

Table 6. *gpt* mutant frequencies in the liver of *gpt* delta mice given 1-MN for 13 weeks

Groups	Animal No.	Cm <sup>R</sup> colonies(x10 <sup>5</sup> )	6-TGR <sup>R</sup> and Cm <sup>R</sup> colonies	Mutant Frequency (x10 <sup>-5</sup> )	Mean ± S.D.	
Male	Control	1	9.8	3	0.31	0.34 ± 0.17
		2	12.3	5	0.41	
		3	15.2	9	0.59	
		4	15.1	2	0.13	
		5	4.0	1	0.25	
	0.075% 1-MN	11	11.4	5	0.26	0.33 ± 0.13
		12	2.1	1	0.47	
		13	5.3	1	0.19	
		14	23.5	5	0.30	
		15	18.2	6	0.33	
	0.15% 1-MN	21	18.0	9	0.61	0.54 ± 0.06
		23	6.1	4	0.49	
		24	24.5	17	0.57	
		25	22.4	11	0.49	
Female	Control	31	7.1	1	0.14	0.17 ± 0.10
		32	50.5	3	0.06	
		33	43.4	10	0.23	
		34	36.0	4	0.11	
		35	18.3	6	0.33	
	0.075% 1-MN	41	41.1	7	0.17	0.17 ± 0.09
		42	36.4	3	0.08	
		43	40.6	6	0.15	
		44	38.0	12	0.32	
		45	49.2	6	0.12	
	0.15% 1-MN	51	25.8	6	0.23	0.20 ± 0.14
		52	29.3	11	0.38	
		53	33.9	7	0.21	
		54	30.2	5	0.17	
		55	55.8	0	0.00	

Table 7. Spi<sup>r</sup> mutant frequencies in the liver of *gpt* delta mice given 1-MN for 13 weeks

Groups	Animal No.	Plaques within XL-1 Blue MRA ( $\times 10^5$ )	Plaque within WL95 (P2)	Mutant Frequency ( $\times 10^{-5}$ )	Mean $\pm$ S.D.	
Male	Control	1	15.8	1	0.06	0.15 $\pm$ 0.06
		2	4	2	0.14	
		3	19.5	4	0.21	
		4	10.9	2	0.18	
	0.075% 1-MN	11	14.1	6	0.43	0.45 $\pm$ 0.16
		12	3.4	1	0.29	
		13	15	10	0.67	
		14	18.4	10	0.55	
		15	15.3	5	0.33	
	0.15% 1-MN	21	16.5	3	0.18	0.40 $\pm$ 0.26
		22	22.8	7	0.31	
		23	4.9	4	0.82	
		24	18	4	0.22	
		25	6.3	3	0.48	
	Female	Control	31	14.9	7	0.47
32			12.3	3	0.24	
33			10.4	1	0.09	
34			10.4	6	0.58	
0.075% 1-MN		41	13.6	1	0.07	0.37 $\pm$ 0.18
		42	20.1	9	0.45	
		43	11.8	4	0.34	
		44	17.6	9	0.51	
		45	10.9	5	0.46	
0.15% 1-MN		51	8.7	0	0.00	0.28 $\pm$ 0.23
		52	12.4	5	0.40	
		53	14.6	3	0.21	
		54	15.5	8	0.52	

Table 8. Changes in parameters for body weight, liver weight, GST-P positive foci

Groups	Animal No.	Final body weight (g)	Liver weight		GST-P	
			Absolute (g)	Relative (g/100g B.W.)	Number(No./cm <sup>2</sup> )	Area (mm <sup>2</sup> /cm <sup>2</sup> )
Cont-1	5	231.3 ± 11.8 <sup>a</sup>	8.4 ± 0.5	3.6 ± 0.1	0.0 ± 0.0	0.0 ± 0.0
600 mg/kg estragole	5	176.6 ± 8.1**	7.0 ± 0.5**	4.0 ± 0.1**	9.48 ± 2.67**	0.03 ± 0.02**
Cont-2	5	220.2 ± 17.1	8.7 ± 0.9	4.0 ± 0.2	0.0 ± 0.0	0.0 ± 0.0
0.5% safrole	5	170.9 ± 4.2 <sup>##</sup>	9.6 ± 0.5	5.6 ± 0.3	0.27 ± 0.40	0.002 ± 0.004

\*\* : significantly different from the cont-1 group at the levels of  $p < 0.001$  (Student's  $t$  -test).

<sup>##</sup> : significantly different from the cont-2 group at the levels of  $p < 0.001$  (Student's  $t$  -test) <sup>a</sup> Mean ± SD.

Table 9. The level of mRNA expression of the up or down-regulated genes in common in estragole or safrole-treated groups.

Regulation	Function	Accession number	Gene Symbol	Estragole	Safrole
				FC Absolute	
Up					
	DNA repair	NM_012861	Mgmt	4.4	3.6
	Cell proliferation	NM_053963	Mimp12	19.9	7.7
		NM_012923	Ccng1	7.9	2.4
	apoptosis	NM_001108099	Mdm2	4.6	2.6
	Other	XM_574584	Adam8	350.0	10.7
		NM_001106536	Mybl2	68.5	10.1
		NM_001012022	Cldn4	9.2	3.3
		NM_133304	Heph	2.6	3.0
		NM_001127524	Aadacl1	2.8	3.0
		NM_001014217	Nhej1	19.7	2.9
		NM_019179	Tyms	9.8	2.2
		NM_012946	Sparcl1	2.8	2.1
		NM_001106707	Nlrc4	2.6	2.0
		NM_138536	Ttf1	2.3	2.0
Down					
	Tumor suppressor	NM_021774	Flit	-65.4	-55.6
		BC168961	Tfdp2	-3.7	-2.0
	Oxidation/metabolism	NM_001014167	Rnls	-3.4	-3.5
		NM_001025762	Smyd3	-7.3	-2.2
	Other	NM_138835	Syt12	-4.6	-6.0
		NM_001108803	Mogat1	-5.6	-4.2
		NM_001100685	Clyb1	-10.9	-3.6
		NM_001009695	Wnt7b	-4.1	-3.4
		XM_574162	Alpk2	-4.3	-3.0
		NM_133614	Slc25a21	-6.1	-2.5
		NM_022184	Cask	-3.0	-2.1
		XM_231528	Cadps2	-11.8	-2.1

