R41

Teratological Study of Piroctone Olamine in Rats

- Subcutaneous Administration during Organogenesis -

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Summary

Piroctone olamine (PO) was administered subcutaneously at 2000, 500, and 100 mg/kg/day to pregnant rats during organogenesis, and its effects on the dams and fetuses were examined. The fetuses were delivered by cesarean section on day 21 of gestation.

Induration due to the drug residue was noted at the injection site of treated animals at any dose. During the administration period, the animals given 2000 mg/kg/day exhibited depression of body weight gain and reduction in food consumption, and those at 500 mg/kg/day also showed slightly reduced food consumption. As to the organ weights, noted were a decrease in the thymus weight and increases in the spleen and adrenal weights at 2000 and 500 mg/kg/day, and slight increases in the liver, kidney, and urinary bladder weights at 2000 mg/kg/day.

The fetal findings were decreases in the number of living fetuses and in the body weight of the living fetuses of either sex at 2000 mg/kg/day. No differences occurred between any treated group and the control group in frequencies of fetuses with external, visceral, or skeletal abnormalities. There appeared skeletal variations, but the frequencies were not dose-related. The delayed ossification in the treated groups was noted in the odontoid process, 5th sternebra, 1st metatarsal, or proximal phalanges of the hindlimbs.

This report deals with effects on dams and fetuses of the subcutaneous administration of piroctone olamine (PO) to pregnant Sprague-Dawley rats during organogenesis.

Materials and Methods

1. Compound

PO supplied by Nippon Hoechst Co., Ltd. (Lot No. N003) was used. The compound forms as white crystals and has the chemical structure shown in Fig. 1.

2. Animal

Eight-week-old Sprague-Dawley rats were obtained from CLEA Japan, Inc. After acclimation, healthy females of 10 - 13 weeks old weighing 198 - 282 g were allowed to mate with males of the same strain, one to one, overnight, and the females in which copulation was confirmed by the presence of sperm in the vaginal smear were separated from the males. The day of the confirmation of copulation was designated as day 0 of gestation. The numbers of the females treated were 26 in the control group, 22 at 100 mg/kg/day, 21 at 500 mg/kg/day, and 24 at 2000 mg/kg/day.

Throughout the acclimation and experimental periods, the animals were housed in a room maintained at a temperature of 22±1°C and a relative humidity of 55±5%, and given a pelleted diet (CLEA Stock Diet CE-2, CLEA) and tap water ad libitum. They were placed in pair in wire-bottom stainless cages during the mating period, and individually in polycarbonate ones during gestation.

3. Dosage and administration

A dose-finding test was carried out prior to the study. PO was given at 5000 and 10000 mg/kg/day subcutaneously to 4 male rats per dose for 20 consecutive days, and 4 male controls received 0.5% carboxymethylcellulose (CMC) in the same way. The PO administration markedly affected the body weight of the animals at either dose and caused deaths in one animal at 5000 mg/kg/day on day 11 of administration and in 3 at 10000 mg/kg/day on days 11, 14, and 15.

From these results, the high dose level for the teratological study was determined as 2000 mg/kg/day. For the medium and low doses, 500 and 100 mg/kg/day were selected, respectively.

PO was suspended in 0.5% CMC at appropriate concentrations (adjusted daily on the weight basis) to give the respective doses in a volume of 5 ml/kg, and each suspension was administered subcutaneously into the back of each animal for 11 days from day 7 through 17 of gestation, with a disposal 2- or 5-ml syringe and needle (gauge 1-1/2). The controls received the same volume of 0.5% CMC alone during the same period.

4. Observations

4.1 Clinical signs of toxicity

The females were observed for behavioral changes and toxic signs every morning throughout gestation. The observation was made also in the evening (15:00 - 17:00) during the administration period.

4.2 Body weight

The animals were weighed on day 0 of gestation and daily during a period from day 7 through 21 of gestation.

4.3 Food consumption

Food consumption during days 0 - 7 of gestation was measured as the total amount, and the mean per day was calculated. For the rest period of gestation, the 24-hr consumption was daily recorded.

4.4 Organ weights

After autopsy on day 21 of gestation, the following organs of each animal were weighed: the brain, pituitary, thyroid, thymus, heart, lung, liver, spleen, pancreas, kidney, adrenal, ovary, uterus, and urinary bladder.

4.5 Observation at delivery by cesarean section and fetal examination

All the animals underwent cesarean section and were autopsied in the morning on day 21 of gestation. At the same time, the intrauterine state was observed, and the number of implantations (living, dead, and resorbed fetuses) was counted. The living fetuses were weighed, sexed, and examined for external abnormalities, and approximately half of them were fixed in alcohol, stained by Dawson's method, and examined for skeletal abnormalities. The remainder were fixed in Bouin's fluid and subjected to visceral observation under a microscope.

5. Statistics

Means were compared by the t test, and frequencies expressed as % were analyzed by the chi-square method.

Results

1. Dams

1.1 Clinical signs of toxicity

Induration at the injection site of the back was noted at any dose. The induration spread more widely in size as the dose increased, and was still noted on the day of cesarean section. The autopsies on these cases revealed the drug residue in the subcutaneous tissue at the site.

1.2 Body weight (Fig. 2 and Table 1)

No depression of weight gain was observed at 100 and 500 mg/kg/day during the study, while the weight gain in the 2000 mg/kg/day group was significantly lower ($P<0.05$) than that of the control group during days 7 - 17 of gestation covering the treatment period.

1.3 Food consumption (Fig. 3 and Table 2)

The animals at 100 mg/kg/day consumed almost as much food as the controls throughout gestation. The consumptions at 500 and 2000 mg/kg/day, however, were reduced during the administration days, when compared with the control one; the reduciton was more marked at 2000 mg/kg/day.

1.4 Organ weights (Table 3)

A decrease in the thymus weight ($P<0.01$, 0.001) and increases in the spleen and adrenal ones ($P<0.001$) were found at 500 and 2000 mg/kg/day. At 2000 mg/kg/day, the liver, kidney, and urinary bladder weights were also increased ($P<0.05$). The brain and uterus weights were slightly decreased, but these were within normal limits. At 100 mg/kg/day, the organ weights examined were comparable to the control values.

2. Fetuses

2.1 Cesarean section findings (Table 4)

At 100 and 500 mg/kg/day, the numbers of corpora lutea per litter were significantly greater ($P<0.05$) than the control value. At 100 mg/kg/day, the number of female living fetuses was also increased ($P<0.05$) as compared with the control, but the sex ratio of the living fetuses was not different from that in the control group. At 2000 mg/kg/day, the changes noted were decreases in the number of living fetuses ($P<0.001$) and in the body weights of the living fetuses of both sexes ($P<0.05$) in comparison with the control values.

External abnormalities were observed in any group except the 500 mg/kg/day group as follows. In the control group, cleft palate occurred in one fetus. At 100 mg/kg/day, abnormalities appeared in 5 fetuses from 4 dams in total: defect of the tail in one fetus, tail with the skin but without coccygeal vertebrae in one fetus, complication of shortening of the lower half of the body, defect of the tail, and oligodactyly of the right forelimb in one fetus (Photo 1) (These 3 fetuses were from different 3 dams.), and cleft palate in 2 fetuses (from the same dam). At 2000 mg/kg/day, abnormalities occurred in 2 fetuses from 2 dams in total: complication of the abnormally curved spina, shortening of the lower half of the body, and defect of the tail (with a trace of skin) in one fetus, and reduction deformity of the left hindlimb in one fetus. The frequencies of fetuses with such abnormalities were not dose-related, and there appeared no significant difference in frequency between either treated group and the control group.

2.2 Skeletal findings (Table 5)

The fetuses with external abnormalities were all examined for skeletal abnormalities. At 100 mg/kg/day, 3 of the 5 fetuses with external abnormalities showed skeletal anomalies: fusion of a sacral vertebral body and arch and absence of the sacral vertebrae except the 1st one in the fetus with defect of the tail; absence of the coccygeal vertebrae in the fetus with the skin only in the tail; and fusion of sacral vertebral arches, absence of the coccygeal vertebrae, fusion and bifurcation of ribs, fusion of ossification centers of sternebrae, absence of an ulna, and absence of phalanges of the right forelimb in the fetus with shortening of the lower half of the body, defect of the tail, and oligodactyly of the right forelimb. At 2000 mg/kg/day, the 2 fetuses had skeletal abnormalities as well: fusion of a thoracic vertebral body and arch, absence of the 11th, 12th, and 13th thoracic vertebrae, and bifurcation of a rib in the fetus with the abnormally curved spina, shortening of the lower half of the body, and the tail with the skin only; and absence of the calcaneus, metatarsus, and phalanges of the left hindlimb in the fetus with reduciton deformity of the limb. (Photo 2).

Among the fetuses without external changes examined, no skeletal anomalies were noted at any dose, except fusion of sacral vertebral bodies in a fetus at 2000 mg/kg/day.

Skeletal variations were noted in the treated and control groups, including an accessory lumbar vertebra (7th), 14th rib, undeveloped 13th rib, and asymmetry of an ossification center of a sternebra. Among the frequencies of fetuses with these variations, a significant difference was noted only as to the 14th rib at 500 mg/kg/day (increase at $P<0.05$).

The ossification of the following bones in the treated groups was delayed as compared with that of the bones in the controls: the odontoid process, center of the 5th sternebra, body of the 1st metatarsal, and proximal phalanges of the hindlimbs. In addition, the frequencies of fetuses with absence of one of the two parts of an ossification center of the 5th sternebra at 100 mg/kg/day and of fetuses with hypoplasia of an ossification center of the 5th sternebra at 2000 mg/kg/day were significantly higher ($P<0.05$) than those of the control fetuses. To the contrary, the ossificaiton of the following bones was more advanced in the treated groups than in the control group: the cervical vertebral bodies, coccygeal vertebral bodies and arches, and calcaneus.

2.3 Visceral findings (Table 6)

The findings were sinistroposition of the heart in 2 fetuses at 100 mg/kg/day and dilatation of the renal pelvis in 3 fetues at 2000 mg/kg/day. These frequencies were included within normal limits.

Discussion

PO was administered to pregnant rats at the subcutaneous doses of 100, 500, and 2000 mg/kg/day for 11 days from day 7 through 17 of gestation, and its effects on the dams and fetuses were examined.

At 500 and 2000 mg/kg/day, reduction of food consumption and/or depression of body weight gain were noted during the administration period. At autopsy, the animals at these doses showed induration due to the drug residue at the injection site of the back, and their thymus, adrenal, and spleen weights were significanlty different from the control ones. These findings are all considered to be attributable to the stress of injections or the inflammatory change at the injection site.

At delivery by cesarean section, the number of female living fetuses at 100 mg/kg/day was greater than the control, but this change is judged to be an incidental one due to an increased number of ova discharged because at this dose i) the sex ratio of the living fetuses was normal and ii) the number of corpora lutea was increased. At 2000 mg/kg/day, the number and body weight of the living fetuses were lowered as compared with those in the control group. These changes seem to have been led by the PO administration secondarily through their dams of which body weight gain was depressed.

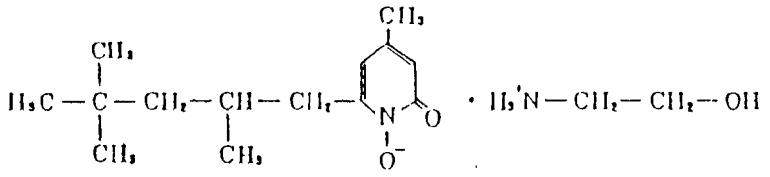
Five fetuses at 100 mg/kg/day and 2 fetuses at 2000 mg/kg/day showed external abnormalities, and most of them also had skeletal malformations. However, the frequencies of fetuses with the abnormalities did not increase dose-relatedly, and the difference in each frequency between either treated group and the control group was not significant. The abnormalities in the two treated groups are, therefore, regarded as the changes produced without any relation to PO.

The 14th rib is recognized to be one of the variations indicative of the teratogenicity of a drug, but the slight increase of fetuses with this variation at 500 mg/kg/day may not be a sign of the teratogenic effect of PO because the frequencies in the treated groups were not dose-related.

