands	(48)	(9)	(3)	(48)
Atrophy				2 (4%)
Infiltration cellular, lymphocytic	41 (85%)	5 (56%)	3 (100%)	41 (85%)
Stomach, forestomach	(47)	(7)	(2)	(44)
Hyperkeratosis	1 (2%)		1 (50%)	1 (2%)
Infiltration cellular, lymphocytic				1 (2%)
Inflammation				2 (5%)
Stomach, glandular	(47)	(7)	(2)	(44)
Cyst	5 (11%)	1 (14%)		
Hyperplasia	2 (4%)			
Infiltration cellular, lymphocytic				1 (2%)
Inflammation				1 (2%)
Mineralization	1 (2%)			2 (5%)
Tongue	(48)	(8)	(3)	(48)
Infiltration cellular, mast cell	1 (2%)			
Mineralization		1 (13%)		
Polyarteritis				1 (2%)
Cardiovascular System				
Heart	(48)	(8)	(3)	(48)
Cardiomyopathy	1 (2%)			
Degeneration, valve				4 (8%)
Hyperplasia, epicardium		1 (13%)		
Infiltration cellular, lymphocytic	1 (2%)			1 (2%)
Necrosis			1 (33%)	1 (2%)
Polyarteritis				1 (2%)
Thrombus	1 (2%)			
Endocrine System				
Adrenal gland	(46)	(9)	(2)	(46)
Accessory adrenal cortical nodule	1 (2%)			
Adrenal gland, cortex	(46)	(8)	(2)	(46)
Hematopoietic cell proliferation	1 (2%)			
Hyperplasia				1 (2%)
Hyperplasia, spindle cell	44 (96%)	4 (50%)	1 (50%)	38 (83%)
Infiltration cellular, lymphocytic	1 (2%)			
Vacuolization cytoplasmic	1 (2%)			2 (4%)
Adrenal gland, medulla	(46)	(8)	(2)	(44)
Inflammation	1 (2%)			
Vacuolization cytoplasmic	1 (2%)			

TABLE C3

Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Endocrine System (continued)				
Islets, pancreatic	(46)	(7)	(3)	(45)
Hyperplasia				2 (4%)
Parathyroid gland	(38)	(7)		(44)
Cyst	1 (3%)			
Ectopic thymus	2 (5%)			1 (2%)
Infiltration cellular, lymphocytic	1 (3%)			1 (2%)
Pituitary gland	(40)	(4)		(42)
Angiectasis				1 (2%)
Cytomegaly	1 (3%)			
Degeneration, cystic, pars distalis	1 (3%)			
Hyperplasia, pars distalis	3 (8%)			8 (19%)
Hypertrophy, pars distalis	2 (5%)			
Polyarteritis				1 (2%)
Thyroid gland	(48)	(8)	(2)	(48)
Cyst, follicle	1 (2%)			
Degeneration				1 (2%)
Ectopic thymus	1 (2%)			
Hyperplasia, follicular cell	1 (2%)			
Infiltration cellular, lymphocytic	2 (4%)			2 (4%)
Inflammation	1 (2%)			
Polyarteritis				1 (2%)
Ultimobranchial cyst	19 (40%)	2 (13%)		20 (42%)
General Body System				
None				
Genital System				
Clitoral gland	(38)	(8)	(1)	(37)
Atrophy	37 (97%)	8 (100%)	1 (100%)	29 (78%)
Infiltration cellular, lymphocytic	1 (3%)			
Inflammation	1 (3%)			
Ovary	(47)	(28)	(28)	(45)
Angiectasis	1 (2%)			1 (2%)
Atrophy	37 (79%)	6 (21%)	1 (4%)	33 (73%)
Congestion	1 (2%)			
Cyst	9 (19%)	11 (39%)	17 (61%)	13 (29%)
Cyst, periovarian tissue	10 (21%)	9 (32%)	7 (25%)	3 (7%)
Hematocyst	4 (9%)		1 (4%)	3 (7%)
Infiltration cellular, lymphocytic	2 (4%)			
Mineralization				1 (2%)
Uterus	(48)	(29)	(28)	(47)
Angiectasis	1 (2%)			
Atrophy	2 (4%)	5 (17%)	2 (7%)	4 (9%)
Dilatation	4 (8%)	2 (7%)	8 (29%)	3 (6%)
Fibrosis				2 (4%)
Hemorrhage				1 (2%)
Hyperplasia, cystic, endometrium	40 (83%)	19 (66%)	17 (61%)	38 (81%)
Inflammation	1 (2%)		1 (4%)	1 (2%)
Vagina	(47)	(8)	(1)	(46)
Atrophy	2 (4%)	5 (63%)	1 (100%)	2 (4%)
Infiltration cellular, lymphocytic	1 (2%)			2 (4%)
Polyarteritis				1 (2%)