Table 10. Final body and organ weights for male *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Group	Control	10 mg/kg MEUG	30 mg/kg MEUG	100 mg/kg MEUG
No. of animal	10	10	10	10
Body weight	300.0 ± 17.4 <sup>a</sup>	325.0 ± 10.4	322.4 ± 13.7	310.2 ± 35.4
Absolute(g)				
Liver	8.09 ± 0.49	8.22 ± 0.41	8.54 ± 0.41	9.43 ± 0.70 <sup>**</sup>
Lung	1.16 ± 0.14	1.15 ± 0.06	1.16 ± 0.11	1.16 ± 0.10
Kidney	1.82 ± 0.11	1.78 ± 0.07	1.84 ± 0.07	1.93 ± 0.08 <sup>*</sup>
Brain	1.93 ± 0.05	1.94 ± 0.03	1.96 ± 0.03	1.96 ± 0.04
Spleen	0.65 ± 0.04	0.65 ± 0.03	0.65 ± 0.03	0.67 ± 0.03
Thymus	0.24 ± 0.05	0.20 ± 0.02	0.22 ± 0.05	0.21 ± 0.03
Heart	0.85 ± 0.06	0.84 ± 0.01	0.84 ± 0.04	0.84 ± 0.04
Adrenal	0.06 ± 0.06	0.04 ± 0.01	0.05 ± 0	0.05 ± 0.00
Gonad	2.93 ± 0.11	2.91 ± 0.09	2.96 ± 0.13	3.00 ± 0.08
Relative(g/100g B.W.)				
Liver	2.45 ± 0.07	2.53 ± 0.08	2.65 ± 0.08	3.09 ± 0.45 <sup>**</sup>
Lung	0.35 ± 0.03	0.35 ± 0.03	0.36 ± 0.03	0.38 ± 0.05
Kidney	0.55 ± 0.01	0.55 ± 0.01	0.57 ± 0.01 <sup>*</sup>	0.63 ± 0.08 <sup>**</sup>
Brain	0.59 ± 0.03	0.60 ± 0.02	0.61 ± 0.03	0.64 ± 0.10
Spleen	0.20 ± 0.01	0.20 ± 0.01	0.2 ± 0.01	0.22 ± 0.04
Thymus	0.07 ± 0.02	0.06 ± 0.01	0.07 ± 0.02	0.07 ± 0.01
Heart	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01	0.28 ± 0.04
Adrenal	0.02 ± 0.02	0.01 ± 0.00	0.01 ± 0.00	0.02 ± 0.00
Gonad	0.89 ± 0.05	0.89 ± 0.03	0.92 ± 0.03	0.99 ± 0.15 <sup>*</sup>

<sup>\*,\*\*</sup>: Significantly different from the controls at the levels of p<0.05 and p<0.01, respectively (Dunnet's test) <sup>a</sup> Mean±SD.

Table 11. Final body and organ weights for female *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Group	Control	10 mg/kg MEUG	30 mg/kg MEUG	100 mg/kg MEUG
No. of animal	10	9	9	9
Body	189.0 ± 5.6	190.3 ± 8.3	187.6 ± 5.3	176.5 ± 9.7
Absolute(g)				
Liver	4.26 ± 0.22	4.34 ± 0.22	4.29 ± 0.22	4.38 ± 0.20
Lung	0.84 ± 0.10	0.8 ± 0.05	0.83 ± 0.09	0.80 ± 0.07
Kidney	1.09 ± 0.04	1.09 ± 0.03	1.09 ± 0.04	1.07 ± 0.04
Brain	1.78 ± 0.03	1.8 ± 0.04	1.77 ± 0.05	1.75 ± 0.04
Spleen	0.41 ± 0.02	0.42 ± 0.02	0.4 ± 0.03	0.40 ± 0.02
Thymus	0.19 ± 0.02	0.19 ± 0.02	0.18 ± 0.02	0.18 ± 0.02
Heart	0.55 ± 0.03	0.54 ± 0.02	0.52 ± 0.02 *	0.50 ± 0.02 **
Adrenal	0.05 ± 0.01	0.05 ± 0.00	0.05 ± 0.00	0.05 ± 0.01
Relative(g/100g B.W.)				
Liver	2.26 ± 0.12	2.28 ± 0.14	2.29 ± 0.11	2.48 ± 0.08 **
Lung	0.45 ± 0.06	0.42 ± 0.04	0.44 ± 0.05	0.45 ± 0.05
Kidney	0.58 ± 0.02	0.58 ± 0.02	0.58 ± 0.02	0.61 ± 0.03 *
Brain	0.94 ± 0.03	0.95 ± 0.04	0.94 ± 0.03	1.00 ± 0.06 *
Spleen	0.22 ± 0.01	0.22 ± 0.01	0.21 ± 0.01	0.23 ± 0.02
Thymus	0.1 ± 0.01	0.09 ± 0.04	0.1 ± 0.01	0.10 ± 0.01
Heart	0.29 ± 0.01	0.29 ± 0.01	0.28 ± 0.01	0.28 ± 0.01
Adrenal	0.03 ± 0.00	0.02 ± 0.00	0.03 ± 0.00	0.03 ± 0.00

\*,\*\* : Significantly different from the controls at the levels of  $p < 0.05$  and  $p < 0.01$ , respectively (Dunnet's test) <sup>a</sup> Mean ± SD.

