

TABLE A1

Summary of the Incidence of Neoplasms in *Ad Libitum*-Fed Male Mice in the 2-Year Gavage Study of Chloral Hydrate<sup>a</sup>

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
<b>Disposition Summary</b>				
Animals initially in study	60	60	60	60
<b>15-Month interim evaluation</b>				
Early deaths				
Moribund		4	2	1
Natural deaths	6	7	10	3
Survivors				
Terminal sacrifice	42	37	36	44
Animals examined microscopically	60	60	60	60
 <b>15-Month Interim Evaluation</b>				
<b>Alimentary System</b>				
Liver	(12)	(12)	(12)	(12)
Hepatocellular adenoma, single	2 (17%)	2 (17%)	2 (17%)	1 (8%)
Hepatocellular adenoma, multiple			1 (8%)	
Hepatocellular carcinoma, single		1 (8%)		2 (17%)
Lymphoma malignant	1 (8%)			
 <b>2-Year Study</b>				
<b>Alimentary System</b>				
Gallbladder	(43)	(10)	(10)	(44)
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Lymphoma malignant	2 (5%)			
Intestine large, cecum	(41)	(5)	(4)	(46)
Lymphoma malignant				1 (2%)
Intestine small	(42)	(7)	(5)	(46)
Lymphoma malignant				1 (2%)
Intestine small, duodenum	(41)	(7)	(4)	(46)
Lymphoma malignant	2 (5%)	1 (14%)		
Intestine small, ileum	(42)	(5)	(5)	(46)
Adenocarcinoma				1 (2%)
Histiocytic sarcoma		1 (20%)		
Lymphoma malignant	2 (5%)		1 (20%)	2 (4%)
Intestine small, jejunum	(42)	(5)	(4)	(46)
Lymphoma malignant	2 (5%)			
Liver	(48)	(48)	(47)	(48)
Carcinoma, bile duct			1 (2%)	
Hemangioma		1 (2%)		
Hepatocellular adenoma, multiple	2 (4%)	8 (17%)	8 (17%)	7 (15%)
Hepatocellular adenoma, single	10 (21%)	11 (23%)	9 (19%)	10 (21%)
Hepatocellular carcinoma		1 (2%)		
Hepatocellular carcinoma, multiple	1 (2%)		3 (6%)	1 (2%)
Hepatocellular carcinoma, single	3 (6%)	9 (19%)	7 (15%)	6 (13%)
Histiocytic sarcoma				1 (2%)
Lymphoma malignant	2 (4%)		2 (4%)	

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<b>2-Year Study</b> (continued)				
<b>Alimentary System</b> (continued)				
Mesentery		(1)		
Lymphoma malignant			1 (100%)	
Pancreas	(46)	(10)	(9)	(48)
Carcinoma, duct		1 (10%)		
Histiocytic sarcoma		1 (10%)		
Lymphoma malignant	1 (2%)		1 (11%)	
Neoplasm NOS			1 (11%)	
Salivary glands	(48)	(10)	(10)	(48)
Lymphoma malignant	1 (2%)	1 (10%)		1 (2%)
Stomach, glandular	(43)	(10)	(10)	(46)
Carcinoma, metastatic, liver			1 (10%)	
<b>Cardiovascular System</b>				
Blood vessel	(48)	(11)	(11)	(48)
Carcinoma, metastatic, pancreas		1 (9%)		
Hepatocellular carcinoma, metastatic, aorta, liver				1 (2%)
Lymphoma malignant	1 (2%)		1 (9%)	
Heart	(48)	(11)	(11)	(48)
Carcinoma, metastatic, liver			1 (9%)	
Carcinoma, metastatic, pancreas		1 (9%)		
Hepatocellular carcinoma, metastatic, liver				2 (4%)
Lymphoma malignant	1 (2%)		1 (9%)	
<b>Endocrine System</b>				
Adrenal gland	(45)	(11)	(10)	(46)
Carcinoma, metastatic, liver			1 (10%)	
Adrenal gland, cortex	(45)	(11)	(10)	(46)
Lymphoma malignant	2 (4%)	1 (9%)		
Adrenal gland, medulla	(45)	(11)	(10)	(45)
Lymphoma malignant	1 (2%)			
Islets, pancreatic	(48)	(10)	(11)	(48)
Carcinoma	1 (2%)			
Parathyroid gland	(47)	(6)	(6)	(42)
Lymphoma malignant	1 (2%)			
Pituitary gland	(42)	(10)	(9)	(46)
Adenoma, pars distalis			1 (11%)	
Thyroid gland	(47)	(11)	(10)	(48)
Adenoma, follicular cell	1 (2%)			
Lymphoma malignant	1 (2%)			
<b>General Body System</b>				
Tissue NOS			(2)	
Hemangiosarcoma				1 (50%)
Hepatocellular carcinoma, metastatic, mediastinum, liver				1 (50%)

