

Table 26. Spi<sup>r</sup> mutant frequencies in the livers of F344 *gpt* delta male rats treated with Furan for 13 weeks

	Animal No.	Plaues within XL-1 Blue MRA (x 10 <sup>5</sup> )	Plaque within WL95 (P2)	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	1	11.25	N.D.	-	
	2	6.39	2	0.31	
	3	12.78	1	0.08	
	4	10.17	N.D.	-	
	5	4.41	N.D.	-	0.20 ± 0.17
2 mg/kg	11	11.25	1	0.09	
	12	4.77	N.D.	-	
	13	5.67	1	0.18	
	14	7.56	2	0.26	
	15	6.12	N.D.	-	0.18 ± 0.09
8 mg/kg	21	15.03	3	0.20	
	22	6.12	N.D.	-	
	23	5.94	3	0.51	
	24	7.38	2	0.27	
	25	6.03	N.D.	-	0.33 ± 0.16

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

Table 27. *gpt* mutant frequencies in the livers of F344 *gpt* delta female 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	31	2.30	1	0.44	
	32	3.15	1	0.32	
	33	3.60	1	0.28	
	34	6.17	N.D.	-	
	35	3.60	N.D.	-	0.34 ± 0.08
2 mg/kg	41	3.65	3	0.82	
	42	3.33	2	0.60	
	43	1.35	N.D.	-	
	44	2.97	2	0.67	
	45	2.48	N.D.	-	0.70 ± 0.11
8 mg/kg	51	2.57	N.D.	-	
	52	6.89	3	0.44	
	53	3.83	3	0.78	
	54	3.15	N.D.	-	
	55	6.35	3	0.47	0.56 ± 0.19

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

Table 28. Spi- mutant frequencies in the livers of F344 *gpt* delta female rats treated with Furan for 13 weeks

	<b>Animal No.</b>	<b>Plaues within XL-1 Blue MRA (x 10<sup>5</sup>)</b>	<b>Plaque within WL95 (P2)</b>	<b>Mutant Frequency (x 10<sup>-5</sup>)</b>	<b>Mean ± S.D.</b>
<b>0 mg/kg</b>	31	1.35	0	-	
	32	7.47	5	0.67	
	33	3.60	1	0.28	
	34	7.29	N.D.	-	
	35	6.03	4	0.66	0.54 ± 0.22
<b>2 mg/kg</b>	41	3.69	1	0.27	
	42	7.02	2	0.28	
	43	1.89	N.D.	-	
	44	5.67	1	0.18	
	45	6.21	N.D.	-	0.24 ± 0.06
<b>8 mg/kg</b>	51	6.48	N.D.	-	
	52	3.69	3	0.81	
	53	5.22	2	0.38	
	54	2.97	N.D.	-	
	55	0.99	N.D.	-	0.60 ± 0.30

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

Table 29. Final body and liver weights for F344 *gpt* delta rats treated with Furan

	4 weeks		8 weeks	
	0 mg/kg	8 mg/kg	0 mg/kg	8 mg/kg
<b>Number of animals</b>	10	10	5	5
<b>Final body weights (g)</b>	249 ± 10 <sup>a)</sup>	244 ± 9	302 ± 11	296 ± 6
<b>Liver weights</b>				
<b>Absolute weights (g)</b>				
Whole	10.15 ± 0.82	10.68 ± 0.65	11.36 ± 0.12	12.90 ± 0.35**
Left lobe	3.32 ± 0.31	3.42 ± 0.35	3.77 ± 0.12	4.40 ± 0.32**
Median lobe	3.75 ± 0.29	4.13 ± 0.21**	4.13 ± 0.21	4.91 ± 0.21**
Right lobe	2.18 ± 0.19	2.34 ± 0.23	2.45 ± 0.20	2.76 ± 0.12*
Caudate lobe	0.91 ± 0.18	0.78 ± 0.112	1.01 ± 0.14	0.82 ± 0.08*
<b>Relative weights (g/100g b.w.)</b>				
Whole	4.07 ± 0.26	4.38 ± 0.14**	3.76 ± 0.12	4.35 ± 0.06**
Left lobe	1.33 ± 0.11	1.40 ± 0.12	1.25 ± 0.03	1.48 ± 0.08**
Median lobe	1.50 ± 0.09	1.70 ± 0.06**	1.37 ± 0.06	1.66 ± 0.07**
Right lobe	0.87 ± 0.07	0.96 ± 0.07*	0.81 ± 0.08	0.93 ± 0.05*
Caudate lobe	0.36 ± 0.07	0.32 ± 0.04	0.33 ± 0.05	0.28 ± 0.03*