Table 12. Hematological data for F344 *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Item	Dose of ME			
	0	10 mg/kg	30 mg/kg	100 mg/kg
Male				
No. of animals examined	10	10	10	10
WBC ( $\times 10^2/\mu\ell$ )	34.9 $\pm$ 5.6	46.1 $\pm$ 7.7	46.5 $\pm$ 5.8	48.7 $\pm$ 7.5
RBS ( $\times 10^4/\mu\ell$ )	923.5 $\pm$ 31.9	964.1 $\pm$ 42.1	919.1 $\pm$ 33.9	945.7 $\pm$ 34.3
Hb (g/dL)	15.8 $\pm$ 0.6	15.6 $\pm$ 0.2	15.4 $\pm$ 0.5	15.8 $\pm$ 0.6
Ht (%)	51.7 $\pm$ 2	51.1 $\pm$ 2.1	50.0 $\pm$ 1.8	51.4 $\pm$ 1.8
MCV (fL)	56.0 $\pm$ 0.5	53.0 $\pm$ 0.4	54.3 $\pm$ 0.3	54.4 $\pm$ 0.5
MCH (pg)	17.2 $\pm$ 0.2	16.2 $\pm$ 0.6	16.7 $\pm$ 0.4	16.7 $\pm$ 0.4
MCHC (g/dL)	30.6 $\pm$ 0.5	30.5 $\pm$ 1	30.8 $\pm$ 0.7	30.8 $\pm$ 0.8
Plt ( $\times 10^4/\mu\ell$ )	74.6 $\pm$ 8.1	66.1 $\pm$ 4.2	71.6 $\pm$ 5.7	70.3 $\pm$ 3.3
Differential leukocyte counts (%)				
Band form neutrophils	1.6 $\pm$ 1.1	1.4 $\pm$ 1.0	2.1 $\pm$ 1.1	1.6 $\pm$ 1.0
Segmented neutrophils	28.5 $\pm$ 9.4	35.4 $\pm$ 8.5	29.5 $\pm$ 6.3	29.9 $\pm$ 6.2
Eosinophils	1.5 $\pm$ 1.0	1.0 $\pm$ 0.3	1.2 $\pm$ 0.5	0.8 $\pm$ 0.7
Basophils	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Lymphocytes	68.0 $\pm$ 8.7	61.9 $\pm$ 8.1	66.7 $\pm$ 6.2	67.7 $\pm$ 6.2
Monocytes	0.3 $\pm$ 0.4	0.2 $\pm$ 0.3	0.5 $\pm$ 0.7	0.2 $\pm$ 0.3
Reticulocytes	1.4 $\pm$ 1.2	2.6 $\pm$ 1.5	2.7 $\pm$ 2.1	4.0 $\pm$ 2.1
Female				
No. of animals examined	10	9	9	9
WBC ( $\times 10^2/\mu\ell$ )	34.9 $\pm$ 5.6	34.6 $\pm$ 10.6	44.8 $\pm$ 8.9*	31.7 $\pm$ 5.6
RBS ( $\times 10^4/\mu\ell$ )	923.5 $\pm$ 31.9	916.5 $\pm$ 31.0	896.7 $\pm$ 29.2	877.0 $\pm$ 56.9
Hb (g/dL)	15.8 $\pm$ 0.6	15.5 $\pm$ 0.6	15.4 $\pm$ 0.4	15.5 $\pm$ 0.8
Ht (%)	51.7 $\pm$ 2	50.9 $\pm$ 1.8	50.0 $\pm$ 1.6	49.1 $\pm$ 2.8
MCV (fL)	56.0 $\pm$ 0.5	55.6 $\pm$ 0.4	55.8 $\pm$ 0.4	56.7 $\pm$ 0.2
MCH (pg)	17.2 $\pm$ 0.2	17.0 $\pm$ 0.2	17.2 $\pm$ 0.4	17.9 $\pm$ 0.5
MCHC (g/dL)	30.6 $\pm$ 0.5	30.5 $\pm$ 0.3	30.8 $\pm$ 0.7	31.5 $\pm$ 1.0
Plt ( $\times 10^4/\mu\ell$ )	74.6 $\pm$ 8.1	72.4 $\pm$ 2.7	59.3 $\pm$ 3.3	84.7 $\pm$ 5.4**
Differential leukocyte counts (%)				
Band form neutrophils	1.1 $\pm$ 0.7	1.3 $\pm$ 0.7	1.9 $\pm$ 0.7	2.0 $\pm$ 1.0
Segmented neutrophils	21.5 $\pm$ 4.6	25.1 $\pm$ 4.1	20.3 $\pm$ 5.0	20.7 $\pm$ 5.3
Eosinophils	1.1 $\pm$ 0.7	1.3 $\pm$ 0.6	1.0 $\pm$ 0.9	0.7 $\pm$ 0.5
Basophils	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Lymphocytes	75.9 $\pm$ 5.2	72.1 $\pm$ 4.2	76.1 $\pm$ 4.9	76.2 $\pm$ 5.7
Monocytes	0.4 $\pm$ 0.4	0.2 $\pm$ 0.3	0.6 $\pm$ 0.5	0.4 $\pm$ 0.4
Reticulocytes	4.4 $\pm$ 2.7	4.4 $\pm$ 3.0	5.9 $\pm$ 2.5	6.6 $\pm$ 4.2

Abbreviations: WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Plt, platelet.

<sup>a</sup> Mean  $\pm$  SD. \*: Significantly different from the controls at the levels of  $p < 0.05$  (Dunnett's test)