The examination revealed delayed ossification in the odontoid process, 5th sternebra, 1st metatarsal, or proximal phalanges of the hindlimbs in the treated groups, as compared with the control values, while it also revealed the results to the contrary; i.e., the ossification in the cervical and coccygeal vertebrae and calcaneus was more advanced in the treated groups than in the control group. Therefore, PO seems to exert little effect on the ossification process of fetuses.

As described above, when administered at the subcutaneous doses of 2000, 500, and 100 mg/kg/day to pregnant rats during organogenesis, PO affected the dams at 2000 mg/kg/day but did not raise the frequencies of fetuses with abnormalities. In conclusion, there is little possibility that PO might exert any teratogenic effects on rat fetuses.

Fig. 1 Chemical structure of piroctone olamine



1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridone monoethanolamine salt

Fig. 2 Body weight changes of female rats treated subcutaneously with piroctone olamine during days 7 – 17 of gestation

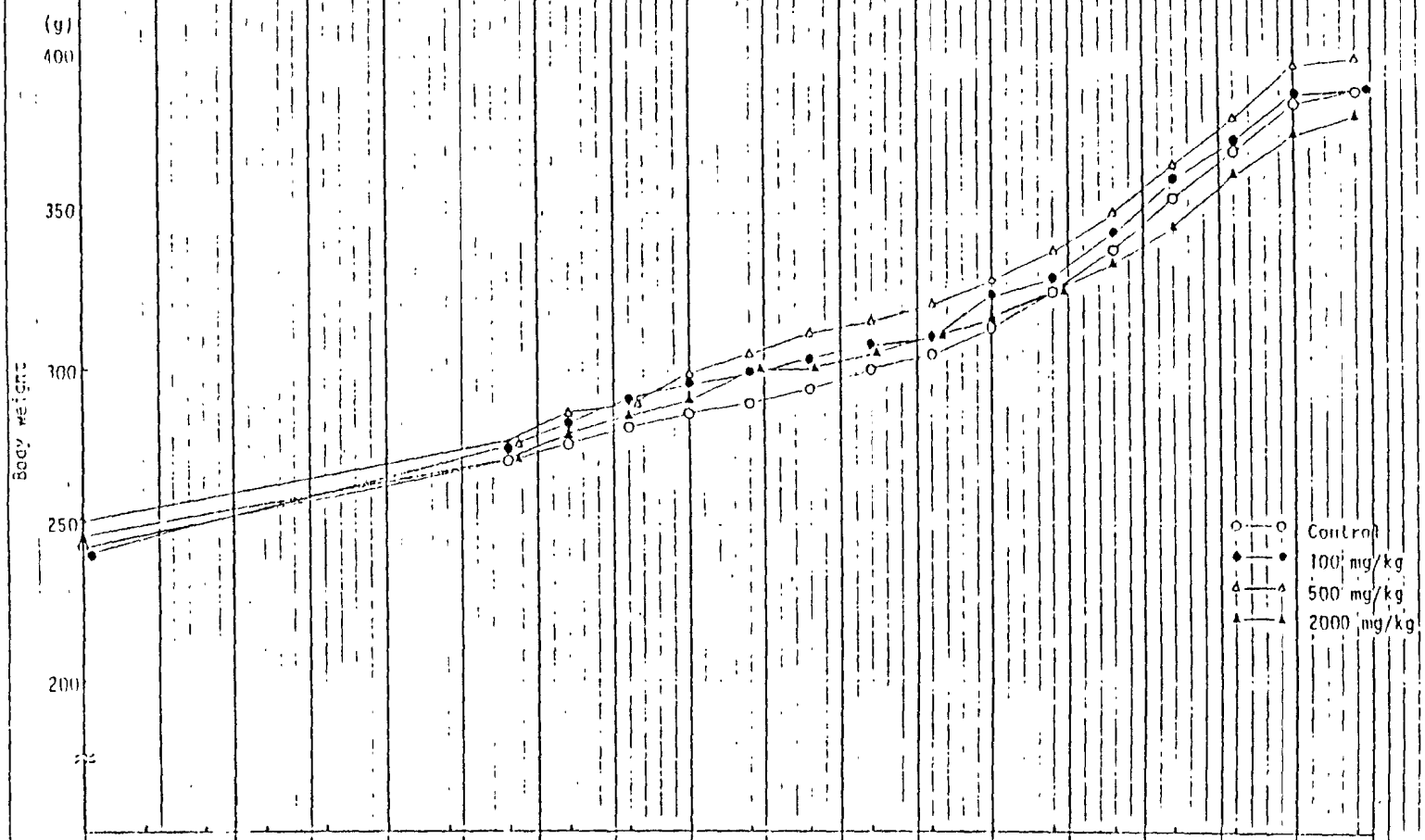


Fig. 3 Food consumption of female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

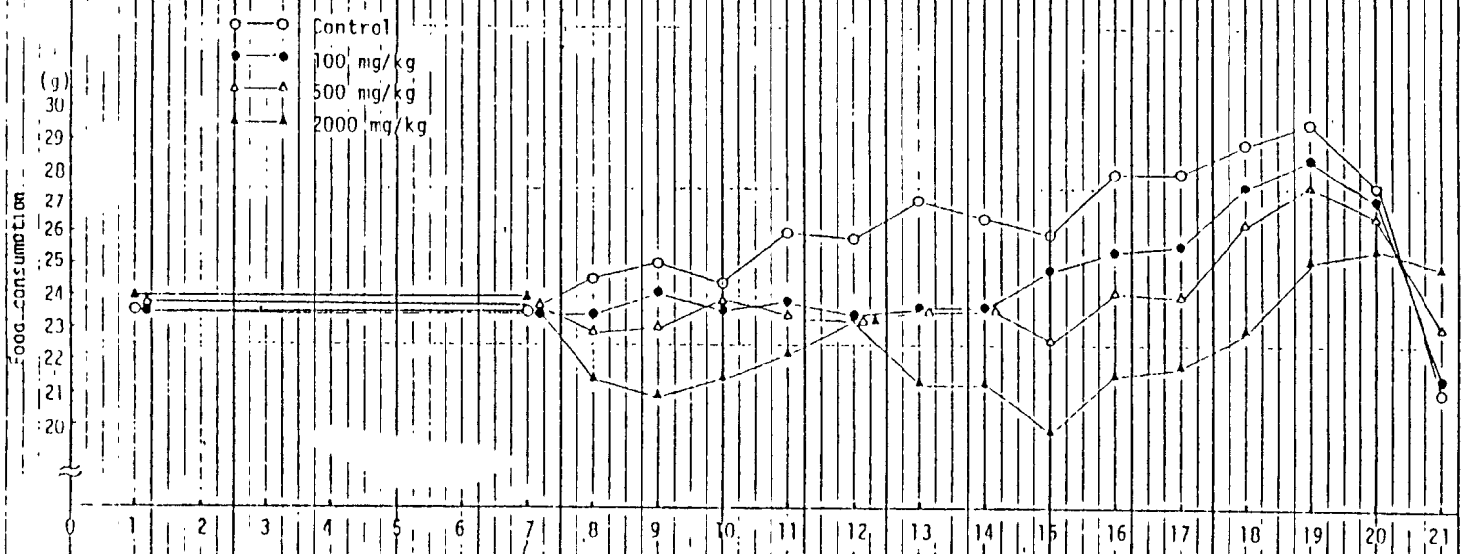


Fig. 3 Food consumption of female rats treated subcutaneously with piroctone olamine during Days 7 - 17 of gestation

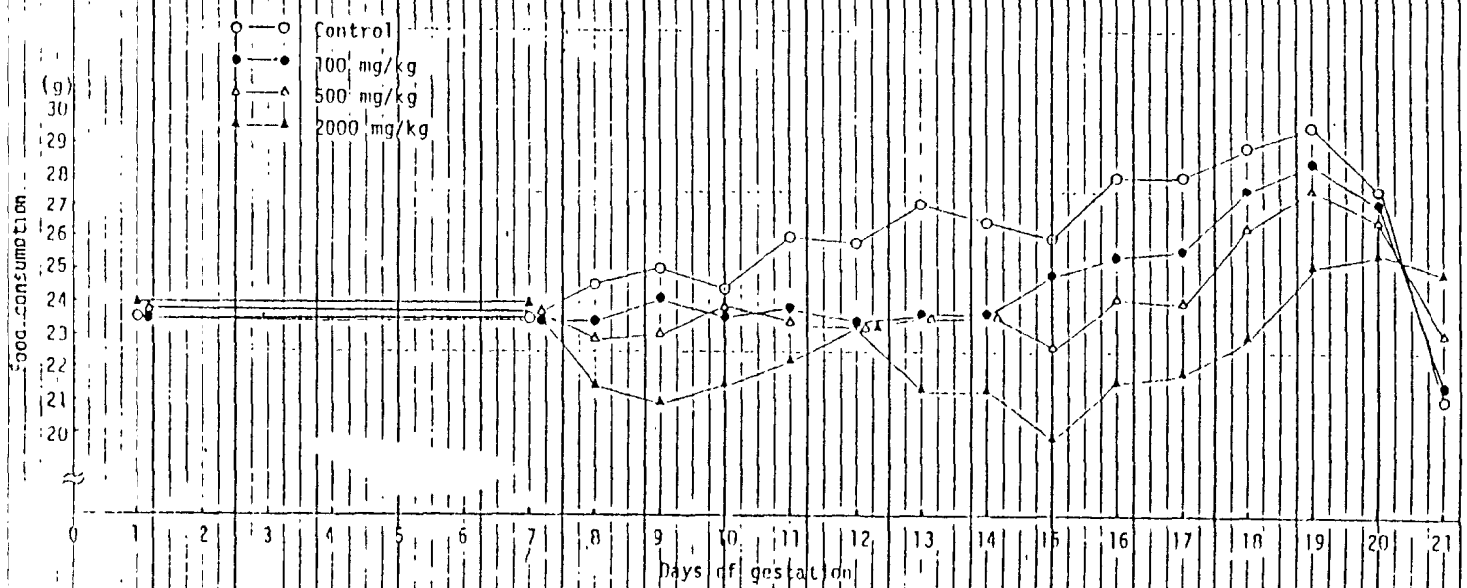


Table 1 Body weight (g) of female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	No. of animals	Days of gestation 0	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Control	26	243.54 ±3.07	271.15 ±2.82	276.54 ±3.18	282.08 ±3.12	286.08 ±3.42	289.15 ±3.51	294.12 ±3.86	300.31 ±3.90	305.69 ±4.11	313.69 ±4.35	324.92 ±4.37	338.85 ±5.18	355.85 ±5.09	370.31 ±5.61	385.31 ±6.13
100 mg/kg	22	241.64 ±3.40	274.00 ±2.95	282.55 ±3.30	291.36 ±3.57	296.18* ±3.26	300.00* ±3.25	303.82 ±3.73	308.36 ±3.70	311.73 ±4.03	323.00 ±4.47	329.00 ±4.25	343.55 ±4.95	362.00 ±4.72	372.91 ±5.52	388.45 ±5.78
500 mg/kg	21	250.67 ±3.83	276.10 ±3.78	286.19 ±3.89	289.43 ±4.32	298.29* ±3.68	305.24** ±4.10	312.29** ±4.40	316.10* ±4.56	321.33* ±4.86	328.48* ±5.22	338.48 ±5.48	350.57 ±5.39	366.86 ±5.86	381.90 ±6.10	398.00 ±6.57
2000 mg/kg	24	245.75 ±4.46	272.00 ±2.60	278.75 ±3.57	284.92 ±3.70	290.42 ±3.59	301.17 ±5.13	301.42 ±3.93	305.92 ±3.77	311.25 ±4.00	316.58 ±4.25	324.83 ±4.39	333.42 ±4.22	346.17 ±4.31	362.58 ±4.95	375.83 ±5.47

Dose	Weight gain (g) 21	21-0	21-7	18-7 (days)
Control	389.00 ±6.54	145.46 ±6.82	117.85 ±4.83	84.69 ±3.15
100 mg/kg	390.82 ±5.78	149.18 ±5.90	116.82 ±3.39	88.00 ±2.82
500 mg/kg	400.76 ±6.87	150.10 ±7.11	124.67 ±4.11	90.76 ±3.01
2000 mg/kg	382.33 ±5.84	136.58 ±6.82	110.33 ±4.03	74.17* ±2.75

Mean(g) ±S.E.