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

**Table 30. Histopathology in the livers of F344 *gpt* delta rats treated with Furan**

	4 weeks		8 weeks	
	0 mg/kg	8 mg/kg	0 mg/kg	8 mg/kg
<b>Number of animals examined</b>	5	5	5	5
<b>Left lobe</b>				
Oval cell proliferation	0	2	0	5
Peripheral basophilic change	0	5	0	5
Centrilobular hepatocyte vacuolation, scattered	0	0	0	3
Hepatocyte apoptosis	0	5	0	2
Subcapsular infiltration of inflammatory cells	0	5	0	3
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<b>Median lobe</b>				
Oval cell proliferation	0	2	0	1
Peripheral basophilic change	0	5	0	2
Centrilobular hepatocyte vacuolation, scattered	0	0	0	0
Hepatocyte apoptosis	0	4	0	0
Subcapsular infiltration of inflammatory cells	0	0	0	0
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Table 30. Histopathology in the livers of F344 *gpt* delta rats treated with Furan (to be continued)

	4 weeks		8 weeks	
	0 mg/kg	8 mg/kg	0 mg/kg	8 mg/kg
<b>Right lobe</b>				
Oval cell proliferation	0	2	0	4
Peripheral basophilic change	0	5	0	3
Centrilobular hepatocyte vacuolation, scattered	0	0	0	2
Hepatocyte apoptosis	0	5	0	3
Subcapsular infiltration of inflammatory cells	0	1	0	0
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<b>Caudate lobe</b>				
Cholangiofibrosis	0	0	0	1
Oval cell proliferation	0	1	0	4
Peripheral basophilic change	0	5	0	5
Centrilobular hepatocyte vacuolation, scattered	0	0	0	3
Hepatocyte apoptosis	0	5	0	0
Subcapsular infiltration of inflammatory cells	0	5	0	4

Table 31. *gpt* mutant frequencies in the caudate lobes of F344 *gpt* delta male rats treated with Furan for 4 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	4.14	1	0.24	0.33 ± 0.08
	2	6.48	2	0.31	
	3	5.45	2	0.37	
	4	7.20	3	0.42	
	5	4.82	N.D.	-	
8 mg/kg	16	5.76	N.D.	-	0.35 ± 0.09
	17	3.83	1	0.26	
	18	5.18	N.D.	-	
	19	5.58	2	0.36	
	20	4.64	2	0.43	

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

Table 32. Spi<sup>r</sup> mutant frequencies in the caudate lobes of F344 *gpt* delta male rats treated with Furan for 4 weeks

	<b>Animal No.</b>	<b>Plaues within XL-1 Blue MRA (x 10<sup>5</sup>)</b>	<b>Plaque within WL95 (P2)</b>	<b>Mutant Frequency (x 10<sup>-5</sup>)</b>	<b>Mean ± S.D.</b>
<b>0 mg/kg</b>	1	15.66	4	0.26	<b>0.23 ± 0.14</b>
	2	15.84	2	0.13	
	3	13.23	N.D.	-	
	4	23.94	3	0.13	
	5	12.06	5	0.41	
<b>8 mg/kg</b>	16	10.62	1	0.09	<b>0.22 ± 0.12</b>
	17	12.15	2	0.16	
	18	8.10	3	0.37	
	19	13.41	N.D.	-	
	20	7.56	2	0.26	

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



Table 33. *gpt* mutant frequencies in the left lobes of F344 *gpt* delta male rats treated with Furan for 8 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	11	7.20	2	0.28	
	12	3.65	2	0.55	
	13	5.27	3	0.57	
	14	2.52	1	0.40	
	15	4.95	2	0.40	0.44 ± 0.12
8 mg/kg	26	4.23	1	0.24	
	27	6.71	2	0.30	
	28	4.05	N.D.	-	
	29	6.30	N.D.	-	
	30	7.11	N.D.	-	0.27 ± 0.04

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

Table 34. Spi<sup>r</sup> mutant frequencies in the left lobes of F344 *gpt* delta male rats treated with Furan for 8 weeks