Table 13. Serum biochemistry for F344 *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Item	Dose of methyl eugenol (P.O.)			
	Cont	10 mg/kg	30 mg/kg	100 mg/kg
Male				
No. of animals examined	10	10	10	10
TP (g/dl)	6.56 ± 0.14 <sup>a</sup>	6.57 ± 0.14	6.65 ± 0.12	6.45 ± 0.20
A/G	1.84 ± 0.05	1.96 ± 0.14	1.93 ± 0.09	2.05 ± 0.12**
Alb (g/dl)	4.25 ± 0.08	4.35 ± 0.10	4.38 ± 0.08	4.33 ± 0.16
T-Bil (mg/dl)	0.04 ± 0.01	0.04 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
Glucose (mg/dl)	172.00 ± 14.72	159.50 ± 16.33	150.70 ± 14.71	160.10 ± 20.52
TG (mg/dl)	134.70 ± 30.59	168.30 ± 21.06	193.90 ± 68.33	188.00 ± 62.09
Phospholipid (mg/dl)	114.10 ± 7.37	119.00 ± 4.64	129.20 ± 10.79*	125.70 ± 15.78
TC (mg/dl)	70.40 ± 2.67	70.10 ± 4.89	72.70 ± 5.21	66.20 ± 7.48
BUN (mg/dl)	18.61 ± 1.55	19.57 ± 1.15	19.86 ± 1.84	19.45 ± 2.40
CRN (mg/dl)	0.33 ± 0.03	0.33 ± 0.02	0.31 ± 0.02	0.29 ± 0.02**
Na (mEq/l)	144.20 ± 0.79	144.80 ± 0.42	144.20 ± 0.92	144.00 ± 1.25
Cl (mEq/l)	104.50 ± 0.85	103.70 ± 0.82	103.30 ± 1.06*	103.20 ± 1.40*
K (mEq/l)	4.35 ± 0.21	4.23 ± 0.19	4.26 ± 0.16	4.16 ± 0.21
Ca (mg/dl)	10.09 ± 0.17	10.07 ± 0.23	10.18 ± 0.20	10.21 ± 0.41
IP (mg/dl)	4.80 ± 0.57	5.18 ± 0.67	5.20 ± 0.52	5.75 ± 0.34**
AST (IU/l)	107.50 ± 23.80	92.60 ± 15.69	83.40 ± 19.96*	78.40 ± 7.83**
ALT (IU/l)	75.00 ± 21.09	63.90 ± 11.11	62.00 ± 22.14	55.40 ± 7.60*
ALP (IU/l)	410.80 ± 22.70	427.10 ± 26.33	409.20 ± 25.68	383.50 ± 35.19
Female				
No. of animals examined	10	9	9	9
TP (g/dl)	7.11 ± 0.33	6.96 ± 0.23	6.83 ± 0.29	6.67 ± 0.27
A/G	2.27 ± 0.15	2.24 ± 0.17	2.28 ± 0.18	2.24 ± 0.11
Alb (g/dl)	4.93 ± 0.22	4.80 ± 0.15	4.74 ± 0.24	4.61 ± 0.17**
T-Bil (mg/dl)	0.06 ± 0.01	0.06 ± 0.01	0.05 ± 0.01*	0.05 ± 0.01**
Glucose (mg/dl)	129.50 ± 18.82	115.78 ± 11.69	133.67 ± 13.35	131.00 ± 18.48
TG (mg/dl)	56.40 ± 22.13	43.00 ± 13.81	69.56 ± 40.40	57.56 ± 21.23
Phospholipid (mg/dl)	176.60 ± 20.15	169.67 ± 12.63	177.89 ± 14.84	177.11 ± 14.26
TC (mg/dl)	103.30 ± 11.20	101.56 ± 8.71	103.89 ± 6.83	102.00 ± 7.21
BUN (mg/dl)	17.11 ± 2.22	15.89 ± 1.22	15.96 ± 1.50	17.01 ± 0.82
CRN (mg/dl)	0.33 ± 0.03	0.34 ± 0.02	0.30 ± 0.02	0.29 ± 0.01**
Na (mEq/l)	144.40 ± 0.52	144.67 ± 0.71	145.00 ± 0.87	145.11 ± 1.54
Cl (mEq/l)	104.90 ± 0.88	105.67 ± 0.87	105.56 ± 0.88	106.78 ± 1.99*
K (mEq/l)	4.06 ± 0.22	3.98 ± 0.17	3.92 ± 0.10	3.94 ± 0.22
Ca (mg/dl)	10.36 ± 0.31	10.09 ± 0.17	10.39 ± 0.21	10.37 ± 0.24
IP (mg/dl)	4.47 ± 0.46	4.40 ± 0.39	4.49 ± 0.56	4.96 ± 0.33**
AST (IU/l)	71.70 ± 13.28	72.89 ± 8.91	64.56 ± 7.58	66.78 ± 9.81
ALT (IU/l)	39.50 ± 5.13	35.44 ± 5.50	35.56 ± 3.81	35.44 ± 6.54
ALP (IU/l)	266.80 ± 34.54	273.78 ± 40.76	275.11 ± 30.70	266.22 ± 29.80

Abbreviations: TP, total protein; Alb, albumin; T-Bil, total bilirubin; TG, triglyceride; TC, Total cholesterol; BUN, blood urea nitrogen; CRN, creatinine; Na, sodium; Cl, [chlorine] K, potassium; Ca, calcium; IP, inorganic phosphate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase \* , \*\* : Significantly different from the controls at the levels of p<0.05 and p<0.01, respectively (Dunnett's test) <sup>a</sup> Mean±SD



Table 14. Histopathological features in the livers of F344 *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks.