* P<0.05

** P<0.01

Table 2 Daily food consumption of female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	No. of animals	Days of gestation														
		0-7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	26	23.58 ±0.47	24.54 ±0.67	25.08 ±0.64	24.38 ±0.67	26.00 ±0.99	25.77 ±0.75	27.15 ±1.17	26.46 ±0.79	25.92 ±0.96	27.92 ±0.89	28.00 ±0.99	28.85 ±0.80	29.62 ±0.73	27.62 ±0.94	21.00 ±1.10
100 mg/kg	22	23.47 ±0.59	23.36 ±0.77	24.18 ±0.79	23.55 ±0.63	23.82 ±0.79	23.45 ±0.98	23.73* ±0.62	23.73* ±0.90	24.82 ±0.87	25.36 ±1.17	25.64 ±0.94	27.55 ±0.84	28.36 ±0.70	27.09 ±1.10	21.45 ±1.89
500 mg/kg	21	23.72 ±0.45	22.86 ±0.80	23.05* ±0.79	23.81 ±0.72	23.43 ±0.78	23.24* ±0.76	23.52* ±0.73	23.62* ±0.68	22.67* ±1.07	24.19** ±0.75	24.00** ±0.79	26.29* ±0.83	27.52* ±0.65	26.48 ±0.74	23.05 ±1.78
2000 mg/kg	24	23.95 ±0.44	21.50* ±0.96	20.92*** ±0.82	21.50** ±0.78	22.25** ±0.59	23.25* ±0.68	21.33*** ±0.69	21.33*** ±0.71	19.83*** ±0.56	21.58*** ±0.96	21.83*** ±0.54	22.92*** ±0.64	25.17*** ±0.68	25.50 ±0.88	24.92* ±1.15

Mean(g/day) ±S.E.

* P<0.05 ** P<0.01 *** P<0.001

Table 3 Organ weights of female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	No. of animals	Final body weight (g)	Brain (g)	Pitu-itary (mg)	Thy-roid (mg)	Thy-mus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pan-creas (g)	Kidney Right (g)	Kidney Left (g)	Adrenal Right (mg)	Adrenal Left (mg)	Ovary Right (mg)	Ovary Left (mg)	Uterus (g)	Urinary bladder (g)
Control	26	389.00 ±6.54	1.87 ±0.02	17.38 ±0.56	19.77 ±0.96	179.27 ±11.23	0.97 ±0.02	1.36 ±0.03	13.51 ±0.44	0.82 ±0.02	0.59 ±0.02	0.97 ±0.02	0.97 ±0.02	46.23 ±1.31	50.65 ±1.24	68.88 ±2.86	71.19 ±2.98	5.34 ±0.17	0.13 ±0.01
100 mg/kg	24	390.82 ±5.78	1.86 ±0.02	17.00 ±0.83	19.41 ±0.88	152.64 ±8.48	0.96 ±0.03	1.40 ±0.03	14.07 ±0.46	0.91 ±0.06	0.56 ±0.02	0.98 ±0.02	1.03 ±0.03	48.18 ±1.72	53.86 ±1.94	69.73 ±3.48	74.73 ±2.46	5.02 ±0.21	0.13 ±0.004
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500 mg/kg	21	400.86 ±6.87	1.87 ±0.01	18.38 ±0.74	21.90 ±1.02	126.57 ±11.62	0.99 ±0.02	1.42 ±0.03	14.67 ±0.39	1.10 ±0.05	0.60 ±0.02	0.98 ±0.03	1.02 ±0.03	55.05 ±1.74	61.29 ±1.56	73.48 ±3.81	74.29 ±3.90	4.92 ±0.16	0.13 ±0.01
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2000 mg/kg	24	384.42 ±5.52	1.82 ±0.01	16.79 ±0.77	17.33 ±0.81	78.96 ±7.28	0.92 ±0.02	1.39 ±0.03	14.95 ±0.45	1.30 ±0.05	0.59 ±0.02	1.06 ±0.03	1.04 ±0.03	60.83 ±1.72	62.17 ±2.27	63.79 ±2.55	62.79 ±3.10	4.49 ±0.20	0.17 ±0.01

Mean ±S.E. *: P<0.05 ** P<0.01 *** P<0.001

Table 4 Cesarean section findings in female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	Control	100 mg/kg	500 mg/kg	2000 mg/kg
No. of pregnant animals	26	22	21	24
No. of corpora lutea	414	376	361	388
Mean±S.E./litter	15.92 ±0.34	17.09* ±0.36	17.19* ±0.39	16.17 ±0.26
No. of implantations	387(93.5%)	361(96.0%)	338(93.6%)	366(94.3%)
Mean±S.E./litter	14.88 ±0.61	16.41 ±0.51	16.10 ±0.56	15.25 ±0.35
No. of living fetuses	370(95.6%)	344(95.3%)	320(94.7%)	325(88.8%)***
Mean±S.E./litter	14.23 ±0.59	15.64 ±0.53	15.24 ±0.55	13.54 ±0.70
No. of males	185(50.0%)	159(46.2%)	157(49.1%)	160(49.2%)
Mean±S.E./litter	7.12 ±0.52	7.22 ±0.39	7.48 ±0.46	6.67 ±0.52
No. of females	185(50.0%)	185(53.8%)	163(50.9%)	165(50.8%)
Mean±S.E./litter	7.12 ±0.49	8.41* ±0.37	7.76 ±0.46	6.88 ±0.61
No. of immature fetuses	3(0.8%)	0	2(0.6%)	3(0.9%)
No. of dead fetuses	0	0	0	0
No. of resorbed fetuses				
Implantation sites	0	0	0	17(4.6%)
Placental remnants	14(3.6%)	12(3.3%)	18(5.3%)	13(3.6%)
Early resorptions	1(0.3%)	3(0.8%)	0	6(1.6%)
Late resorptions	2(0.5%)	2(0.6%)	0	5(1.4%)
Macerated fetuses	0	0	0	0
No. of dams of fetuses with external abnormalities	1(3.85%)	4(18.18%)	0	2(8.70%)
No. of fetuses with external abnormalities	(a) 1(0.27%)	(b) 5(1.45%)	0	(c) 2(0.62%)
Body weight of the living fetuses				
Male Mean±S.E./litter	5.42 ±0.07	5.31 ±0.07	5.42 ±0.06	5.15* ±0.09
Female Mean±S.E./litter	5.04 ±0.10	5.10 ±0.15	5.04 ±0.07	4.75* ±0.06

* P<0.05 *** P<0.001

a) Cleft palate

b) Cleft palate (2 fetuses (from the same dam)); Defect of the tail (1); Skin only in the tail (1); Shortening of the lower half of the body, defect of the tail, and oligodactyly of the right forelimb (1)

c) Abnormally curved spine, shortening of the lower half of the body, and skin only in the tail (1); Reduction deformity of the left hindlimb (1)

Table 5-1 Skeletal findings in fetuses from female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	Control		100 mg/kg		500 mg/kg		2000 mg/kg	
		(%)		(%)		(%)		(%)
No. of dams examined	26		22		21		23	
No. of fetuses examined	193		175		164		169	
Dams of fetuses with abnormalities	0	0.	4	18.2	0	0	3	13.0
Fetuses with abnormalities	0	0	5	2.9	0	0	3	1.8
Dams of fetuses with variations	25	96.2	19	86.4	21	100	21	91.3
Fetuses with variations	88	45.6	62	35.4	97	59.1	86	50.9
No. of fetuses with abnormalities								
Cleft palate	0	0	2	1.1	0	0	0	0
Fusion of a thoracic vertebral body & arch	0	0	0	0	0	0	1	0.6
Fusion of a sacral vertebral body & arch	0	0	1	0.6	0	0	0	0
Fusion of sacral vertebral bodies	0	0	0	0	0	0	1	0.6
Fusion of sacral vertebral arches	0	0	1	0.6	0	0	0	0
Absence of the thoracic vertebrae 11 - 13	0	0	0	0	0	0	1	0.6
Absence of the sacral vertebrae 2-4	0	0	1	0.6	0	0	0	0
Absence of the coccygeal vertebrae	0	0	2	1.1	0	0	0	0
Furion & bifurcation of ribs	0	0	1	0.6	0	0	0	0
Bifurcation of a rib	0	0	0	0	0	0	1	0.6
Fusion of ossification centers of sternebrae	0	0	1	0.6	0	0	0	0
Absence of an ulna	0	0	1	0.6	0	0	0	0
Absence of phalanges of a forelimb	0	0	1	0.6	0	0	0	0
Absence of the tarsus, metatarsus, & phalanges of a hindlimb	0	0	0	0	0	0	1	0.6
No. of fetuses with variations								
Accessory lumbar vertebra	4	2.1	4	2.3	3	1.8	3	1.8
14th rib	88	45.6	62	35.4	96	58.5*	85	50.3
Undeveloped 13th rib	0	0	0	0	0	0	1	0.6
Asymmetry of an ossification center of a sternebra	1	0.5	0	0	1	0.6	0	0

* $P < 0.05$

Table 5-2 Skeletal findings in fetuses from female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation (continued)

Dose		Control		100 mg/kg		500 mg/kg		2000 mg/kg	
No. of fetuses with ossification			(%)		(%)		(%)		(%)
Nasal bone		193	100	175	100	164	100	169	100
Frontal bone		193	100	175	100	164	100	169	100
Parietal bone		193	100	175	100	164	100	169	100
Occipital bone		193	100	175	100	164	100	169	100
Lacrimal bone		193	100	175	100	164	100	169	100
Maxilla		193	100	175	100	164	100	169	100
Mandibule		193	100	175	100	164	100	169	100
Hyoid bone		193	100	175	100	164	100	169	100
Palatine bone		193	100	173	98.9	164	100	169	100
Odontoid process		174	90.2	144	82.3*	138	84.2	137	81.1*
Cervical vertebral bodies	1	26	13.5	36	20.6	43	26.2**	50	29.6***
	2	34	17.6	35	20.0	36	22.0	34	20.1
	3	42	21.8	62	35.4***	64	39.0***	52	30.8
	4	53	27.5	68	38.9*	69	42.1**	57	33.7
	5	64	33.2	73	41.7	79	48.2**	79	46.8**
	6	78	40.4	86	49.1	86	52.4*	86	50.9*
	7	146	75.7	147	84.0*	131	79.9	145	85.8*
Cervical vertebral arches	1-7	193	100	175	100	164	100	169	100
Thoracic vertebral bodies & arches	1-10	193	100	175	100	164	100	169	100
	11-13	193	100	175	100	164	100	168	99.4
Including the cases with:									
Hypoplasia in the bodies	1-11	0	0	0	0	0	0	0	0
	12	0	0	1	0.6	0	0	0	0
	13	0	0	1	0.6	0	0	0	0
Splitting in the body	13	1	0.5	0	0	0	0	0	0
Lumbar vertebral bodies & arches	1-6	189	97.9	171	97.7	161	98.2	165	97.6
Including the case with Hypoplasia in the bodies	2-3	0	0	1	0.6	0	0	0	0
Sacral vertebral bodies & arches	1	193	100	175	100	164	100	168	99.4
	2-4	193	100	174	99.4	164	100	168	99.4
Coccygeal vertebral bodies	1-4	193	100	172	98.3	164	100	168	99.4
	5	192	99.5	172	98.3	164	100	168	99.4
	6	167	86.5	161	92.0	159	97.0***	157	92.9*
	7	100	51.8	113	64.6*	114	69.5***	109	64.5*
	8	25	13.0	43	24.6**	47	28.7***	48	28.4***
	9	0	0	3	1.7	13	7.9***	11	6.5***
	10	0	0	0	0	1	0.6	0	0
No. of ossified coccygeal vertebral bodies/fetus (Mean±S.E.)		6.47 ±0.13		6.76 ±0.14		7.05** ±0.13		6.89* ±0.16	
Coccygeal vertebral arches	1	193	100	173	98.9	164	100	168	99.4
	2	193	100	170	97.1	163	99.4	166	98.2
	3	171	88.6	151	86.3	148	90.2	139	82.3
	4	12	6.2	31	17.7***	42	25.6***	39	23.1***
Ribs	1-10	193	100	175	100	164	100	169	100
	11-12	193	100	175	100	164	100	168	99.4
	13	193	100	175	100	164	100	167	98.8