	Animal No.	Plaues within XL-1 Blue MRA (x 10 <sup>5</sup> )	Plaque within WL95 (P2)	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	11	14.13	4	0.28	
	12	10.62	12	1.13	
	13	10.71	2	0.19	
	14	7.38	N.D.	-	
	15	5.04	N.D.	-	0.53 ± 0.52
8 mg/kg	26	11.25	3	0.27	
	27	10.44	2	0.19	
	28	9.27	1	0.11	
	29	9.90	1	0.10	
	30	10.80	1	0.09	0.15 ± 0.08

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

Table 35. *gpt* mutant frequencies in the caudate lobes of F344 *gpt* delta male rats treated with Furan for 8 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	11	9.27	3	0.32	0.24 ± 0.10
	12	4.82	1	0.21	
	13	11.25	4	0.36	
	14	8.24	1	0.12	
	15	5.85	1	0.17	
8 mg/kg	26	5.27	1	0.19	0.37 ± 0.16
	27	3.78	2	0.53	
	28	5.04	N.D.	—	
	29	4.28	2	0.47	
	30	10.04	3	0.29	

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

Table 36. Spi<sup>-</sup> mutant frequencies in the caudate lobes of F344 *gpt* delta male rats treated with Furan for 8 weeks

	Animal No.	Plaues within XL-1 Blue MRA (x 10 <sup>5</sup> )	Plaque within WL95 (P2)	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	11	12.06	N.D.	-	
	12	7.11	15	2.11	
	13	20.61	3	0.15	
	14	11.79	6	0.51	
	15	7.02	4	0.57	0.83 ± 0.87
8 mg/kg	26	10.44	4	0.38	
	27	13.23	1	0.08	
	28	9.63	3	0.31	
	29	8.82	1	0.11	
	30	15.57	1	0.06	0.19 ± 0.15

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

**Table 37. Final body and liver weights for B6C3F<sub>1</sub> *gpt* delta mice treated with Furan for 4 weeks**

	Male			Female		
	0 mg/kg	2 mg/kg	15 mg/kg	0 mg/kg	2 mg/kg	15 mg/kg
<b>Final body weight (g)</b>	28.2 ± 1.4 <sup>a)</sup>	28.9 ± 0.7	29.7 ± 1.9	21.8 ± 1.0	22.2 ± 1.3	22.5 ± 0.9
<b>Organ weight</b>						
<b>Absolute weight (g)</b>						
<b>Liver</b>	1.28 ± 0.06	1.32 ± 0.04	1.56 ± 0.01**	1.06 ± 0.07	1.04 ± 0.10	1.15 ± 0.07*
<b>Relative weight (g/10g b.w.)</b>						
<b>Liver</b>	0.45 ± 0.02	0.46 ± 0.02	0.53 ± 0.02**	0.46 ± 0.15	0.47 ± 0.02	0.51 ± 0.01**

<sup>a)</sup>: Mean ± S.D.

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

**Table 38. Final body and liver weights for B6C3F<sub>1</sub> *gpt* delta mice treated with Furan for 13 weeks**

	Male			Female		
	0 mg/kg	2 mg/kg	15 mg/kg	0 mg/kg	2 mg/kg	15 mg/kg
<b>Final body weight (g)</b>	35.7 ± 1.3 <sup>a)</sup>	34.4 ± 1.7	33.1 ± 1.0*	25.2 ± 2.0	24.3 ± 0.9	24.8 ± 0.5
<b>Organ weight</b>						
<b>Absolute weight (g)</b>						
<b>Liver</b>	1.59 ± 0.03	1.64 ± 0.10	1.73 ± 0.15	1.12 ± 0.15	1.09 ± 0.05	1.31 ± 0.04
<b>Relative weight (g/10g b.w.)</b>						
<b>Liver</b>	0.45 ± 0.03	0.48 ± 0.03	0.52 ± 0.04**	0.44 ± 0.03	0.45 ± 0.02	0.53 ± 0.02**

<sup>a)</sup>: Mean ± S.D.