Sex	Groups	Male				Female			
		Cont	10 mg/kg	30 mg/kg	100 mg/kg	Cont	10 mg/kg	30 mg/kg	100 mg/kg
		10	10	10	10	10	9	9	9
	Survival rate	100%	100%	100%	100%	100%	90%	90%	90%
Liver	Altered foci	0 <sup>a</sup> (0 <sup>b</sup> )	1(10)	0(0)	1(10)	0(0)	0(0)	0(0)	0(0)
	Focal necrosis	3(30)	3(30)	3(30)	6(60)	2(20)	3(33.3)	2(22.2)	2(22.2)
Spleen	Single cell necrosis	4(40)	6(60)	3(30)	2(20)	7(70)	6(66.7)	1(11.1)	3(33.3)
	Centrilobular hepatocell hypertrophy	0(0)	0(0)	0(0)	2(20)	0(0)	0(0)	0(0)	0(0)
Lung	Microgranuloma	1(10)	0(0)	0(0)	1(10)	5(50)	5(55.6)	2(22.2)	0(0)
	Angiectasis	2(20)	2(20)	2(20)	1(10)	0(0)	0(0)	0(0)	0(0)
Kidney	Brown pigmentation	0(0)	0(0)	0(0)	0(0)	0(0)	5(55.6)**	5(55.6)**	4(44.4)*
	Fibrosis	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)	0(0)
Heart	Focal hemorrhage	0(0)	0(0)	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)
	Mineralization	0(0)	6(60)**	1(10)	1/10	0(0)	0(0)	1(11.1)	1(11.1)
Tongue	Collection of foam cell	1(10)	0(0)	0(0)	0(0)	1(10)	0(0)	0(0)	1(11.1)
	Osseous metaplasia	0(0)	0(0)	1(10)	0(0)	1(10)	0(0)	1(11.1)	0(0)
Mammary gland	Hyalin cast	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	Tubular regeneration	8(80)	8(80)	10(100)	9(90)	0(0)	0(0)	0(0)	0(0)
thyroid gland	Mineralization	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)	1(11.1)
	Inflammatory cell infiltration	0(0)	0(0)	1(10)	0(0)	1(10)	1(11.1)	0(0)	1(11.1)
Parotid gland	Focal myocardial inflammation	10(100)	9(90)	9(90)	8(80)	1(10)	2(22.2)	1(11.1)	0(0)
	Fibrotic degeneration	0(0)	1(10)	1(10)	0(0)	1(10)	1(11.1)	2(22.2)	0(0)
Pituitary gland	Endocardial proliferation	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)	0(0)
	Arteritis	0(0)	0(0)	0(0)	1(10)	0(0)	0(0)	0(0)	0(0)
Salivary gland	Inflammatory cell infiltration	1(10)	0(0)	0(0)	1(10)	0(0)	0(0)	0(0)	0(0)
	Proliferation	4(40)	2(20)	6(60)	2(20)	0(0)	0(0)	0(0)	0(0)
Cecum	Granuloma	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)	0(0)
	Ultimobranchial cyst	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)	0(0)
Pancreas	Mineralization	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	Focal hyperplasia of anterior lobe	0(0)	1(10)	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)
Epididymis	Spinal cord cervical	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)
	Demyelination	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)
Prostate gland	Breastbone	8(80)	9(90)	9(90)	10(100)	9(90)	9(100)	7(77.8)	9(100)
	Nonsuppurative necrosis	8(80)	9(90)	9(90)	10(100)	9(90)	9(100)	7(77.8)	9(100)
Ovary	Vacuolar degeneration	0(0)	0(0)	0(0)	0(0)	1(10)	0(0)	0(0)	0(0)
	Loss of the mucosal epithelium	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(11.1)	0(0)
Harder gland	Inflammatory cell infiltration	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	Atrophy of exocrine gland	1(10)	1(10)	0(0)	4(40)	0(0)	0(0)	1(11.1)	1(11.1)
Adrenal gland	Nesidioblastosis	0(0)	1(10)	0(0)	0(0)	4(40)	2(22.2)	0(0)	1(11.1)
	Inflammatory cell infiltration	0(0)	2(20)	0(0)	0(0)	-	-	-	-
Cortical hyperplasia	Prostatitis	1(10)	0(0)	0(0)	0(0)	-	-	-	-
	Cyst	-	-	-	-	2(20)	1(11.1)	0(0)	0(0)
Fibrosis	Fibrosis	1(10)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	Inflammatory cell infiltration	1(10)	0(0)	1(10)	1(10)	2(20)	1(11.1)	1(11.1)	1(11.1)
Cortical hyperplasia	Cortical hyperplasia	0(0)	1(10)	0(0)	1(10)	1(10)	1(11.1)	0(0)	0(0)

<sup>a</sup>: The number of animals with histopathological lesions. <sup>b</sup>: The incidence(%) of histopathological lesions - : Not examined  
<sup>\*</sup>, <sup>\*\*</sup>, <sup>\*\*\*</sup>: Significantly different from the controls at the levels of  $p < 0.05$ , 0.01, respectively (Fisher's exact test)

Table 15. *gpt* MFs in the liver of males *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Groups	Animal No.	Cm <sup>R</sup> colonies(x10 <sup>5</sup> )	6-TG <sup>R</sup> and Cm <sup>R</sup> colonies	Mutant Frequency (x10 <sup>-5</sup> )	Mean±S.D.
Control	1	3.4	2	0.59	0.53 ± 0.18
	2	4.5	2	0.44	
	3	4.5	3	0.67	
	4	2.9	2	0.69	
	5	7.6	2	0.27	
10 mg/kg MEUG	11	9.5	4	0.42	0.79 ± 0.34
	12	4.8	6	1.25	
	13	3.0	2	0.66	
	14	1.9	2	1.03 <sup>a</sup>	
	15	5.3	3	0.57	
30 mg/kg MEUG	21	2.5	1	0.40	0.79 ± 0.42
	22	5.5	8	1.45	
	23	4.9	3	0.61	
	24	7.3	7	0.96	
	25	3.6	2	0.55	
100 mg/kg MEUG	31	6.0	12	2.20	1.35 ± 0.60*
	32	4.1	3	0.73	
	33	8.3	8	0.96	
	34	3.5	4	1.14	
	35	3.6	6	1.69	

\*: Significantly different from the control group at p<0.05 (Dunnet's test).

<sup>a</sup>: Data of animal No.14 was excluded for the calculation of MF because of the poor packaging efficiency of the transgene.

Table 16. Spi<sup>-</sup> MFs in the liver of males *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Groups	Animal No.	Plaques within XL-1 Blue MRA (x10 <sup>5</sup> )	Plaque within XL-1 Blue MRA (P2)	Mutant Frequency (x10 <sup>-5</sup> )	Mean±S.D.
Control	1	7.3	1	0.14	0.32 ± 0.27
	2	4.1	1	0.25	
	3	5.9	1	0.17	
	4	8.4	6	0.72	
	5	8.6	1	0.12	
10 mg/kg MEUG	11	9.5	4	0.42	0.31 ± 0.11
	12	7.6	2	0.27	
	13	6.9	3	0.44	
	14	8.8	2	0.23	
	15	10.4	2	0.19	
30 mg/kg MEUG	21	7.8	3	0.38	0.41 ± 0.24
	22	8.8	2	0.23	
	23	6.8	1	0.15	
	24	7.2	5	0.70	
	25	6.7	4	0.60	
100 mg/kg MEUG	31	7.0	5	0.72	0.85 ± 0.40*
	32	6.9	2	0.29	
	33	7.8	10	1.29	
	34	4.2	5	1.20	
	35	4.1	3	0.74	

\*: Significantly different from the control group at p<0.05 (Dunnet's test).