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

Table 5-3 Skeletal findings in fetuses from female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation (continued)

Dose		Control		100 mg/kg		500 mg/kg		2000 mg/kg	
No. of fetuses with ossification (continued)			(%)		(%)		(%)		(%)
Ossification centers of sternebrae	1	193	100	175	100	164	100	169	100
	2	193	100	175	100	164	100	169	100
	3	192	99.5	175	100	164	100	169	100
	4	192	99.5	175	100	164	100	169	100
	5	190	98.5	167	95.4	163	99.4	155	91.7**
	6	192	99.5	175	100	164	100	169	100
Including the cases with:									
Hypoplasia		26	13.5	30	17.1	26	15.9	38	22.5*
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	1	0.6
	5	26	13.5	29	16.6	26	15.9	38	22.5*
	6	0	0	1	0.6	1	0.6	1	0.6
Splitting		0	0	0	0	0	0	1	0.6
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	1	0.6
	4	0	0	0	0	0	0	1	0.6
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	1	0.6
Absence of one of the two parts		1	0.5	9	5.1*	2	1.2	4	2.4
	1	0	0	0	0	0	0	0	0
	2	0	0	1	0.6	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	1	0.5	8	4.6*	2	1.2	4	2.4
	6	0	0	0	0	0	0	0	0
Clavicle		193	100	175	100	164	100	169	100
Scapula		193	100	175	100	164	100	169	100
Humerus		193	100	175	100	164	100	169	100
Radius		193	100	175	100	164	100	169	100
Ulna		193	100	174	99.4	164	100	169	100
Metacarpals (bodies)	1	0	0	0	0	0	0	0	0
	2-4	193	100	174	99.4	164	100	169	100
	5	192	99.5	174	99.4	164	100	169	100
Phalanges of the forelimbs									
Proximal	1	0	0	0	0	0	0	0	0
	2	175	90.7	162	92.6	155	94.5	155	91.7
	3	192	99.5	174	99.4	164	100	169	100
	4	192	99.5	173	98.9	164	100	169	100
	5	169	87.6	158	90.3	153	93.3	155	91.7
Middle	2-5	0	0	0	0	0	0	0	0
Distal	1	185	95.9	168	96.0	150	91.5	155	91.7
	2	193	100	174	99.4	164	100	169	100
	3	193	100	175	100	164	100	169	100
	4	193	100	174	99.4	164	100	169	100
	5	189	97.9	173	98.9	162	98.8	163	96.5

* $P < 0.05$
** $P < 0.01$

Table 5-4 Skeletal findings in fetuses from female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation (continued)

Dose		Control		100 mg/kg		500 mg/kg		2000 mg/kg	
No. of fetuses with ossification (continued)			(%)		(%)		(%)		(%)
Ilium		193	100	175	100	164	100	169	100
Ischium		193	100	175	100	164	100	169	100
Pubis		193	100	175	100	164	100	169	100
Femur		193	100	175	100	164	100	169	100
Tibia		193	100	175	100	164	100	169	100
Fibula		193	100	175	100	164	100	169	100
Tarsus Astragalus		0	0	0	0	0	0	0	0
Calcaneus		3	1.6	11	6.3**	19	11.6***	35	20.7***
Metatarsals (bodies)	1	161	83.4	138	78.9	130	79.3	118	69.8***
	2-5	193	100	175	100	164	100	168	99.4
Phalanges of the hindlimbs									
Proximal	1	0	0	0	0	2	1.2	0	0
	2	69	35.8	69	39.4	58	35.4	54	32.0
	3	111	57.5	95	54.3	71	43.3**	67	39.6***
	4	108	56.0	92	52.6	70	42.7*	66	39.1**
	5	28	14.5	21	12.0	17	10.4	30	17.8
Middle	2-5	0	0	0	0	0	0	0	0
Distal	1	191	99.0	173	98.9	164	100	168	99.4
	2	193	100	174	99.4	164	100	168	99.4
	3	193	100	174	99.4	164	100	168	99.4
	4	193	100	174	99.4	164	100	168	99.4
	5	191	99.0	174	99.4	163	99.4	168	99.4

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

Table 6 Visceral abnormalities in fetuses from female rats treated subcutaneously with piroctone olamine during days 7 - 17 of gestation

Dose	Control	100 mg/kg	500 mg/kg	2000 mg/kg
No. of dams examined	26	22	21	22
No. of fetuses examined	178	168	155	149
No. of dams with fetuses showing abnormalities	1(3.85%)	2(9.09%)	0	3(13.64%)
No. of fetuses with abnormalities	1(0.56%)	2(1.19%)	0	3(2.01%)
Cleft palate	1(0.56%)	0	0	0
Sinistroposition of the heart	0	2(1.19%)	0	0
Dilatation of the renal pelvis	0	0	0	3(2.01%)

Photo 1 Shortening of the lower half of the body, defect of the tail, and oligodactyly of the right forelimb in a fetus at 100 mg/kg/day

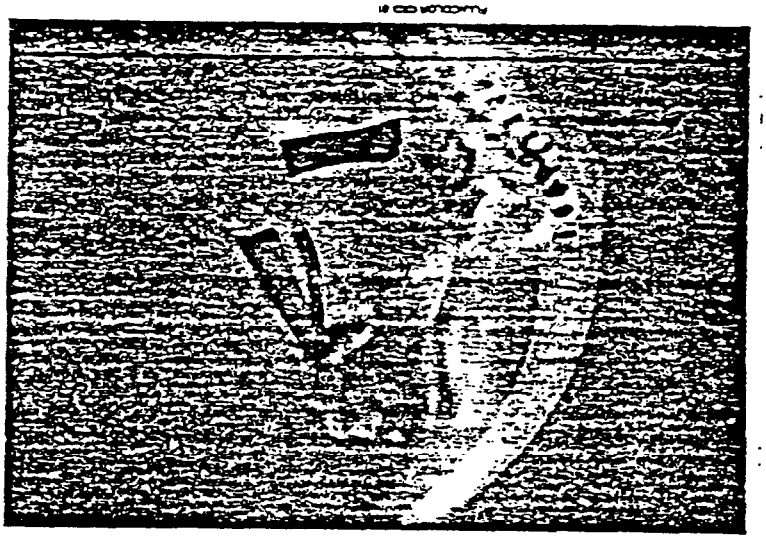

Photo 2 Absence of the calcaneus, metatarsus, and phalanges of the left hindlimb in a fetus at 2000 mg/kg/day

Individual Data: 1 BODY WEIGHT OF FEMALES DURING GESTATION

Rate Piroctone olamine 0 mg/kg (Control) s.c.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain 21-0	21-7	18-7
1 1-1	312							292	294	306	306	310	316	326	330	340	350	360	370	410	420	430	118	138	98
2 2	330							266	266	278	280	274	280	294	298	290	314	328	354	368	382	384	154	118	88
3 3	328							280	286	292	296	296	308	316	312	316	328	346	368	380	390	410	162	130	88
4 2-1	322							314	262	284	290	290	282	286	292	304	314	332	350	366	384	400	178	146	96
5 2	326							280	286	292	298	304	309	314	320	330	340	364	378	386	404	424	198	144	98
6 3	312							288	288	276	272	280	288	286	292	304	318	332	354	354	370	376	124	130	98
7 4	310							256	264	270	272	276	282	288	288	292	302	332	340	346	372	382	122	126	84
8 3-1	338							272	274	276	286	290	294	294	298	312	328	334	352	360	384	372	134	100	80
9 2	310							286	290	290	296	302	300	306	306	310	322	326	330	340	348	342	92	56	44
10 3	312							270	264	270	272	280	280	280	292	298	310	320	332	350	362	366	74	96	72
11 4	312							284	286	288	298	306	310	304	324	334	346	364	376	390	412	414	102	130	92
12 5	310							282	288	294	298	304	300	310	316	330	344	360	374	400	418	408	148	136	92
13 6	318							264	270	272	274	282	286	286	294	300	316	328	340	382	378	382	124	118	76
14 4-1	342							298	304	316	330	332	338	350	358	378	386	376	420	442	460	472	130	174	122
15 2	324							252	254	262	266	262	262	272	278	292	300	320	318	332	340	350	104	98	66
16 3	338							252	260	258	262	264	264	272	282	288	300	328	330	352	366	354	120	102	78
17 4	332							260	260	264	272	266	270	282	278	290	294	298	316	332	324	330	98	70	56
18 5-1	340							264	268	280	276	274	286	290	300	308	314	330	342	368	378	378	138	114	78
19 2	340							264	272	282	278	284	286	296	306	310	322	344	354	382	422	432	132	138	90
20 3	326							286	300	306	306	310	314	318	310	336	342	362	380	400	422	430	124	144	94
21 4	334							268	262	274	268	276	280	286	292	298	306	320	334	346	356	368	134	110	78
22 6-1	264							302	318	316	324	330	342	350	358	362	376	410	414	430	448	452	188	150	112
23 2	340							274	280	280	288	292	296	306	310	316	328	340	348	364	374	378	138	108	74
24 3	328							264	270	270	280	286	292	300	298	306	316	336	350	364	370	378	140	114	86
25 4	340							276	282	286	290	296	300	304	298	316	322	332	352	364	376	386	146	110	76
26 5	338							268	272	272	280	282	282	298	300	300	312	332	354	370	380	376	138	106	86
27																									
28																									
No.	26							26																	
Mean	330.54							277.69	276.54	282.08	286.08	289.15	296.12	300.31	305.69	312.69	324.92	338.81	352.85	370.31	385.31	388.00	57.46	111.31	94.69
S	1138.5							1682.4	1864.5	1939.8	1878.8	1774.4	1614.7	1902.5	1990.0	1284.0	1348.8	1748.8	1807.1	2048.8	2446.1	2770.0	302.45	1743.3	1455.5
S.D.	33.73							41.38	43.20	43.92	42.93	42.88	40.16	43.91	44.22	35.83	36.73	41.82	42.53	45.23	49.46	52.63	17.28	41.73	38.17
S.E.	7.07							8.12	8.48	8.62	8.43	8.41	8.06	8.90	8.71	7.03	7.22	8.21	8.37	8.88	9.71	10.33	3.39	8.19	7.49
t																									

Individual Data: 2 BODY WEIGHT OF FEMALE DURING GESTATION

Rats Piroctone bismine 100 mg/kg s.c.