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

**Table 39. Histopathology in the livers of B6C3F<sub>1</sub> *gpt* delta mice treated with Furan for 4 weeks**

	Male			Female		
	0 mg/kg	2 mg/kg	15 mg/kg	0 mg/kg	2 mg/kg	15 mg/kg
<b>Number of animals examined</b>	5	5	5	5	5	5
<b>Liver</b>						
<b>Centrilobular hepatocyte hypertrophy</b>	0	2	5	0	0	1
<b>Subcapsular infiltration of inflammatory cells</b>	0	0	1	0	0	3

**Table 40. Histopathology in the livers of B6C3F<sub>1</sub> *gpt* delta mice treated with Furan for 13 weeks**

	Male			Female		
	0 mg/kg	2 mg/kg	15 mg/kg	0 mg/kg	2 mg/kg	15 mg/kg
<b>Number of animals examined</b>	5	5	5	5	5	5
<b>Liver</b>						
<b>Centrilobular hepatocyte hypertrophy</b>	0	1	0	0	0	0
<b>Focal necrosis</b>	0	0	1	0	0	0
<b>Subcapsular infiltration of inflammatory cells</b>	0	5	5	0	4	5



Table 41. *gpt* mutant frequencies in the livers of B6C3F<sub>1</sub> *gpt* delta male mice treated with Furan for 4 weeks

Dose	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	8.19	2	0.24	0.37 ± 0.23
	2	3.24	2	0.62	
	3	4.77	2	0.42	
	4	24.21	1	0.04	
	5	3.87	2	0.52	
2 mg/kg	11	15.57	4	0.26	0.31 ± 0.28
	12	3.83	3	0.78	
	13	22.37	4	0.18	
	14	3.33	1	0.30	
	15	20.97	1	0.05	
15 mg/kg	21	14.45	6	0.42	0.27 ± 0.13
	22	15.30	N.D.	-	
	23	18.63	4	0.21	
	24	16.92	3	0.18	
	25	10.53	N.D.	-	

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

**Table 42. Spi<sup>r</sup> mutant frequencies in the livers of B6C3F<sub>1</sub> *gpt* delta male mice treated with Furan for 4 weeks**

Dose	Animal No.	Plaques within XL-1 Blue MRA (x 10 <sup>5</sup> )	Plaques within WL95 (P2)	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	1	8.01	N.D.	-	
	2	4.41	N.D.	-	
	3	2.97	N.D.	-	
	4	21.51	8	0.37	
	5	4.50	2	0.44	0.41 ± 0.23
2 mg/kg	11	17.19	8	0.47	
	12	3.96	2	0.51	
	13	14.58	2	0.14	
	14	3.24	1	0.31	
	15	23.40	12	0.51	0.39 ± 0.16
15 mg/kg	21	10.98	5	0.46	
	22	7.92	3	0.38	
	23	29.97	7	0.23	
	24	20.79	9	0.43	
	25	7.56	4	0.53	0.41 ± 0.11

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

Table 43. *gpt* mutant frequencies in the livers of B6C3F1 *gpt* delta female mice treated with Furan for 4 weeks

Dose	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	31	2.16	N.D.	-	0.33 ± 0.14
	32	7.70	3	0.39	
	33	14.09	5	0.35	
	34	23.27	3	0.13	
	35	6.93	3	0.43	
2 mg/kg	41	6.39	1	0.16	0.22 ± 0.08
	42	14.27	3	0.21	
	43	3.69	1	0.27	
	44	18.81	6	0.32	
	45	14.94	2	0.13	
15 mg/kg	51	25.25	7	0.28	0.41 ± 0.12
	52	17.51	9	0.51	
	53	14.40	5	0.35	
	54	4.68	N.D.	-	
	55	7.97	4	0.50	

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

**Table 44. Spi<sup>-</sup> mutant frequencies in the livers of B6C3F1 *gpt* delta female mice treated with Furan for 4 weeks**

Dose	Animal No.	Plaques within XL-1 Blue MRA (x 10 <sup>5</sup> )	Plaques within WL95 (P2)	Mutant Frequency (x 10 <sup>-5</sup> )	Mean ± S.D.
0 mg/kg	31	1.68	5	1.07	0.46 ± 0.34
	32	11.79	3	0.25	
	33	21.96	8	0.36	
	34	23.13	6	0.26	
	35	10.62	4	0.38	
2 mg/kg	41	10.89	7	0.64	0.39 ± 0.24
	42	16.74	3	0.18	
	43	3.15	1	0.32	
	44	20.07	3	0.15	
	45	17.28	11	0.64	
15 mg/kg	51	30.42	10	0.33	0.37 ± 0.11
	52	21.60	7	0.32	
	53	16.56	5	0.30	
	54	6.39	N.D.	0.00	
	55	12.87	7	0.54	

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