Table 17. *gpt* MFs in the liver of females *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Groups	Animal No.	Cm <sup>R</sup> colonies(x10 <sup>5</sup> )	6-TG <sup>R</sup> and Cm <sup>R</sup> colonies	Mutant Frequency (x10 <sup>-5</sup> )	Mean±S.D.
Control	41	10.5	1	0.10	0.21 ± 0.13
	42	14.9	2	0.14	
	43	13.1	5	0.38	
	44	13.3	4	0.30	
	45	18.0	2	0.11	
10 mg/kg MEUG	51	6.0	3	0.50	0.38 ± 0.18
	52	7.5	4	0.53	
	54	6.2	3	0.48	
	55	10.7	3	0.28	
	56	8.8	1	0.11	
30 mg/kg MEUG	61	9.5	4	0.42	0.53 ± 0.19
	62	7.8	2	0.25	
	63	10.3	7	0.68	
	64	8.8	6	0.68	
	65	4.8	3	0.62	
100 mg/kg MEUG	71	8.9	10	1.12	1.23 ± 0.59*
	72	3.1	7	2.25	
	73	5.0	4	0.81	
	74	5.6	5	0.90	
	75	5.7	6	1.05	

\*: Significantly different from the control group at p<0.05 (Dunnet's test).

Table 18. Spi MFs in the liver of females *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Groups	Animal No.	Plaues within XL-1 Blue MRA (x10 <sup>5</sup> )	Plaque within XL-1 Blue MRA (P2)	Mutant Frequency (x10 <sup>-5</sup> )	Mean±S.D.
Control	41	17.9	2	0.11	0.15 ± 0.07
	42	24.8	2	0.08	
	43	16.5	4	0.24	
	44	20.9	4	0.19	
	45	35.1	4	0.11	
10 mg/kg MEUG	51	9.2	0	0.00	0.15 ± 0.10
	52	18.6	4	0.22	
	54	11.3	2	0.18	
	55	18.7	2	0.11	
	56	16.1	4	0.25	
30 mg/kg MEUG	61	18.9	5	0.27	0.20 ± 0.09
	62	13.1	4	0.31	
	63	20.1	2	0.10	
	64	14.0	2	0.14	
	65	11.2	2	0.18	
100 mg/kg MEUG	71	9.5	7	0.74	0.33 ± 0.26*
	72	9.3	1	0.11	
	73	6.9	3	0.43	
	74	10.0	2	0.20	
	75	10.5	2	0.19	

\*: Significantly different from the control group at p<0.05 (Dunnet's test)

Table 19. Mutation spectra of *gpt* mutant colonies in the livers of F344 *gpt* delta rats given 0, 10, 30 or 100 mg/kg MEUG for 13 weeks

Sex		Control		10 mg/kg MEUG		30 mg/kg MEUG		100 mg/kg MEUG	
		Number (%)	Mutation frequency ( $10^{-5}$ )	Number (%)	Mutation frequency ( $10^{-5}$ )	Number (%)	Mutation frequency ( $10^{-5}$ )	Number (%)	Mutation frequency ( $10^{-5}$ )
Male	Base substitution								
	Transversions								
	GC-TA	3 <sup>a</sup> (37.5)	0.16 ± 0.16	2(18.2)	0.08 ± 0.17	3(15.0)	0.09 ± 0.13	4(15.4)	0.19 ± 0.17
	GC-CG	0	0	2(18.2)	0.12 ± 0.22	1(5.0)	0.04 ± 0.08	5(19.2)	0.20 ± 0.23
	AT-TA	0	0	0	0	3(15.0)	0.10 ± 0.16	0	0
	AT-CG	1(12.5)	0.04 ± 0.10	1(9.1)	0.02 ± 0.05	0	0	1(3.8)	0.04 ± 0.08
	Transitions								
	GC-AT	3(37.5)	0.12 ± 0.11	3(27.3)	0.15 ± 0.21	7(35.0)	0.31 ± 0.09	8(30.8)	0.29 ± 0.21
	AT-GC	1(12.5)	0.04 ± 0.10	2(18.2)	0.06 ± 0.09	4(20.0)	0.16 ± 0.10	4(15.4)	0.15 ± 0.17
	Deletion								
	Single bp	0	0	1(9.1)	0.07 ± 0.15	2(10.0)	0.06 ± 0.09	1(3.8)	0.06 ± 0.13
	Over 2 bp	0	0	0	0	0	0	1(3.8)	0.04 ± 0.08
	Insertion	0	0	0	0	0	0	0	0
	Complex	0	0	0	0	0	0	2(7.7)	0.09 ± 0.13
Total	8	0.53 ± 0.18	11	0.79 ± 0.34	20	0.79 ± 0.42	26	1.35 ± 0.60*	
Female	Base substitution								
	Transversions								
	GC-TA	2(18.2)	0.03 ± 0.04	1(9.1)	0.03 ± 0.07	3(16.7)	0.19 ± 0.25	5(17.9)	0.23 ± 0.32
	GC-CG	1(9.1)	0.01 ± 0.03	2(18.2)	0.06 ± 0.08	0	0	2(7.1)	0.13 ± 0.29
	AT-TA	0	0	0	0	2(11.1)	0.04 ± 0.09	2(7.1)	0.10 ± 0.15
	AT-CG	0	0	0	0	1(5.6)	0.02 ± 0.04	0	0
	Transitions								
	GC-AT	4(36.4)	0.06 ± 0.07	3(27.3)	0.08 ± 0.08	9(50.0)	0.23 ± 0.18	6(21.4)	0.21 ± 0.17
	AT-GC	1(9.1)	0.02 ± 0.03	2(18.2)	0.06 ± 0.08	2(11.1)	0.05 ± 0.06	8(28.6)	0.24 ± 0.28
	Deletion								
	Single bp	2(18.2)	0.06 ± 0.07	0	0	1(5.6)	0.03 ± 0.06	0	0
	Over 2 bp	0	0	2(18.2)	0.06 ± 0.08	0	0	2(7.1)	0.07 ± 0.16
	Insertion	0	0	1(9.1)	0.02 ± 0.04	0	0	1(3.6)	0.04 ± 0.09
	Complex	1(9.1)	0.02 ± 0.03	0	0	0	0	2(7.1)	0.10 ± 0.15
Total	11	0.21 ± 0.13	11	0.38 ± 0.18	18	0.53 ± 0.19	28	1.23 ± 0.59*	

<sup>a</sup> Number of colonies with independent mutations.