No. \ Days	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain 7-0	14-7	21-7
1 1-4	230							218	226	202	202	212	206	220	222	222	222	220	224	224	224	214	164	128	58
2 2	244							238	238	200	218	202	206	226	224	230	242	242	242	208	208	220	206	134	106
3 6	228							224	224	224	226	226	232	228	232	228	208	226	228	246	242	268	140	102	74
4 3-5	238							232	232	238	232	200	206	216	234	234	232	250	264	272	272	270	154	118	92
5 6	248							250	250	258	264	270	278	272	270	278	232	232	246	266	286	276	150	116	76
6 7	240							234	234	230	232	200	204	202	210	218	220	244	260	270	276	276	156	120	84
7 3-7	242							238	230	236	232	200	218	214	208	212	220	226	242	242	276	274	112	100	68
8 8	238							246	250	238	238	230	238	234	204	206	226	220	244	266	270	270	92	114	88
9 10	246							236	236	230	236	242	244	246	230	216	232	226	232	232	238	242	106	86	78
10																									
11 11	250							236	202	206	212	216	226	228	226	228	250	228	232	208	226	224	124	138	106
12																									
13 4-6	242							232	230	236	232	230	220	220	220	226	242	250	238	230	214	202	122	120	96
14 7	242							240	242	250	260	260	260	264	270	282	230	236	238	234	222	232	120	92	98
15 8	232							234	238	238	236	230	238	230	232	220	230	220	238	230	238	260	128	96	94
16 9	240							230	232	236	230	208	228	230	232	232	234	240	250	230	234	236	146	116	80
17 1-6	236							232	238	236	230	232	238	230	234	238	234	238	238	232	232	238	162	126	106
18 7	242							238	230	240	234	234	238	230	236	234	230	236	232	234	236	238	156	120	94
19 8	242							230	238	234	236	238	232	236	238	238	230	230	236	230	236	232	150	102	76
20 1-6	242							238	230	238	234	238	230	232	232	236	250	260	230	234	230	240	156	122	92
21 7	240							236	234	236	230	230	236	230	230	234	242	236	236	230	234	240	160	124	90
22 8	240							232	230	232	238	230	230	232	232	236	230	238	238	238	232	236	136	114	86
23 9	242							236	230	236	238	234	240	232	240	238	230	232	236	234	234	240	128	154	120
24 10	238							234	234	236	236	236	236	238	232	236	234	238	238	234	236	232	164	128	84
25																									
26																									
27																									
28																	* P < 0.05								
No.	22							22																	
Mean	241.64							236.00	232.55	231.36	231.18	230.00	232.32	228.36	231.73	233.00	232.00	242.55	242.00	232.91	238.45	240.82	162.18	116.82	82.00
S	1326.1							1292.0	1251.5	1255.5	1253.3	1258.0	1233.3	1234.7	1234.4	1222.0	1212.8	1304.7	1304.7	1284.5	1276.5	1284.7	1085.5	1320.3	1820.0
S.D.	15.12							13.84	15.06	16.74	15.35	16.13	17.42	17.38	18.71	20.94	17.71	23.20	22.15	25.87	22.09	22.10	37.68	15.90	22.13
S.E.	3.40							2.95	3.30	3.57	3.26	3.44	3.73	3.70	3.99	4.47	4.25	4.95	4.72	5.52	4.78	4.78	8.04	3.39	4.82
t	0.476							0.495	0.307	0.367	0.117	0.237	0.271	0.250	0.039	0.486	0.663	0.649	0.525	0.328	0.369	0.305	0.405	0.168	0.270

Individual Data: 3 BODY WEIGHT OF FEMALES DURING GESTATION

Rats Piroctone olamine 500 mg/kg s.c.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain 21-0	21-7	18-7
1 7-2	224							276	282	292	294	292	296	298	296	300	298	296	280	280	296	310	176	134	84
2 8	246							284	290	296	298	300	296	298	324	322	344	324	280	320	406	410	164	126	96
3 9	308							272	288	294	302	306	314	328	320	332	346	360	370	388	406	400	156	122	92
4 12-1	240							284	286	292	294	304	308	310	314	330	330	348	340	368	374	386	136	102	66
5 11	320							302	314	334	336	338	342	344	350	370	374	382	410	436	440	436	166	134	108
6 12	326							242	261	266	270	280	282	280	280	282	290	300	316	330	340	354	128	112	74
7 13	324							284	300	300	302	286	322	324	322	338	350	366	380	376	434	440	166	156	96
8 14	322							272	280	286	300	312	316	320	330	340	360	372	376	416	430	436	214	160	120
9 3-13	324							278	282	292	300	310	322	324	332	340	356	362	376	394	410	410	186	132	98
10 14	322							264	278	280	286	298	300	300	306	312	320	336	350	370	376	388	176	124	88
11 15	352							272	286	286	296	306	310	308	314	328	336	344	362	374	378	404	152	132	90
12 16	352							254	264	276	274	278	284	286	292	298	312	316	328	350	364	352	70	98	54
13 4-15	364							296	304	314	318	324	328	330	340	340	354	368	382	398	410	410	186	114	86
14																									
15 11	358							278	284	294	302	304	308	314	322	330	330	342	356	368	386	380	136	102	78
16 12	340							282	290	300	312	322	328	332	332	346	356	364	382	400	428	430	190	148	102
17 5-9	356							286	296	304	304	310	314	320	326	334	340	354	374	380	400	406	150	120	78
18 10	348							294	312	320	318	326	330	336	346	350	362	368	386	404	424	422	154	128	92
19 11	322							244	250	260	264	268	268	272	282	286	292	302	324	336	348	346	124	102	80
20 6-11	310							304	318	318	326	340	350	356	366	376	374	406	424	438	448	456	206	152	120
21 12	348							252	262	278	280	286	290	294	294	298	312	326	334	350	354	360	110	98	82
22 13	354							268	284	286	298	302	314	314	308	316	332	346	352	374	376	370	146	122	94
23																									
24																									
25																									
26																									
27																									
28																									

* P < 0.05, ** P < 0.01

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	21-0	21-7	18-7
No.	21							21																	
Mean	324.67							276.10	288.19	292.43	298.57 *	305.24 **	312.57 **	316.10 *	322.33	328.48 *	338.48	350.57	366.86	381.90	398.00	400.76	150.10	124.67	90.76
S	4150.7							1987.8	1959.2	2049.1	2074.3	2088	2138.3	2231.8	2196.7	2242.7	2263.1	2207.1	2142.9	2153.3	2138	2188.8	2133.8	2092.7	2030.8
S.D.	12.54							12.20	12.83	12.81	12.54	12.78	13.17	13.37	13.26	13.42	13.12	12.70	12.86	12.77	13.11	14.49	12.58	12.32	13.79
S.E.	3.23							3.28	3.39	3.32	3.29	3.30	3.40	3.46	3.44	3.46	3.38	3.27	3.31	3.29	3.37	3.73	3.24	3.17	3.56
t	2.428							2.070	2.941	2.921	2.934	3.117	3.174	3.264	3.1	3.194	3.918	3.857	3.934	3.895	3.407	2.233	2.467	2.918	2.320

Individ . Data: 4 BODY WEIGHT OF FEMALES ING GESTATION

Rats . Piroctone olamine 2000 mg/kg B.C.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain 4-0	21-7	18-7
1	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
4	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
5	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
6	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
7	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
8	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
9	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
10	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
11	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
12	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
13	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
14	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
15	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
16	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
17	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
18	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
19	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
20	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
21	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
22	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
23	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
24	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
25																									
26																									
27																									
28																	* P < 0.05								
No.	[illegible]																								
Mean	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
S	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
S.D.	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
S.E.	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
t	[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Individual Data: 5 FOOD CONSUMPTION OF FEMALES DURING GESTATION

Rats · Piroctone olamine 0 mg/kg (Control) s.c.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain -	-	-
1								23.7	25	26	28	28	30	30	28	30	26	30	28	30	25	32			
2								23.7	22	22	27	22	27	28	26	24	30	27	30	28	26	26			
3								22.3	27	22	30	26	26	28	26	24	30	26	30	24	28	27			
4								22.7	30	27	26	26	30	30	26	27	28	28	25	26	30	30			
5								26.6	28	30	30	30	28	22	30	27	30	30	22	22	27	22			
6								20.9	26	27	26	27	27	27	30	30	30	30	30	28	26	22			
7								27.1	27	26	27	28	26	28	27	28	30	30	26	26	28	26			
8								25.4	22	26	26	22	26	22	26	27	26	22	28	30	30	26			
9								22.4	30	30	22	30	22	26	27	30	27	27	22	27	30	27			
10								27.1	22	27	22	30	27	22	28	30	27	22	30	27	30	30			
11								27.0	27	27	28	26	27	30	22	27	26	26	30	22	22	30			
12								27.7	28	30	26	26	30	27	26	26	30	22	28	22	27	28			
13								30.9	26	26	26	26	26	30	30	22	26	28	27	30	30	30			
14								22.4	28	26	22	26	30	30	28	30	22	27	28	28	22	22			
15								27.6	27	27	30	27	22	30	22	22	27	27	27	30	30	27			
16								27.1	30	22	22	30	30	30	22	28	26	27	28	27	26	30			
17								30.0	22	30	30	30	30	26	30	30	22	22	26	26	22	28			
18								22.6	26	26	26	30	30	22	27	27	27	26	30	28	27	27			
19								22.9	28	27	26	22	22	27	26	28	30	26	28	30	26	28			
20								22.1	30	22	30	26	30	22	27	28	27	30	22	30	28	22			
21								27.4	22	22	30	22	28	30	22	27	22	30	30	28	27	30			
22								30.6	30	22	26	26	30	26	27	27	27	28	30	28	27	22			
23								28.0	22	27	27	30	27	28	26	26	22	30	30	30	26	28			
24								27.1	27	22	27	26	27	28	26	26	22	30	30	28	27	30			
25								22.4	27	28	22	22	22	22	30	28	30	30	30	27	27	28			
26								22.9	30	26	27	28	28	30	27	30	28	30	26	30	28	28			
27																									
28																									
No.								26																	
Mean								23.58	27.54	26.65	27.38	26.00	25.77	27.15	26.46	25.23	27.73	28.00	28.85	27.63	27.63	27.00			
S								144.65	273.46	278.15	276.15	633.00	262.63	477.38	690.46	603.85	115.35	433.04	417.73	347.65	526.15	286.00			
S.D.								2.47	3.63	3.46	3.44	5.03	3.87	5.77	4.05	4.91	4.54	5.03	4.07	3.77	4.80	5.67			
S.E.								0.47	0.67	0.64	0.67	0.99	0.75	1.17	0.79	0.96	0.87	0.99	0.80	0.74	0.94	1.10			
t																									

Individ Data: 6 FOOD CONSUMPTION OF FEMAI DURING GESTATION

Rats Piro one olamine 100 mg/kg s.c.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain -	-	-
1 1 - 4								26.8	20	24	28	24	20	20	26	20	22	22	22	26	24	24			
2 5								25.7	26	24	22	24	24	24	20	26	24	26	22	24	24	22			
3 1								23.4	24	20	22	24	20	20	22	20	28	24	24	26	24	28			
4 2 - 5								23.7	22	22	24	26	24	26	26	20	22	28	24	24	22	46			
5 6								23.7	22	22	24	24	24	24	22	20	20	22	20	20	24	22			
6 7								23.4	20	24	24	22	22	20	22	20	22	24	28	26	40	28			
7 3 - 7								22.0	22	24	24	20	20	26	28	24	26	24	20	28	30	20			
8 8								23.1	26	22	26	26	24	28	22	20	24	24	20	20	28	20			
9 10								20.0	26	22	20	20	20	20	24	28	24	24	22	20	28	28			
10																									
11 12								21.7	24	28	24	20	20	24	22	24	22	20	26	22	34	20			
12																									
13 4 - 6								24.1	28	22	24	26	28	28	28	24	24	26	20	26	24	26			
14 7								22.2	28	20	20	20	28	26	20	22	20	26	24	28	20	22			
15 8								22.9	24	22	20	20	20	28	22	20	22	28	26	30	28	20			
16 9								22.5	26	28	24	20	28	26	22	28	20	24	20	24	20	20			
17 5 - 8								22.4	26	22	24	20	20	22	22	22	24	20	24	20	20	22			
18 7								22.4	28	28	20	20	28	22	22	22	20	20	26	26	24	26			
19 8								23.7	24	20	22	20	20	20	26	22	20	26	20	24	24	22			
20 1 - 1								24.9	22	28	20	20	22	24	22	26	26	20	20	24	26	24			
21 7								25.7	24	20	22	26	28	24	24	26	26	26	20	28	26	20			
22 8								26.4	20	26	24	26	26	22	20	22	26	24	28	28	28	28			
23 9								28.0	20	22	20	22	22	26	28	24	24	26	22	20	20	22			
24								26.6	20	22	20	24	20	20	22	24	22	20	28	28	28	22			
25																									
26																									
27																									
28																									
No.								22											* P < 0.05						
Mean								23.47	23.36	24.25	23.55	23.22	23.55	23.23	23.23	23.83	23.36	23.64	23.25	23.54	23.69	23.45			
S								16.21	20.09	28.27	28.45	25.27	44.74	25.36	27.34	30.27	23.09	40.09	22.65	22.05	33.25	19.21			
S.D.								3.77	4.43	5.20	5.96	5.20	6.53	5.91	5.30	5.49	5.20	6.39	4.75	4.70	5.75	8.88			
S.E.								0.79	0.77	0.79	0.83	0.79	0.85	0.83	0.80	0.87	0.79	0.94	0.84	0.70	1.00	1.89			
t								0.145	1.155	0.891	0.897	1.685	1.911	2.446	2.371	0.838	1.746	1.715	1.668	2.007	0.175	1.215			

Individual Data: 7 FOOD CONSUMPTION OF FEMALES DURING GESTATION

Rats Piroctone olamine 500 mg/kg s.c.

