

TABLE A2

Statistical Analysis of Primary Neoplasms in *Ad Libitum*-Fed Male Mice in the 2-Year Gavage Study of Chloral Hydrate

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
<b>Harderian Gland: Adenoma</b>				
Overall rate <sup>a</sup>	5/47 (11%)	6/16 (38%)	2/12 (17%)	5/47 (11%)
Adjusted rate <sup>b</sup>	10.9%	42.4%	20.8%	10.9%
Terminal rate <sup>c</sup>	5/41 (12%)	5/6 (83%)	1/1 (100%)	5/44 (11%)
First incidence (days)	757 (T)	666	738	757 (T)
Poly-3 test <sup>d</sup>	NA	— <sup>e</sup>	—	P=0.6264N
<b>Harderian Gland: Adenoma or Carcinoma</b>				
Overall rate	5/47 (11%)	7/16 (44%)	2/12 (17%)	5/47 (11%)
Adjusted rate	10.9%	49.5%	20.8%	10.9%
Terminal rate	5/41 (12%)	6/6 (100%)	1/1 (100%)	5/44 (11%)
First incidence (days)	757 (T)	666	738	757 (T)
Poly-3 test	NA	—	—	P=0.6264N
<b>Liver: Hepatocellular Adenoma</b>				
Overall rate	12/48 (25%)	19/48 (40%)	17/47 (36%)	17/48 (35%)
Adjusted rate	25.2%	40.8%	37.8%	36.2%
Terminal rate	9/41 (22%)	14/37 (38%)	15/36 (42%)	16/44 (36%)
First incidence (days)	511	639	668	713
Poly-3 test	P=0.2362	P=0.0792	P=0.1373	P=0.1722
<b>Liver: Hepatocellular Carcinoma</b>				
Overall rate	4/48 (8%)	10/48 (21%)	10/47 (21%)	7/48 (15%)
Adjusted rate	8.5%	21.4%	22.0%	14.7%
Terminal rate	2/41 (5%)	5/37 (14%)	5/36 (14%)	4/44 (9%)
First incidence (days)	689	666	668	629
Poly-3 test	P=0.3737	P=0.0716	P=0.0631	P=0.2713
<b>Liver: Hepatocellular Adenoma or Carcinoma</b>				
Overall rate	16/48 (33%)	25/48 (52%)	23/47 (49%)	22/48 (46%)
Adjusted rate	33.4%	52.6%	50.6%	46.2%
Terminal rate	11/41 (27%)	16/37 (43%)	17/36 (47%)	19/44 (43%)
First incidence (days)	511	639	668	629
Poly-3 test	P=0.2154	P=0.0437	P=0.0684	P=0.1430
<b>Lung: Alveolar/bronchiolar Adenoma</b>				
Overall rate	13/48 (27%)	8/20 (40%)	4/16 (25%)	11/48 (23%)
Adjusted rate	27.8%	45.0%	29.4%	23.4%
Terminal rate	12/41 (29%)	7/9 (78%)	3/5 (60%)	10/44 (23%)
First incidence (days)	709	736	738	662
Poly-3 test	NA	—	—	P=0.4012N
<b>Lung: Alveolar/bronchiolar Carcinoma</b>				
Overall rate	2/48 (4%)	4/20 (20%)	1/16 (6%)	3/48 (6%)
Adjusted rate	4.3%	21.7%	7.4%	6.4%
Terminal rate	2/41 (5%)	2/9 (22%)	1/5 (20%)	3/44 (7%)
First incidence (days)	757 (T)	639	757 (T)	757 (T)
Poly-3 test	NA	—	—	P=0.5010

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
<b>Lung: Alveolar/bronchiolar Adenoma or Carcinoma</b>				
Overall rate	15/48 (31%)	11/20 (55%)	5/16 (31%)	14/48 (29%)
Adjusted rate	32.0%	59.3%	36.7%	29.7%
Terminal rate	14/41 (34%)	8/9 (89%)	4/5 (80%)	13/44 (30%)
First incidence (days)	709	639	738	662
Poly-3 test	NA	—	—	P=0.4930N
<b>All Organs: Malignant Lymphoma</b>				
Overall rate	5/48 (10%)	3/48 (6%)	5/48 (10.4%)	5/48 (10%)
Adjusted rate	10.7%	6.6%	10.6%	10.7%
Terminal rate	3/41 (7%)	2/37 (5%)	2/36 (5.6%)	4/44 (9.1%)
First incidence (days)	744	736	353	713
Poly-3 test	P=0.4761	P=0.3674N	P=0.6262N	P=0.6269N
<b>All Organs: Benign Neoplasms</b>				
Overall rate	27/48 (56%)	27/48 (56%)	20/48 (42%) <sup>f</sup>	25/48 (52%)
Adjusted rate	56.6%	57.6%	43.6%	52.9%
Terminal rate	24/41 (59%)	21/37 (57%)	17/36 (47%)	23/44 (52%)
First incidence (days)	511	639	668	662
Poly-3 test	P=0.3184N	P=0.5417	P=0.1461N	P=0.4394N
<b>All Organs: Malignant Neoplasms</b>				
Overall rate	12/48 (25%)	19/48 (40%)	20/48 (42%)	17/48 (35%)
Adjusted rate	25.5%	39.7%	41.7%	35.4%
Terminal rate	7/41 (17%)	9/37 (24%)	9/36 (25%)	13/44 (30%)
First incidence (days)	689	639	353	629
Poly-3 test	P=0.2596	P=0.1034	P=0.0715	P=0.2037
<b>All Organs: Benign or Malignant Neoplasms</b>				
Overall rate	34/48 (71%)	36/48 (75%)	33/48 (69%)	35/48 (73%)
Adjusted rate	70.8%	75.0%	68.8%	72.9%
Terminal rate	27/41 (66%)	25/37 (68%)	22/36 (61%)	31/44 (71%)
First incidence (days)	511	639	353	629
Poly-3 test	P=0.5213	P=0.4100	P=0.5012N	P=0.5000

(T)Terminal sacrifice

NA Not applicable

<sup>a</sup> Number of neoplasm-bearing animals/number of animals with tissue examined microscopically<sup>b</sup> Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality<sup>c</sup> Observed incidence at terminal kill<sup>d</sup> 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.<sup>e</sup> Tissue was examined microscopically only when it was observed to be abnormal at necropsy; thus, statistical comparisons with the vehicle controls are not appropriate.<sup>f</sup> Includes one animal with a neoplasm of uncertain malignancy