\*: Significantly different from the control group at  $p < 0.05$

Table 20. Final body and organ weights for F344 *gpt* delta rats treated with Furan for 13 weeks

	Male			Female		
	0 mg/kg	2 mg/kg	8 mg/kg	0 mg/kg	2 mg/kg	8 mg/kg
Final body weights (g)	357±21 <sup>a)</sup>	361±21	328±27*	195±10	189±5	187±7
Organ weights						
Absolute weights (g)						
Brain	1.92±0.06	1.94±0.06	1.88±0.03	1.78±0.04	1.77±0.04	1.75±0.03
Thymus	0.21±0.02	0.20±0.01	1.90±0.03	0.18±0.01	0.18±0.02	0.17±0.01
Lungs	1.05±0.06	1.12±0.10	1.03±0.08	0.77±0.06	0.79±0.03	0.76±0.05
Heart	0.90±0.05	0.91±0.04	0.84±0.05**	0.58±0.03	0.57±0.04	0.54±0.03
Spleen	0.65±0.03	0.66±0.04	0.67±0.04	0.43±0.04	0.41±0.02	0.46±0.03
Liver	9.46±0.71	9.75±0.86	10.37±1.00	4.75±0.39	4.69±0.23	5.81±0.28**
Adrenals	0.045±0.005	0.048±0.004	0.050±0.011	0.052±0.003	0.051±0.009	0.051±0.007
Kidneys	2.01±0.14	2.09±0.18	1.98±0.14	1.24±0.17	1.14±0.07	1.23±0.08
Testes	2.98±0.14	3.04±0.09	2.92±0.12			
Relative weights (g/100g b.w.)						
Brain	0.54±0.03	0.54±0.02	0.58±0.05	0.92±0.04	0.94±0.03	0.94±0.04
Thymus	0.059±0.005	0.057±0.004	0.057±0.008	0.091±0.006	0.093±0.006	0.089±0.009
Lungs	0.30±0.02	0.31±0.03	0.32±0.03	0.40±0.03	0.42±0.02	0.41±0.03
Heart	0.25±0.01	0.25±0.01	0.26±0.02	0.30±0.02	0.30±0.01	0.29±0.01
Spleen	0.18±0.01	0.18±0.01	0.21±0.01**	0.22±0.02	0.22±0.01	0.24±0.02**
Liver	2.65±0.06	2.70±0.11	3.16±0.12**	2.44±0.16	2.50±0.11	3.11±0.13**
Adrenals	0.013±0.001	0.013±0.001	0.015±0.004	0.027±0.002	0.026±0.003	0.027±0.004
Kidneys	0.56±0.03	0.58±0.04	0.605±0.03*	0.64±0.10	0.61±0.03	0.66±0.05
Testes	0.84±0.03	0.85±0.05	0.90±0.07			

a): Mean ± SD

\*,\*\*): Significantly different from the 0 mg/kg group at  $p < 0.05$  and  $0.01$ , respectively.

Table 21. Hematology for F344 *gpt* delta rats treated with Furan for 13 weeks

	Male			Female		
	0 mg/kg	2 mg/kg	8 mg/kg	0 mg/kg	2 mg/kg	8 mg/kg
RBC ( $\times 10^4/\mu\text{L}$ )	1003 $\pm$ 43 <sup>a)</sup>	1003 $\pm$ 56	937 $\pm$ 114	881 $\pm$ 54	883 $\pm$ 36	847 $\pm$ 75
Hb (g/dL)	15.6 $\pm$ 0.6	16.1 $\pm$ 0.7	15.4 $\pm$ 1.8	15.2 $\pm$ 0.9	15.0 $\pm$ 0.6	14.7 $\pm$ 1.3
Ht (%)	52.9 $\pm$ 2.2	54.0 $\pm$ 3.1	51.2 $\pm$ 5.7	49.3 $\pm$ 2.9	49.8 $\pm$ 2.0	47.5 $\pm$ 4.0
MCV (fL)	52.7 $\pm$ 0.4	53.8 $\pm$ 0.4*	54.7 $\pm$ 0.3**	56.0 $\pm$ 0.4	56.4 $\pm$ 0.3	56.1 $\pm$ 0.5
MCH (pg)	15.5 $\pm$ 0.5	16.1 $\pm$ 0.3**	16.4 $\pm$ 0.3*	17.2 $\pm$ 0.3	16.9 $\pm$ 0.3	17.3 $\pm$ 0.3
MCHC (g/dL)	29.4 $\pm$ 0.9	29.9 $\pm$ 0.5	30.0 $\pm$ 0.5	30.8 $\pm$ 0.6	30.0 $\pm$ 0.7*	30.9 $\pm$ 0.4
PLT ( $\times 10^4/\mu\text{L}$ )	74.6 $\pm$ 8.6	78.2 $\pm$ 4.0	87.2 $\pm$ 6.6**	86.0 $\pm$ 11.2	76.8 $\pm$ 4.5	83.5 $\pm$ 9.9
WBC ( $\times 10^2/\mu\text{L}$ )	46.6 $\pm$ 4.9	58.4 $\pm$ 10.1**	54.6 $\pm$ 9.9	40.4 $\pm$ 9.8	39.5 $\pm$ 9.8	35.4 $\pm$ 10.5
Differential cell counts (%)						
Band	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Seg	37.1 $\pm$ 6.2	39.9 $\pm$ 8.6	35.6 $\pm$ 9.0	28.5 $\pm$ 7.8	28.6 $\pm$ 7.8	27.7 $\pm$ 4.7
Eosino	1.4 $\pm$ 0.7	1.2 $\pm$ 0.8	1.0 $\pm$ 0.6	1.6 $\pm$ 1.3	0.8 $\pm$ 0.6	1.0 $\pm$ 1.1
Baso	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Lymph	61.0 $\pm$ 6.0	58.6 $\pm$ 8.7	63.3 $\pm$ 9.0	69.4 $\pm$ 7.6	70.2 $\pm$ 8.3	70.8 $\pm$ 4.5
Mono	0.5 $\pm$ 0.6	0.3 $\pm$ 0.4	0.2 $\pm$ 0.2	0.5 $\pm$ 0.5	0.4 $\pm$ 0.5	0.4 $\pm$ 0.4
Ebl	1.6 $\pm$ 1.5	2.4 $\pm$ 1.7	1.6 $\pm$ 1.5	4.0 $\pm$ 2.6	2.1 $\pm$ 1.5	2.0 $\pm$ 1.6

a): Mean  $\pm$  SD

\*,\*\*: Significantly different from the 0 mg/kg group at  $p < 0.05$  and  $0.01$ , respectively.



Table 22. Serum biochemistry for F344 *gpt* delta rats treated with Furan for 13 weeks

	Male			Female		
	0 mg/kg	2 mg/kg	8 mg/kg	0 mg/kg	2 mg/kg	8 mg/kg
TG (g/dL)	7.1±0.1 <sup>a)</sup>	7.1±0.3	7.0±0.2	6.7±0.2	7.0±0.2*	7.1±0.3**
A/G	2.2±0.1	2.3±0.1	2.5±0.2**	2.4±0.2	2.8±0.2**	3.0±0.2**
ALB (g/dL)	4.9±0.1	4.9±0.1	5.0±0.2	4.7±0.2	5.1±0.1**	5.3±0.2**
T-Bil (mg/dL)	0.05±0.01	0.05±0.01	0.06±0.01**	0.05±0.01	0.07±0.01**	0.07±0.01**
T-Cho (mg/dL)	72±6	71±7	71±16	104±16	93±6	91±8
Glu (mg/dL)	161±17	148±18	129±13**	111±9	113±17	105±11
TG (mg/dL)	106±30	103±52	64±23*	31±9	21±4*	28±11
PL (mg/dL)	117±8	116±17	113±21	177±20	162±10*	158±10**
BUN (mg/dL)	17.5±1.4	18.4±2.4	26.4±21.6*	16.5±1.9	15.9±1.6	15.7±1.7
CRN (mg/dL)	0.31±0.02	0.30±0.02	0.38±0.37*	0.29±0.05	0.29±0.03	0.27±0.05
Ca (mg/dL)	11.0±0.2	11.3±0.4	11.0±0.3	10.5±0.2	10.7±0.2	11.1±0.3**
P (mg/dL)	6.1±0.7	6.7±0.6	6.7±0.7	6.5±0.7	6.2±0.5	6.5±0.7
Na (mEq/dL)	145±1	146±1	146±1	145±1	146±1	145±1
K (mEq/dL)	4.4±0.2	4.3±0.4	4.2±0.2	4.3±0.4	4.0±0.3	4.1±0.4
Cl (mEq/dL)	104±1	103±1	105±1	107±1	106±1	105±2
AST (IU/L)	98±20	91±15	110±23	83±6	83±11	86±8
ALT (IU/L)	57±12	50±5	51±9	42±4	38±5	36±4*
ALP (IU/L)	537±49	626±73**	630±64**	461±73	438±59	442±61
γ-GTP (IU/L)	3.0±0.0	3.0±0.0	3.0±0.0	3.0±0.0	3.0±0.0	3.0±0.0

<sup>a)</sup>: Mean ± SD

\*,\*\*): Significantly different from the 0 mg/kg group at  $p < 0.05$  and  $0.01$ , respectively.

Table 23. Histopathology in the livers of F344 *gpt* delta rats treated with Furan for 13 weeks

		Males			Females		
		0 mg/kg	2 mg/kg	8 mg/kg	0 mg/kg	2 mg/kg	8 mg/kg
Number of animals examined		10	10	10	10	10	10
Liver							
Bile ducts	Cholangiofibrosis	0	6	7	0	0	4
	Bile duct proliferation	1	4	9	2	2	10
	Oval cell proliferation	0	5	10	0	5	10
Hepatocytes	Apoptosis	0	0	5	0	0	6
	Vacuolation	0	1	5	0	0	0
Kupffer cells	Pigmentation	0	0	5	0	10	10

Table 24. Micronucleus test with bone marrow in F344 *gpt* delta rats treated with Furan for 13 weeks

	Male			Female		
	No. of animals examined	MNPCE (%)	PCE/PCE + NCE (%)	No. of animals examined	MNPCE (%)	PCE/PCE + NCE (%)
0 mg/kg	5	0.13 ± 0.07 <sup>a)</sup>	22.8 ± 6.8	5	0.14 ± 0.09	26.3 ± 6.1
2 mg/kg	5	0.18 ± 0.07	23.5 ± 7.4	5	0.14 ± 0.02	28.1 ± 7.2
8 mg/kg	5	0.32 ± 0.07*	20.8 ± 3.3	5	0.17 ± 0.08	39.0 ± 3.1**

MNPCE : Micronucleated polychromatic erythrocytes, PCE : Polychromatic erythrocytes, NCE : Normochromatic erythrocytes

a): Mean ± S.D.

\*,\*\*: Significantly different from the 0 mg/kg group at  $p < 0.05$  and  $0.01$ , respectively.

Table 25. *gpt* mutant frequencies in the livers of F344 *gpt* delta male rats treated with Furan for 13 weeks

	Animal No.	Cm <sup>R</sup> colonies (x 10 <sup>5</sup> )	6-TG <sup>R</sup> and Cm <sup>R</sup> colonies	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	1	7.16	N.D.	-	
	2	5.85	1	0.17	
	3	4.95	1	0.20	
	4	9.05	1	0.11	
	5	7.38	1	0.14	0.15 ± 0.04
2 mg/kg	11	8.46	1	0.12	
	12	6.57	N.D.	-	
	13	15.57	1	0.06	
	14	10.44	3	0.29	
	15	9.54	N.D.	-	0.16 ± 0.12
8 mg/kg	21	10.44	2	0.19	
	22	7.07	1	0.14	
	23	6.21	3	0.48	
	24	7.25	2	0.28	
	25	7.83	4	0.51	0.29 ± 0.19

N.D.: No mutant colonies were detected on the plate, with those data being excluded from the calculation of mutant frequency.