TABLE C3

Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Hematopoietic System				
Bone marrow	(48)	(8)	(1)	(46)
Depletion		1 (13%)		
Hyperplasia	3 (6%)	1 (13%)		2 (4%)
Infarct				1 (2%)
Myelofibrosis	1 (2%)	1 (13%)		
Lymph node	(48)	(15)	(6)	(48)
Hyperplasia, lymphoid, bronchial	1 (2%)			
Hyperplasia, lymphoid, inguinal		1 (7%)		
Lymph node, mandibular	(48)	(9)	(4)	(47)
Hematopoietic cell proliferation		1 (11%)		
Hemorrhage	1 (2%)			
Hyperplasia				1 (2%)
Hyperplasia, lymphoid	8 (17%)			3 (6%)
Lymph node, mesenteric	(47)	(11)	(4)	(43)
Atrophy	1 (2%)	2 (18%)		1 (2%)
Hematopoietic cell proliferation	1 (2%)	1 (9%)		
Hemorrhage	2 (4%)	1 (9%)		1 (2%)
Hyperplasia, lymphoid	2 (4%)			1 (2%)
Hyperplasia, reticulum cell	1 (2%)			
Infiltration cellular, lymphocytic	1 (2%)			
Spleen	(47)	(20)	(15)	(46)
Atrophy	1 (2%)	2 (10%)	1 (7%)	1 (2%)
Congestion	3 (6%)	2 (10%)	1 (7%)	
Hematopoietic cell proliferation	4 (9%)	4 (20%)	2 (13%)	9 (20%)
Hyperplasia, lymphoid	21 (45%)	2 (10%)	4 (27%)	12 (26%)
Infarct				1 (2%)
Infiltration cellular, lymphocytic	1 (2%)			
Thymus	(38)	(6)	(4)	(37)
Atrophy, cortex	27 (71%)	1 (17%)	1 (25%)	15 (41%)
Congestion				1 (3%)
Cyst	1 (3%)			
Ectopic parathyroid gland	1 (3%)			
Hyperplasia, lymphoid, medulla	16 (42%)			22 (59%)
Integumentary System				
Mammary gland	(46)	(6)	(2)	(47)
Hyperplasia	1 (2%)	1 (17%)		1 (2%)
Infiltration cellular, lymphocytic	1 (2%)			
Lactation	1 (2%)			5 (11%)
Skin	(48)	(8)	(6)	(48)
Infiltration cellular, lymphocytic	1 (2%)			
Musculoskeletal System				
Bone	(48)	(8)	(3)	(47)
Fibrous osteodystrophy, turbinate				10 (21%)
Bone, femur	(48)	(8)	(2)	(47)
Fibrous osteodystrophy	13 (27%)			9 (19%)
Bone, sternum	(48)	(8)	(3)	(47)
Fibrous osteodystrophy, multifocal	36 (75%)	2 (25%)	1 (33%)	33 (70%)
Skeletal muscle	(48)	(8)	(3)	(48)
Infiltration cellular, lymphocytic	2 (4%)			2 (4%)

TABLE C3

Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Nervous System				
Brain, cerebellum	(48)	(8)	(3)	(48)
Mineralization, thalamus	1 (2%)			
Brain, cerebrum	(48)	(8)	(3)	(48)
Developmental malformation	1 (2%)			
Gliosis	1 (2%)			
Infiltration cellular, lymphocytic				2 (4%)
Mineralization, multifocal, thalamus	31 (65%)	4 (50%)		24 (50%)
Necrosis	1 (2%)			
Spinal cord, thoracic	(48)	(8)	(3)	(48)
Infiltration cellular, lymphocytic	1 (2%)			1 (2%)
Respiratory System				
Larynx	(44)	(4)	(2)	(42)
Infiltration cellular, lymphocytic	1 (2%)			
Lung	(48)	(8)	(4)	(48)
Congestion	1 (2%)			1 (2%)
Hyperplasia, alveolar epithelium	2 (4%)			1 (2%)
Infiltration cellular, histiocytic	2 (4%)			2 (4%)
Infiltration cellular, lymphocytic	40 (83%)	2 (25%)	2 (50%)	38 (79%)
Inflammation				1 (2%)
Nose	(48)	(8)	(3)	(47)
Focal cellular change				1 (2%)
Special Senses System				
Eye	(45)	(5)		(46)
Inflammation, cornea				1 (2%)
Harderian gland	(48)	(10)	(5)	(47)
Hyperplasia		1 (10%)	1 (20%)	1 (2%)
Infiltration cellular, lymphocytic	14 (29%)	2 (20%)	2 (40%)	16 (34%)
Lacrimal gland	(41)	(5)	(2)	(43)
Atrophy	1 (2%)			
Infiltration cellular, lymphocytic	25 (61%)	3 (60%)		26 (60%)
Zymbal's gland	(48)	(6)	(1)	(45)
Atrophy	1 (2%)			
Hyperplasia, squamous	1 (2%)			
Inflammation				1 (2%)
Urinary System				
Kidney	(48)	(9)	(3)	(48)
Accumulation hyaline droplet		1 (11%)		1 (2%)
Amyloid deposition, glomerulus	2 (4%)			
Cyst, renal tubule	10 (21%)	1 (11%)		2 (4%)
Glomerulosclerosis	2 (4%)	2 (22%)		1 (2%)
Hydronephrosis	2 (4%)			1 (2%)
Hyperplasia, renal tubule	1 (2%)			

TABLE C3

Summary of the Incidence of Nonneoplastic Lesions in Regimen C Female Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	10 mg/kg	25 mg/kg	50 mg/kg
Urinary System (continued)				
Kidney (continued)	(48)	(9)	(3)	(48)
Infiltration cellular, lymphocytic	42 (88%)	4 (23%)	2 (67%)	39 (81%)
Mineralization	1 (2%)			1 (2%)
Necrosis, renal tubule	1 (2%)			
Nephropathy	7 (15%)			2 (4%)
Pigmentation, renal tubule				1 (2%)
Vacuolization cytoplasmic, renal tubule	1 (2%)			
Urinary bladder	(47)	(8)	(2)	(45)
Fibrosis, adventitia	1 (2%)			
Infiltration cellular, lymphocytic	41 (87%)		1 (50%)	37 (82%)