

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

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TABLE E1

Summary of the Incidence of Neoplasms in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate<sup>a</sup>

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

TABLE E1

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

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

TABLE E1

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

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

**TABLE E1**

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

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

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

b Primary neoplasms: all neoplasms except metastatic neoplasms

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

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

TABLE E2

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

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

TABLE E2

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

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

(T)Terminal sacrifice

(NA)Not applicable

- a Number of neoplasm-bearing animals/number of animals with tissue examined microscopically
- b Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
- c Observed incidence at terminal kill
- d Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in a dose group is indicated by N.
- e Not applicable; no neoplasms in animal group
- f Tissue was examined microscopically only when it was observed to be abnormal at necropsy; thus, statistical comparisons with the vehicle controls are not appropriate.



## Chloral Hydrate, NTP TR 502 E-9

**TABLE E3**

**Summary of the Incidence of Nonneoplastic Lesions in Regimen E Male Mice in the 2-Year Gavage Study of Chloral Hydrate<sup>a</sup>**

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

<sup>a</sup> Number of animals examined microscopically at the site and the number of animals with lesion

**E-10 Chloral Hydrate, NTP TR 502**

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

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

# Chloral Hydrate, NTP TR 502 E-11

**TABLE E3**

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

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

**E-12 Chloral Hydrate, NTP TR 502**

**TABLE E3**

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

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

**Chloral Hydrate, NTP TR 502 E-13**

**TABLE E3**

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

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