Days / No.	Days of gestation 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain -	-	-
1 1-2								24.0	18	14	22	26	26	24	22	24	22	20	20	26	30	24			
2 8								24.8	28	24	24	20	20	24	26	24	24	26	24	28	26	26			
3 9								23.1	20	22	26	26	24	26	20	20	26	24	24	26	22	28			
4 2-9								24.9	20	20	28	20	20	22	22	20	22	20	24	26	28	26			
5 11								21.1	26	24	28	28	20	26	24	26	28	24	30	30	28	30			
6 12								21.7	22	26	24	26	20	24	22	22	20	22	20	24	26	24			
7 13								20.9	26	14	24	20	24	20	26	22	20	20	22	20	22	26			
8 14								26.9	20	26	20	26	20	24	28	20	28	24	20	20	20	20			
9 3-15								23.1	22	20	24	24	26	26	28	22	24	20	24	28	28	18			
10 16								23.4	26	21	28	22	22	20	26	20	20	22	24	24	24	12			
11 17								22.0	24	24	20	20	20	20	24	22	20	20	26	24	28	24			
12 4-18								22.1	20	26	26	26	24	18	26	22	22	22	22	26	20	10			
13 5-19								26.8	20	24	22	26	22	20	22	20	24	24	20	22	20	28			
14																									
15 11								20.6	24	20	20	20	18	22	20	16	26	22	28	20	24	14			
16 12								24.3	26	26	18	26	28	28	24	22	24	26	26	24	20	24			
17 8-9								27.1	28	24	24	22	20	22	20	26	22	26	20	28	26	26			
18 10								22.9	26	20	22	24	24	24	24	14	22	24	28	28	26	20			
19 11								21.4	20	18	22	16	26	20	20	16	22	26	28	26	22	20			
20 6-11								26.6	26	26	24	20	20	24	20	28	28	24	24	30	28	18			
21 14								20.6	16	20	18	22	20	20	18	16	20	20	24	22	20	10			
22 15								28.7	20	20	26	28	24	20	24	24	24	28	24	26	28	16			
23																									
24																									
25																									
26																									
27																									
28																		* P < 0.05,		** P	0.01				
No.								21																	
Mean								23.72	22.36	22.05	23.81	23.83	23.24	23.52	23.62	23.67	24.19	24.00	24.28	25.22	26.08	23.05			
S								85.52	268.57	260.95	215.31	217.11	263.81	223.24	196.15	482.67	238.24	264.00	274.28	175.24	237.24	125.16			
S.D.								2.92	3.66	3.61	3.28	3.59	3.49	3.34	3.14	4.91	3.44	3.63	3.81	3.36	3.40	3.14			
S.E.								0.45	0.80	0.79	0.72	0.78	0.76	0.73	0.68	1.07	0.75	0.79	0.83	0.65	0.74	0.28			
t								2.214	1.633	2.031	0.587	1.972	2.359	2.427	2	2.259	3.106	3.055	3.201	2.078	1.977	1.019			

Indivi l Data: 8 FOOD CONSUMPTION OF FEM S DURING GESTATION

Rats Piroctone olamine 2000 mg/kg s.c.

Days / No.	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Gain		
								Days of gestation																	
1 / - 10								25.2	22	22	22	22	18	18	18	18	26	22	20	22	24	26			
2 11								22.6	18	14	20	24	26	20	22	22	28	20	24	30	30	34			
3 12								25.4	[illegible]	22	24	26	20	22	20	18	20	20	26	20	20	26			
4 13								22.3	22	20	20	26	24	22	24	22	24	24	20	24	24	40			
5 14								20.9	14	16	20	20	20	18	20	18	20	20	22	20	20	24			
6 3 - 15								25.1	16	16	22	26	22	22	18	26	26	22	26	24	24	22			
7 16								24.3	20	16	24	22	20	22	18	20	20	18	24	24	16	16			
8 17								22.4	22	26	26	24	22	24	24	22	20	20	24	26	22	30			
9 18								22.9	24	20	22	22	24	22	18	22	22	16	22	22	30	28			
10 4 - 19								22.6	16	20	20	18	20	22	24	20	20	26	24	26	22	20			
11 20								25.4	26	28	26	24	24	20	22	20	18	20	24	26	30	20			
12 21								24.9	24	26	24	24	26	18	28	20	22	24	24	22	28	18			
13 22								24.7	18	20	22	22	20	24	20	24	16	24	26	24	30	20			
14 23								22.1	26	22	22	22	26	20	26	20	20	22	24	22	22	24			
15 24								27.1	20	24	26	20	24	20	24	18	22	20	22	28	28	26			
16 5 - 25								22.9	24	20	20	26	24	28	20	20	16	24	20	22	22	18			
17 26								27.1	24	20	20	16	16	16	16	16	16	24	16	28	20	20			
18 27								26.6	26	20	18	24	24	24	20	20	26	26	26	28	20	20			
19 6 - 28								27.1	20	24	26	24	22	26	26	22	26	24	24	28	28	26			
20 29								26.9	26	18	22	20	22	26	20	18	22	24	26	30	28	26			
21 30								27.7	25	22	26	16	26	26	22	20	18	18	22	26	26	26			
22 31								24.1	20	20	22	20	24	16	16	12	18	22	24	26	26	24			
23 7 - 32								22.9	26	16	16	22	24	16	20	20	16	24	14	26	30	20			
24 33								27.7	18	20	16	24	20	20	20	18	36	20	24	20	22	24			
25																									
26																									
27																									
28																									
No.								24									* P < 0.05,		** P < 0.01		*** P < 0.01				
Mean								23.92	20.50	22.92	20.50	22.25	22.25	22.42	22.42	22.83	22.42	22.42	22.42	22.42	22.50	24.92			
S								106.88	514.00	361.83	408.00	487.50	458.50	447.42	447.42	521.83	511.83	459.42	433.83	515.42	424.00	532.83			
S.D.								2.16	4.73	4.48	4.53	4.71	4.68	4.67	4.67	4.76	4.73	4.67	4.65	4.67	4.50	4.63			
S.E.								0.44	0.96	0.91	0.92	0.96	0.95	0.95	0.95	0.96	0.96	0.94	0.94	0.94	0.88	0.94			
t								0.526	2.619	4.055	3.804	3.783	3.483	3.785	4.281	5.340	4.840	5.315	5.221	4.447	4.615	3.464			

Individual Data: 9 CESAREAN SECTION FINDINGS

Rats — Piroctone olamine — 0 mg/kg (Control) — s.c.

Dam No.	No. of corpora lutea	No. of implantations	No. of living fetuses: Total	Males	Females	Immature fetuses	No. of dead fetuses	No. of resorbed fetuses: Implantsites	Placental remnants	Early resorp.	Late resorp.	Macerated fetuses	External abnormalities	Body weight of living fetuses: Male (g)	Female (g)		
1 1-1	16	16	16	8	8									5.83	4.94		
2 2	18	15	14	7	7				1					5.43	5.42		
3 2	16	16	16	10	6									5.05	5.03		
4 3-1	19	19	17	11	6				3				a	4.78	4.59		
5 3	17	16	13	8	5				3					5.18	4.43		
6 2	16	14	14	8	6									5.84	5.33		
7 4	15	13	13	6	7									4.67	5.50		
8 3-1	13	13	13	4	9									5.53	5.36		
9 3	13	4	4	3	1	(3)								4.80	4.01		
10 2	15	15	15	10	5									5.45	5.08		
11 4	16	16	16	10	6									5.37	4.75		
12 1	18	18	19	6	13	(1)								5.44	4.84		
13 1	18	18	16	8	8				3					5.38	4.76		
14 4-1	19	19	19	10	9									5.30	5.04		
15 3	15	13	13	8	4				1					5.45	5.48		
16 3	17	17	17	11	6									5.33	4.78		
17 4	13	11	10	4	6						1			5.43	4.87		
18 5-1	17	17	16	6	10				1					5.49	5.08		
19 3	17	17	16	11	5				1					5.44	5.13		
20 3	15	14	14	8	6									6.13	5.77		
21 4	14	13	13	4	9									5.46	5.16		
22 6-1	16	16	15	8	7						1			5.53	5.15		
23 3	15	14	14	5	9									5.53	5.33		
24 3	15	13	13	6	6				1					6.01	5.38		
25 4	16	16	13	7	6				3	1				5.36	5.35		
26 5	14	13	13	4	9									5.59	5.40		
27																	
28													a Cleft	palate	in 1 fetus		
29																	
30																	
No. of litters	26	26	26	26	26									26	26		
Total	415	387	370	185	185	(3)	0	0	14	1	2	0	1				
%		93.5	95.6	50.0	50.0	(0.8)			3.6	0.3	0.5		0.32				
Mean	15.92	14.88	14.23	7.12	7.12									5.43	5.04		
Sum of squares	23.846	33.65	222.62	176.65	156.65									3.0357	2.0217		
S.D.	1.22	2.09	2.98	2.64	2.50									0.35	0.53		
S.E.	0.34	0.61	0.59	0.52	0.49									0.07	0.10		
t test																	

Individual Data: 10 CESAREAN SECTION FINDINGS

Rats Piroctone amine 100 mg/kg s.c.

	Dam No.	No. of corpora lutea	No. of implantations	No. of living fetuses: Total	Males	Females	Immature fetuses	No. of dead fetuses	No. of resorbed fetuses: Implant sites	Placental remnants	Early resorp.	Late resorp.	Macerated fetuses	External abnormalities	Body weight of living fetuses: Male (g)	Female (g)		
1	1-4	16	16	16	8	8									5.25	4.91		
2	5	17	17	16	7	9						1		a	5.41	5.04		
3	6	16	12	12	6	6									5.49	5.19		
4	2-5	18	18	18	8	10								b	4.96	4.71		
5	6	16	14	14	6	8								c	5.37	5.05		
6	7	15	14	14	7	7									5.51	5.24		
7	3-7	20	20	18	8	10				2					4.83	4.57		
8	8	16	16	14	8	6				2					5.43	4.95		
9	10	15	14	14	5	9									5.24	4.73		
10																		
11	11	18	17	17	6	11									5.33	5.07		
12																		
13	4-6	17	17	17	11	6									5.48	5.22		
14	7	16	14	14	8	6									5.17	4.89		
15	8	18	18	18	7	11									4.69	4.60		
16	9	18	18	13	5	8				4		1			5.67	7.99		
17	5-6	18	18	18	7	11								d	5.32	5.13		
18	7	17	17	16	7	9					1				5.55	4.95		
19	8	16	13	11	5	6				1	1				5.80	5.55		
20	6-8	18	18	18	9	9									4.53	4.27		
21	7	18	18	15	8	7				2	1				5.04	5.02		
22	8	16	15	14	5	9				1					5.86	5.52		
23	9	22	22	22	12	10									5.21	4.87		
24	10	15	15	15	6	9									5.60	4.65		
25																		
26																		
27																		
28																		
29																		
30																		
No. of litters		22	22	22	22	22									22	22		
Total		376	361	344	159	185	0	0	0	12	3	2	0	5				
%			95.0	85.3	46.2	53.8				3.3	0.8	0.6		1.45				
Mean		17.09*	16.41	15.64	7.23	8.41*									5.31	5.10		
Sum of squares		57.818	119.32	131.09	69.504	63.318									2.4001	10.677		
S.D.		1.69	2.38	2.50	1.82	1.74									0.34	0.71		
S.E.		0.36	0.51	0.53	0.39	0.37									0.07	0.15		
t test		2.365	1.886	1.750	0.168	2.042									1.145	0.316		

[a] Defect of the tail in 1 fetus; [b] Tail with the skin only (without the coccygeal vertebrae) in 1 fetus; [c] Cleft palate in 2 fetuses; [d] Shortening of the lower half of the body, defect of the tail, and oligodactyly of the right forelimb

* $P < 0.05$

Individual Data: 11 CESAREAN SECTION FINDINGS

Rats | Piroctone olamine | 500 mg/kg | s.c.

Dam No.	No. of corpora lutea	No. of implantations	No. of living fetuses: Total	Males	Females	Immature fetuses	No. of dead fetuses	No. of resorbed fetuses: Implantations	Placental remnants	Early resorp.	Late resorp.	Macerated fetuses	External abnormalities	Body weight of living fetuses: Male (g)	Female (g)		
1 1:2	12	16	16	10	6									5.50	5.04		
2 8	16	12	10	3	7				2					5.88	5.22		
3 7	16	16	16	9	7									5.43	5.13		
4 2-7	12	12	12	6	6									5.58	4.31		
5 11	22	22	22	10	12									4.80	4.35		
6 12	16	13	13	7	6									5.28	5.22		
7 13	16	16	15	7	8				1					5.84	5.06		
8 14	19	17	15	4	11				2					5.91	5.49		
9 3-13	18	18	18	11	7									5.36	4.90		
10 14	18	16	15	5	10				1					5.39	5.37		
11 15	16	16	16	8	8									5.36	4.93		
12 16	16	15	14	10	4				1					5.45	5.16		
13 4-5	20	20	15	8	7	(1)			5					4.97	5.14		
14																	
15 11	16	13	13	5	8									5.48	5.13		
16 12	17	17	16	9	7				1					5.41	4.93		
17 5-9	17	17	15	8	7				2					5.69	5.38		
18 10	16	15	15	7	8									5.20	5.08		
19 11	17	14	13	8	5				1					5.43	5.11		
20 1-11	20	20	19	8	11				1					5.86	5.01		
21 14	16	16	15	8	7	(1)			1					5.38	4.85		
22 15	17	17	17	6	11									5.11	4.96		
23																	
24																	
25																	
26																	
27																	
28																	
29																	
30																	
No. of litters	21	21	21	21	21									21	21		
Total	361	338	330	157	173	(3)	0	0	18	0	0	0	0				
%		93.6	96.7	47.7	50.7	(0.6)			5.3								
Mean	17.19	16.10	15.24	7.48	7.76									5.42	5.04		
Sum of squares	63.238	131.81	127.81	82.238	89.810			* P = 0.05						1.5957	2.0158		
S.D.	1.78	2.57	2.53	2.09	2.12									0.38	0.32		
S.E.	0.39	0.56	0.55	0.46	.46									0.06	0.07		
t test	2.475	1.438	0.330	0.5[illegible]	.943									0.036	0.020		

Individual Data: 12 CESAREAN SE[illegible] – FINDINGS

Rats Pirocto[illegible]olamine 2000 mg/kg s.c.

Dam No.	No. of corpora lutea	No. of implan-tations	No. of living fetuses: Total	Males	Females	Immature fetuses	No. of dead fetuses	No. of resorbed fetuses: Implant sites	Placental remnants	Early resorp.	Late resorp.	Macerated fetuses	External abnor-malities	Body weight of living fetuses: Male (g)	Female (g)
1 1-10	17	17	0	0	0			17						-	-
2 11	17	15	15	9	6									5.10	5.10
3 12	16	15	12	7	5				2		1			4.66	4.47
4 13	18	16	15	8	7				1					5.23	4.60
5 14	14	13	11	7	4	(1)			2					5.51	4.76
6 2-15	15	15	15	9	6	(1)								5.05	4.99
7 16	16	15	15	9	6									4.95	4.76
8 17	16	15	15	4	11									5.17	4.60
9 18	16	16	16	10	6									4.74	4.34
10 3-17	15	13	13	4	8									5.00	5.00
11 18	15	14	14	11	3									5.67	5.31
12 19	15	15	15	8	7									5.12	4.98
13 20	16	15	15	6	9	(1)								5.38	4.58
14 21	16	16	15	6	9				1					5.33	4.69
15 22	16	15	14	7	7				1					5.65	5.06
16 4-14	16	16	13	6	6					2	2			4.83	4.87
17 15	15	15	11	3	8				2	1	1			4.11	4.30
18 16	20	19	18	7	11					1			a	4.77	4.22
19 5-13	17	16	14	6	8				1		1			4.93	4.74
20 14	16	14	13	10	3					1				5.63	5.38
21 15	15	11	11	8	3								b	5.78	5.00
22 17	17	17	16	4	12				1					5.86	4.55
23 6-16	16	16	16	4	12									4.96	4.46
24 17	18	18	15	7	8				2	1				5.10	4.76
25															
26															
27															
28															
29															
30															
No. of litters	24	24	24	24	24									23	23
Total	388	366	325	160	165	(3)	0	17	13	6	5	0	2		
%		94.3	88.8	49.2	50.8	(0.9)		4.6	3.6	1.6	1.4		0.62		
Mean	16.17	15.25	13.54	6.67	6.88									5.15*	4.76*
Sum of squares	32,333	18,500	267.96	151.33	205.63									3.7698	2.1077
S.D.	1.27	1.73	3.41	2.57	3.01									0.41	0.31
S.E.	0.26	0.35	0.70	0.52	0.61									0.09	0.06
t test	0.565	0.510	0.761	0.608	0.308									2.458	2.293

[a] Abnormally curved spina, tail with the skin only, and shortening of the lower half of the body in 1 fetus; [b] Reduction deformity of the left hindlimb in 1 fetus

* $P < 0.05$

Individual Data: 13-1 ORGAN WEIGHTS OF FEMALES

Rats | Piroctone olamine | 0 mg/kg (Control) | s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
1-1	430	1.77	19	18	132	1.10	1.39	14.93	0.88	0.78	1.18	1.17	51	53	91	90	6.38	0.14
2	384	1.59	16	22	222	0.94	1.34	13.37	0.73	0.48	0.86	0.77	45	53	70	55	4.96	0.12
3	400	1.81	16	12	63	0.92	1.35	13.39	0.77	0.61	0.93	1.00	50	56	65	50	5.49	0.10
2-1	400	1.98	15	18	148	1.08	1.27	16.68	0.80	0.67	1.09	1.05	45	50	55	88	6.05	0.15
2	424	1.88	17	19	228	1.13	1.32	19.39	0.73	0.54	1.04	1.09	49	45	93	64	5.20	0.15
3	376	1.72	19	19	171	0.85	1.16	11.90	0.74	0.48	0.79	0.85	43	43	64	55	5.16	0.14
4	382	1.74	11	10	164	0.86	1.09	11.39	0.81	0.74	0.93	0.87	33	43	53	46	5.65	0.13
3-1	372	1.73	15	16	215	0.94	1.32	11.92	0.72	0.68	0.90	0.96	51	53	63	55	6.18	0.11
2	342	1.94	22	20	217	1.03	1.46	14.11	0.59	0.78	0.97	0.92	37	43	99	76	2.75	0.16
3	356	1.92	18	20	207	0.80	1.25	10.04	1.08	0.45	0.84	0.83	42	49	44	75	5.06	0.13
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 13-2 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
3-4	414	1.91	18	21	162	0.92	1.36	13.84	0.81	0.49	0.88	0.85	46	53	88	85	6.28	0.21
5	408	1.82	14	15	96	0.91	1.42	11.95	0.72	0.49	0.96	0.92	38	49	81	71	6.03	0.12
6	382	1.93	16	23	203	1.24	1.50	13.42	0.77	0.61	0.89	0.91	49	43	61	85	6.28	0.21
4-1	472	1.76	20	22	286	1.07	1.60	12.90	0.94	0.56	1.13	1.11	41	45	76	104	6.32	0.13
2	350	2.02	21	16	148	0.86	1.35	11.97	1.02	0.58	0.93	0.93	45	53	54	76	4.81	0.11
3	354	1.94	13	25	199	0.87	1.43	11.21	0.78	0.40	0.94	0.96	46	51	79	70	5.54	0.12
4	330	1.90	17	26	132	0.86	1.32	11.77	0.81	0.49	0.84	0.82	34	47	76	62	3.68	0.10
5-1	378	1.88	20	25	194	0.90	1.33	11.89	0.80	0.62	1.01	0.98	65	65	73	54	4.81	0.09
2	392	1.90	15	20	119	0.92	1.36	12.84	0.90	0.52	1.01	1.04	49	49	60	82	4.68	0.11
3	430	1.74	16	17	211	1.00	1.41	14.82	0.64	0.49	1.13	1.11	45	49	78	72	5.31	0.10
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 13-3 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
5-4	368	1.81	18	13	88	1.04	1.14	12.60	0.83	0.59	0.95	1.06	48	45	63	59	5.41	0.16
6-1	452	1.88	21	34	216	1.09	1.50	16.68	1.04	0.70	0.99	0.98	56	65	75	85	6.06	0.11
2	378	1.88	23	23	126	0.90	1.63	12.72	0.70	0.71	0.97	0.96	52	54	53	98	5.25	0.09
3	378	1.86	19	22	177	1.03	1.48	14.29	0.94	0.58	1.01	0.98	48	53	55	64	5.79	0.14
4	386	1.89	18	20	299	1.06	1.43	15.75	0.98	0.75	1.16	1.11	48	59	55	62	5.19	0.09
5	376	1.98	16	18	233	0.97	1.13	12.06	0.83	0.64	0.96	0.92	46	45	78	68	4.53	0.11
26																		
Mean	389.00	1.87	17.38	19.77	179.27	0.97	1.36	13.51	0.82	0.59	0.97	0.97	46.33	50.65	68.88	71.19	5.34	0.13
Sum of squares	27770.	0.1708	204.15	604.62	81943.	0.2851	0.4588	124.96	0.3705	0.2936	0.2570	0.2675	1112.6	1005.9	5318.7	5780.0	17.803	0.0254
S.D.	33.33	0.08	2.86	4.92	57.25	0.11	0.14	2.24	0.12	0.11	0.10	0.10	6.67	6.34	14.59	15.31	0.84	0.03
S.E.	6.54	0.02	0.56	0.96	11.23	0.02	0.03	0.44	0.02	0.02	0.02	0.02	1.31	1.24	2.86	2.98	0.17	0.01
t test																		

