

Table 4

Selected treatment-related nonneoplastic lesions of liver and thyroid in male and female rats and mice.

Dose (mg/kg)	0	3	15	50
Male rat				
Liver	49	50	50	50
Numbered examined				
Hepatocyte hypertrophy	1 (2%)* [1.0] ^a	44 (88%)* [2.1]	50 (100%)* [3.0]	50(100 %)* [3.8]
Basophilic focus	16(33%)	21(42%)	11(22%)	11(22%)
Clear cell focus	39 (80%)*	37 (74%)	35 (70%)	29 (58%)*
Eosinophilic focus	3 (6%)*	3 (6%)	12 (24%)*	15 (30%)*
Hyperplasia, nodular	0	0	3	0
Fatty change	32 (65%)*	37 (74%)	48 (96%)*	48 (96%)*
Cholangiofibrosis	0	0	1 (2%)	1 (2%)
Inflammation chronic	1 (2%)*	2 (4%)	0	5 (10%)
Pigmentation	0 **	0	1 (2%)	6 (12%)*
Oval cell hyperplasia	0 *	0	2 (4%)	3 (6%)
Thyroid, Number examined	45	45	48	46
Thyroid gland follicle hypertrophy	1**(2%) [1.2]	26**(58%) [1.4]	34**(70%) [2.0]	23**(50%) [2.4]
Female Rat				
Liver	50	49	50	47
Number examined				
Hepatocyte hypertrophy	0 **	48 (98%)* [1.9]	49 (100%)* [3.0]	45 (96%)* [3.9]
Basophilic focus	44 (88%)	43 (88%)	40 (80%)	33 (70%)*
Clear cell focus	35 (70%)	21 (43%)	26 (52%)	31 (66%)
Eosinophilic focus	5 (10%)*	7 (14%)	21 (42%)*	31 (66%)*
Fatty change	15 (30%)*	12 (24%)	28 (56%)*	39 (83%)*
Cholangiofibrosis	0 **	0	0	3 (6%)
Hyperplasia, nodular	0 **	0	2 (4%)	7 (15%)*
Hepatocyte Necrosis	4 (8%)*	2 (4%)	1 (2%)	8 (17%)
Bile duct cyst	2 (4%)*	2 (4%)	5 (10%)	7 (15%)*
Oval cell hyperplasia	1 (2%)	3 (6%)	3 (6%)	10 (21%)*
Uterus	50	50	50	49
Numbered examined				
Vaginal polyp	0	0	0	1(2%)
Uterus histiocytic sarcoma	0*	0	0	2(4%)
Uterus metaplasia	0**	0	1(2%)	4(8%)*
Cervix Hyperplasia	0*	0	0	2 (4%)
Thyroid, Number examined	45	49	47	42
Thyroid gland Follicle hypertrophy	8(16%)* [1.1]	17 (34%) [1.3]	22**(47%) [1,4]	35**(83%) [1.9]

Dose (mg/kg)	0	3	30	100
Male mouse				
Liver	50	49	50	49
Number examined				
Centrilobular, hepatocyte, hypertrophy	0**	28(56%)* [1.6]	46(92%)* [3.8]	48(96%)* [3.9]
Fatty change	17(34%)	25(50%)	17(34%)	5(10%)
Necrosis, focal	2(4%)*	2(4%)	16(32%)*	2(4%)
Kupffer cell pigmentation	5(10%)*	15(30%)*	33(66%)*	25(50%)*
Clear cell focus	10	13	20*	7
Thyroid				
Number examined				
Thyroid gland Follicle, hypertrophy	25** [1.3]	35* [1.5]	41* [1.5]	45* [2.4]
Female mouse				
Liver	50	49	50	49
Number examined				
Centrilobular hypertrophy	0**	7(14%)* [1.0]	45(90%)* [2.0]	47(96%)* [3.6]
Eosinophilic focus	3(6%)*	2(4%)	16(32%)*	15(31%)*
Fatty change	18(36%)*	18(37%)	39(78%)*	20(41%)*
Hemorrhage	4(8%)*	1(2%)	4(8%)	5(10%)

Table 4 (continued)

Dose (mg/kg)	0	3	30	100
Necrosis, focal	1(2%)*	1(2%)	4(8%)	3(6%)
Kupffer cell pigmentation	3(6%)*	10(20%)*	24(48%)*	27(55%)*
Thyroid gland	50	49	48	47
Number examined				
Thyroid gland Follicle, hypertrophy	24 [1.3]	31 [1.5]	37** [1.5]	42** [2.4]

Trend statistic under control column; pairwise statistic under dose columns:
*p ≤ 0.05 **p ≤ 0.01.

^a Average severity grade of lesions in affected animals: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked.