

Table 3

Treatment-related carcinogenic effects in male and female Wistar Han rats and B6C3F1 mice.

Dose (mg/kg)	0	3	15	50
Male rats liver, Number examined	49	50	50	50
Hepatocellular adenoma	3* (6%)	2 (4%)	4 (8%)	8 (16%)
Hepatocellular carcinoma	0	0	0	2 (4%)
Hepatocellular adenoma or carcinoma	3** (6%)	2 (4%)	4 (8%)	9* (18%)
Hepatocholangioma	0*	0	0	2
Hepatocholangioma, hepatocellular adenoma or hepatocellular carcinoma ^a	3** (6%)	2 (4%)	4 (8%)	11* (22%)
Male rats thyroid, Number examined	45	45	48	46
Thyroid gland:	1*	3	2	6*
follicular cell adenoma	(2%)	(7%)	(4%)	(13%)
Thyroid gland:	0	2	1	0
follicular cell carcinoma	(0%)	(4%)	(2%)	(0%)
Thyroid gland	1	5	3	6*
follicular cell adenoma or carcinoma ^b	(2%)	(11%)	(6%)	(13%)
Male rats pituitary, Number examined	49	49	50	50
Pituitary gland: pars distalis or unspecified site adenoma ^c	19** (39%)	12 (24%)	22 (44%)	35** (70%)
Female rats liver, Number examined	50	49	50	47
Hepatocellular adenoma	3** (6%)	2 (4%)	8 (16%)	16** (34%)
Hepatocellular carcinoma	0**	0	1 (2%)	6** (13%)
Hepatocellular adenoma or carcinoma	3** (6%)	2 (4%)	8 (16%)	17** (36%)
Cholangiocarcinoma	0*	0	0	2 (4%)
Hepatocholangioma	0**	0	0	8** (17%)
Hepatocholangioma, hepatocellular adenoma, or hepatocellular carcinoma ^d	3** (6%)	2 (4%)	8 (16%)	21** (45%)
Female rats uterus, Number examined	50	50	50	49
Uterus, metaplasia, squamous	0	2 (4%)	5* (10%)	6* (12%)
Cervix, squamous hyperplasia	2** (4%)	3 (6%)	4 (8%)	8* (16%)
Uterus polyp, stromal	4 (8%)	12* (24%)	11* (22%)	9 (18%)
Uterus, stromal sarcoma	0	0	1 (2%)	0
Uterus stromal polyp or stromal sarcoma ^e	4 (8%)	12* (24%)	12* (24%)	9 (18%)
Vaginal polyp	0*	0	0	2 (4%)

Dose (mg/kg)	0	3	30	100
Male mice liver, Number examined	50	50	50	50
Hepatocellular adenoma	23** (46%)	35* (70%)	49** (98%)	40** (80%)
Hepatocellular carcinoma	18** (36%)	15 (30%)	30* (60%)	45** (90%)
Hepatoblastoma	1** (2%)	1 (2%)	16** (32%)	5* (10%)
Hepatocellular adenoma, carcinoma, or hepatoblastoma ^f	31** (62%)	40 (80%)	49** (98%)	47** (94%)
Female mice liver, Number examined	50	49	50	49
Hepatocellular adenoma	5** (10%)	7 (14%)	32** (64%)	46** (94%)
Hepatocellular carcinoma	4** (8%)	2 (4%)	6 (12%)	27** (55%)

Table 3 (continued)

Dose (mg/kg)	0	3	30	100
Hepatocellular adenoma or carcinoma ^g	8** (16%)	8 (16%)	33** (66%)	47** (96%)

*P ≤ 0.05; **P ≤ 0.01.

Historical Data:

Male rats – liver tumors

^aHistorical controls, gavage corn oil: ^a3/99 (3.1% ± 4.3%), range.0%–6%.

^aHistorical controls, all routes:^a4/299 (1.4% ± 2.5%), range.0%–6%.

Male rats – Thyroid tumors

^bHistorical controls, gavage corn oil: 4/95 (4.1% ± 2.7%), range.2%–6%.

^bHistorical controls, all routes: 5/295 (1.7% ± 2.4%), range.0%–6%.

Male rats – Pituitary tumors

^cHistorical controls, gavage corn oil: 40/99 (40.4% ± 2.3%), range 39%–42%.

^cHistorical controls, all routes:101/298 (33.9% ± 5.7%), range.28%–42%.

Female rats – liver tumors

^dHistorical controls, gavage corn oil:4/100 (4.0% ± 2.8%), range.2%–6%.

^dHistorical controls, all routes:6/300 (2.0% ± 2.2%), range.0%–6%.

Female rats - uterus

Historical controls, all routes.

^e29/194 (15.1% ± 6.3%), range.8%–22%.

Male mice – liver tumors

^fHistorical controls, gavage corn oil: 221/300 (73.7% ± 6.1%), range.62%–78%.

^fHistorical controls, all routes: 545/700 (77.3% ± 8.3%), range.62%–90%.

Female mice – liver tumors

^gHistorical controls, gavage corn oil: 85/300 (28.3% ± 10.2%), range.16%–40%.

^gHistorical controls, all routes: 320/698 (45.9% ± 21.9%), range.16%–82%.