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<b>2-Year Study</b> (continued)				
<b>Genital System</b>				
Coagulating gland	(46)	(10)	(10)	(48)
Carcinoma, metastatic, liver			1 (10%)	
Lymphoma malignant		1 (10%)	1 (10%)	
Epididymis	(46)	(10)	(11)	(48)
Carcinoma, metastatic, liver			1 (9%)	
Histiocytic sarcoma			1 (9%)	
Lymphoma malignant	1 (2%)	1 (10%)	2 (18%)	
Lymphoma malignant, unilateral				1 (2%)
Schwannoma benign				1 (2%)
Preputial gland	(46)	(10)	(11)	(48)
Lymphoma malignant	1 (2%)			
Prostate	(46)	(10)	(11)	(48)
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Lymphoma malignant	1 (2%)	1 (10%)	2 (18%)	
Seminal vesicle	(46)	(11)	(14)	(48)
Carcinoma, metastatic, liver			1 (7%)	
Lymphoma malignant	1 (2%)	1 (9%)	2 (14%)	
Testes	(45)	(11)	(10)	(48)
Adenoma, interstitial cell	1 (2%)			1 (2%)
Lymphoma malignant			1 (10%)	
<b>Hematopoietic System</b>				
Bone marrow	(47)	(10)	(10)	(48)
Hemangiosarcoma, metastatic, spleen	1 (2%)			
Lymphoma malignant	1 (2%)			
Lymph node	(48)	(15)	(17)	(48)
Histiocytic sarcoma, bronchial		1 (7%)		
Histiocytic sarcoma, renal		1 (7%)		
Lymphoma malignant, axillary	1 (2%)			
Lymphoma malignant, inguinal				1 (2%)
Lymphoma malignant, lumbar	1 (2%)	1 (7%)		
Lymphoma malignant, renal	2 (4%)			
Sarcoma, metastatic, uncertain primary site			1 (6%)	
Lymph node, mandibular	(48)	(10)	(9)	(45)
Lymphoma malignant	2 (4%)		3 (33%)	3 (7%)
Lymph node, mesenteric	(47)	(13)	(16)	(48)
Carcinoma, metastatic, liver			1 (6%)	
Carcinoma, metastatic, pancreas		1 (8%)		
Hemangiosarcoma				1 (2%)
Hemangiosarcoma, metastatic, spleen	1 (2%)			
Histiocytic sarcoma		2 (15%)	1 (6%)	
Lymphoma malignant	4 (9%)	2 (15%)	4 (25%)	4 (8%)
Spleen	(47)	(16)	(17)	(48)
Hemangiosarcoma	1 (2%)		2 (12%)	2 (4%)
Histiocytic sarcoma		1 (6%)		
Lymphoma malignant	5 (11%)	2 (13%)	3 (18%)	3 (6%)
Thymus	(29)	(6)	(4)	(35)
Carcinoma, metastatic, liver			1 (25%)	
Hepatocellular carcinoma, metastatic, liver				1 (3%)
Lymphoma malignant	2 (7%)	1 (17%)	2 (50%)	2 (6%)

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<b>2-Year Study</b> (continued)				
<b>Integumentary System</b>				
Mammary gland	(5)		(2)	
Lymphoma malignant	1 (20%)			
Skin	(48)	(10)	(10)	(48)
Fibroma	1 (2%)			
Keratoacanthoma				1 (2%)
<b>Musculoskeletal System</b>				
Bone, femur	(46)	(11)	(12)	(48)
Lymphoma malignant	1 (2%)			
Bone, sternum	(47)	(11)	(12)	(48)
Hemangiosarcoma				1 (2%)
Lymphoma malignant	1 (2%)			
Skeletal muscle	(47)	(10)	(11)	(48)
Carcinoma, metastatic, liver			1 (9%)	
Lymphoma malignant			1 (9%)	1 (2%)
Rhabdomyosarcoma			1 (9%)	
<b>Nervous System</b>				
Brain, cerebrum	(47)	(10)	(9)	(48)
Lymphoma malignant			1 (11%)	
<b>Respiratory System</b>				
Larynx	(46)	(11)	(11)	(47)
Lymphoma malignant	1 (2%)			
Lung	(48)	(20)	(16)	(48)
Alveolar/bronchiolar adenoma	12 (25%)	6 (30%)	3 (19%)	9 (19%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)	2 (10%)	1 (6%)	2 (4%)
Alveolar/bronchiolar carcinoma	2 (4%)	4 (20%)	1 (6%)	3 (6%)
Carcinoma, metastatic, liver			1 (6%)	
Carcinoma, metastatic, pancreas		1 (5%)		
Hepatocellular carcinoma, metastatic, liver	1 (2%)			2 (4%)
Hepatocellular carcinoma, metastatic, multiple, liver			2 (13%)	
Lymphoma malignant	2 (4%)	1 (5%)	2 (13%)	2 (4%)
Nose	(47)	(11)	(12)	(48)
Carcinoma			1 (8%)	
Lymphoma malignant	1 (2%)			
<b>Special Senses System</b>				
Eye	(46)	(11)	(11)	(48)
Lymphoma malignant, unilateral				1 (2%)
Harderian gland	(47)	(16)	(12)	(47)
Adenoma	5 (11%)	6 (38%)	2 (17%)	5 (11%)
Carcinoma		1 (6%)		
Lymphoma malignant	2 (4%)			
Lymphoma malignant, bilateral			1 (8%)	
Lacrimal gland	(47)	(10)	(10)	(46)
Lymphoma malignant		1 (10%)		

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<b>2-Year Study</b> (continued)				
<b>Urinary System</b>				
Kidney	(46)	(10)	(10)	(48)
Carcinoma, metastatic, pancreas		1 (10%)		
Lymphoma malignant	2 (4%)		2 (20%)	1 (2%)
Urinary bladder	(46)	(10)	(11)	(48)
Lymphoma malignant	2 (4%)	1	(9%) 1	(2%)
<b>Neoplasm Summary</b>				
Total animals with primary neoplasms <sup>b</sup>				
15-Month interim evaluation	3	3	3	3
2-Year study	34	36	33	35
Total primary neoplasms				
15-Month interim evaluation	3	3	3	3
2-Year study	95	72	77	78
Total animals with benign neoplasms				
15-Month interim evaluation	2	2	3	1
2-Year study	27	27	19	25
Total benign neoplasms				
15-Month interim evaluation	2	2	3	1
2-Year study	33	34	24	36
Total animals with malignant neoplasms				
15-Month interim evaluation	1	1		2
2-Year study	12	19	20	17
Total malignant neoplasms				
15-Month interim evaluation	1	1		2
2-Year study	62	38	53	42
Total animals with metastatic neoplasms				
2-Year study	2	1	4	2
Total metastatic neoplasms				
2-Year study	3	5	13	9
Total animals with uncertain neoplasms- benign or malignant				
2-Year study			1	
Total uncertain neoplasms				
2-Year study			1	

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

<sup>b</sup> Primary neoplasms: all neoplasms except metastatic neoplasms