Individual Data: 14-1 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 100 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pitu-ttary (mg)	Thy-roid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pan-creas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
1-4	424	1.86	16	17	164	0.93	1.45	15.95	1.01	0.59	1.00	1.04	43	59	87	58	4.90	0.13
5	420	1.83	18	16	226	0.99	1.38	14.79	1.16	0.58	1.02	1.08	56	71	56	83	5.00	0.16
6	366	1.91	17	18	180	0.91	1.64	14.89	0.98	0.48	0.94	1.01	50	55	34	97	3.72	0.14
7-8	370	1.56	15	14	149	0.93	1.39	11.58	0.47	0.44	0.88	0.94	55	56	57	72	4.48	0.14
9	396	1.98	14	15	111	0.97	1.52	12.50	0.93	0.59	1.12	1.26	55	58	86	71	3.05	0.16
10	396	1.12	12	18	236	0.92	1.42	13.98	1.15	0.59	1.05	1.02	54	48	54	70	4.30	0.09
11-12	374	1.91	15	22	126	0.96	1.34	14.13	0.89	0.44	1.01	0.95	56	45	50	72	5.09	0.11
13	370	1.29	19	15	108	1.18	1.30	16.40	0.58	0.51	0.88	0.94	42	48	68	80	4.22	0.11
14	362	1.22	14	21	159	0.95	1.39	10.72	0.59	0.42	0.82	0.84	53	56	78	72	4.66	0.12
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 14-2 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 100 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
3 - 12	424	1.22	16	20	203	0.84	1.40	13.15	1.05	0.68	0.88	1.10	40	48	83	22	4.58	0.13
4 6	403	1.83	16	18	245	0.83	1.36	13.11	1.34	0.67	0.84	0.88	50	54	68	26	5.89	0.12
7	332	1.84	13	23	95	0.78	1.33	10.64	0.64	0.48	0.76	0.77	48	53	43	21	4.52	0.11
8	360	1.83	10	27	161	0.86	1.50	11.15	0.70	0.46	0.84	0.90	40	43	68	26	4.45	0.14
5 - 5	386	1.94	16	15	146	0.86	1.37	13.34	1.40	0.60	1.01	0.86	61	47	77	22	4.24	0.13
6	388	1.93	20	20	135	0.71	1.33	12.04	0.70	0.53	0.93	1.03	52	53	71	34	4.38	0.11
7	378	1.86	15	15	138	0.90	1.37	13.71	1.00	0.55	1.07	1.03	45	46	74	45	4.63	0.12
8	372	1.72	19	14	133	1.09	1.43	14.22	1.07	0.51	1.17	1.37	38	43	88	56	5.10	0.09
6 - 1	410	1.83	13	31	140	1.36	1.35	13.34	1.33	0.53	1.06	1.08	35	38	65	80	6.51	0.13
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 14-3 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 100 mg/kg S.C.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
7	410	1.31	20	25	129	1.10	1.82	19.44	1.06	0.53	0.78	1.13	45	63	99	98	6.00	0.15
8	376	1.03	20	18	145	1.03	1.40	15.71	0.79	0.66	1.11	1.03	40	43	78	73	4.99	0.13
9	450	1.13	38	20	138	1.08	1.53	14.99	0.57	0.68	1.14	1.16	63	70	88	84	7.11	0.14
10	382	1.24	33	36	97	0.83	1.41	14.38	0.73	0.67	0.89	1.02	40	45	70	73	5.38	0.13
Mean	390.83	1.86	17.00	19.41	152.14	0.96	1.40	14.07	0.91	0.56	0.98	1.03	48.18	53.86	69.73	74.73	5.02	0.13
Sum of squares	15437.	0.1177	218.00	319.33	33347	0.3333	0.4040	89.376	1.4015	0.1351	0.3213	0.3183	1361.3	1140.6	5862.14	2780.4	20.830	0.0093
S.D.	32.10	0.07	3.89	4.14	39.29	0.12	0.14	3.17	0.36	0.08	0.11	0.13	8.05	9.10	16.33	16.53	1.00	0.02
S.E.	5.78	0.03	0.83	0.88	8.48	0.03	0.03	0.46	0.06	0.03	0.03	0.03	1.73	1.94	3.48	3.46	0.31	0.004
t test	0.285	0.344	0.394	0.273	1.837	0.337	0.966	0.873	1.423	1.333	0.363	1.365	0.918	1.434	0.189	0.894	1.312	0.013

Individual Data: 15-1 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 500 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
1-7	410	1.97	19	18	86	0.81	1.48	13.38	0.92	0.59	0.88	0.98	52	66	64	60	4.90	0.17
8	410	1.85	15	20	246	1.22	1.63	15.35	1.54	0.66	1.03	1.11	47	51	40	82	4.13	0.11
9	400	1.86	16	15	130	0.97	1.38	15.20	0.88	0.50	1.02	1.10	68	65	91	66	5.34	0.15
2-9	386	1.90	15	22	80	1.10	1.38	12.33	0.80	0.67	1.12	1.05	56	61	54	52	4.07	0.14
11	436	1.90	23	18	142	0.93	1.57	15.45	1.25	0.61	1.03	1.02	61	73	77	81	6.02	0.13
12	354	1.80	28	22	106	0.79	1.44	13.25	1.03	0.73	0.97	0.80	55	72	52	62	3.44	0.15
13	440	1.91	16	28	186	1.10	1.41	18.02	1.45	0.73	1.04	1.23	73	57	101	62	5.06	0.13
14	436	1.82	20	22	154	1.04	1.44	15.18	1.45	0.70	1.00	1.06	66	64	107	130	5.34	0.21
5-12	410	1.90	19	25	64	0.97	1.44	13.33	0.75	0.59	1.07	1.11	58	63	70	65	4.93	0.11
3-13	388	1.80	16	27	104	0.94	1.23	12.46	1.07	0.53	0.85	0.92	68	68	77	70	4.60	0.12
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 15-2 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 500 mg/kg u.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
3 - 1	406	1.78	18	30	146	1.11	1.45	16.72	1.17	0.62	0.96	0.90	55	56	82	83	4.27	0.16
2	352	1.83	19	26	94	0.83	1.32	12.06	1.09	0.48	0.93	0.84	52	48	70	70	4.34	0.11
4 - 1	410	1.88	19	18	81	1.01	1.55	16.86	1.15	0.64	1.11	1.22	48	54	76	84	4.61	0.14
2																		
11	350	1.86	16	19	121	1.01	1.32	14.12	0.88	0.56	1.07	1.04	50	70	58	72	5.08	0.14
12	410	1.89	15	21	122	1.02	1.42	16.41	1.36	0.67	0.99	1.12	50	70	102	80	5.86	0.12
5 - 1	405	1.90	18	20	211	0.88	1.16	14.94	1.08	0.48	1.01	1.01	52	63	78	60	4.36	0.11
2	411	1.90	18	18	186	1.00	1.55	14.41	1.24	0.45	1.17	1.18	52	52	63	58	5.97	0.13
3	346	1.80	18	19	95	0.96	1.18	11.83	0.85	0.52	0.75	0.79	45	58	72	71	4.07	0.14
6 - 1	416	1.84	16	20	122	1.17	1.58	15.38	1.30	0.66	1.07	1.10	48	58	88	104	5.35	0.13
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 15-3 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 500 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
6-14	350	1.91	16	22	102	0.88	1.46	12.41	0.82	0.63	0.80	0.87	45	62	59	58	4.94	0.11
6-15	390	1.86	17	30	20	0.92	1.47	13.88	0.94	0.60	0.91	0.99	55	56	62	78	4.35	0.11
21																		
Mean	400.86	1.82	18.38	21.90	** 126.57	0.99	1.42	14.62	*** 1.10	0.60	0.98	1.02	*** 55.05	*** 61.29	73.48	74.29	4.92	0.13
Sum of squares	19845.	0.0649	226.95	437.81	56717.	0.2570	0.3203	63.758	1.0764	0.1335	0.2626	0.3348	1277.0	1016.3	6105.2	6404.3	11.148	0.0123
S.D.	31.50	0.06	3.37	4.68	53.25	0.11	0.13	1.79	0.23	0.08	0.11	0.13	7.99	7.13	17.47	17.89	0.75	0.02
S.E.	6.87	0.01	0.74	1.02	11.62	0.02	0.03	0.39	0.05	0.02	0.03	0.03	1.74	1.56	3.81	3.90	0.16	0.01
t test	1.242	0.126	1.097	1.512	3.236	0.511	1.584	1.927	5.338	0.295	0.256	1.581	4.124	5.406	0.982	0.641	1.803	0.676

** P < 0.01, *** P < 0.001

Individual Data: 16-1 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 2000 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
1-10	220	1.78	18	20	120	0.92	1.43	14.41	1.26	0.42	0.96	0.95	53	62	54	42	0.21	0.10
11	226	1.86	20	22	122	1.16	1.40	19.88	1.53	0.66	1.34	1.33	65	82	62	62	4.22	0.33
12	248	1.87	13	14	142	0.91	1.35	18.00	1.52	0.61	1.31	1.05	22	76	63	65	3.26	0.38
13	252	1.87	16	14	44	0.86	1.32	10.82	0.86	0.55	0.95	1.87	53	58	58	60	5.35	0.20
14	240	1.62	11	14	42	0.78	1.21	14.07	1.20	0.48	0.78	1.76	53	58	78	52	3.50	0.11
2-11	290	1.78	21	12	58	0.90	1.36	12.88	1.26	0.53	0.98	0.92	54	50	76	52	4.12	0.18
12	238	1.80	16	13	57	0.77	1.95	10.82	0.88	0.48	0.88	0.88	53	48	72	46	4.77	0.16
13	414	1.86	34	16	148	0.98	1.80	16.91	1.63	0.57	1.11	1.02	53	58	40	20	5.11	0.15
14	286	1.88	18	22	102	0.81	1.38	16.16	1.26	0.68	1.03	1.03	70	63	84	63	5.16	0.16
3-12	232	1.82	12	20	75	0.88	1.28	12.73	0.88	0.51	1.03	0.90	55	65	64	33	3.88	0.36
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 16-2 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 2000 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
3-18	325	1.81	11	18	83	0.97	1.43	14.40	1.37	0.70	1.20	1.26	58	56	50	66	4.49	0.16
19	374	1.81	15	21	55	0.77	1.37	13.37	0.96	0.43	1.05	1.03	70	68	43	50	5.07	0.13
20	370	1.79	18	18	100	0.90	1.40	12.38	1.70	0.56	0.87	0.88	45	47	47	77	5.49	0.17
21	380	1.91	11	18	41	0.90	1.34	14.07	1.07	0.63	1.08	1.08	75	65	53	74	4.41	0.17
22	372	1.78	13	13	57	0.88	1.41	16.76	1.37	0.60	0.96	0.91	63	60	67	63	4.51	0.20
4-14	384	1.81	21	21	78	0.93	1.37	16.63	1.50	0.56	0.96	0.96	55	50	71	64	4.48	0.18
15	344	1.83	15	14	100	1.08	1.34	14.93	1.66	0.67	1.13	1.11	67	65	58	53	4.97	0.15
16	408	1.86	15	20	31	0.98	1.44	18.17	1.40	0.63	1.24	1.25	63	60	60	97	4.60	0.14
5-17	434	1.83	17	13	38	1.14	1.34	16.15	1.40	0.73	1.15	1.15	60	73	83	73	3.93	0.13
18	403	1.87	20	16	110	0.91	1.38	13.59	1.49	0.78	1.09	1.19	58	64	84	52	4.41	0.14
Mean																		
Sum of squares																		
S.D.																		
S.E.																		
t test																		

Individual Data: 16-3 ORGAN WEIGHTS OF FEMALES

Rats Piroctone olamine 2000 mg/kg s.c.

Animal No.	Body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) Right	Kidney (g) Left	Adrenal (mg) Right	Adrenal (mg) Left	Ovary (mg) Right	Ovary (mg) Left	Uterus (g)	Urinary bladder (g)
5-16	284	1.68	24	14	60	0.88	1.28	15.51	1.54	0.72	1.14	1.20	63	67	54	90	4.05	0.14
17	405	1.83	14	20	74	0.98	1.53	14.44	1.30	0.50	1.07	1.07	72	74	67	72	5.35	0.14
6-16	398	1.91	19	16	39	0.80	1.45	14.05	1.41	0.66	1.23	1.20	63	65	79	52	4.71	0.12
17	388	1.81	17	18	98	1.00	1.28	14.60	1.57	0.51	0.96	1.03	52	55	52	83	5.55	0.12
24																		
Mean	384.42	1.82*	16.79	17.33	78.96***	0.92	1.39	14.95*	1.30***	0.59	1.06*	1.04*	60.83***	62.17***	63.79	62.79	4.49**	0.17*
Sum of squares	16808.	0.0998	325.96	363.33	29257.	0.2378	0.4468	112.74	1.5510	0.1975	0.4425	0.4273	1631.3	2841.3	3578.0	5302.0	23.162	0.1111
S.D.	37.03	0.07	3.76	3.97	35.67	0.10	0.14	2.21	0.26	0.09	0.14	0.14	8.42	11.11	12.47	15.18	1.00	0.07
S.E.	5.52	0.01	0.77	0.81	7.28	0.02	0.03	0.45	0.05	0.02	0.03	0.03	1.72	2.27	2.55	3.10	0.20	0.01
t test	0.531	2.316	0.630	1.916	2.362	1.642	0.634	2.279	8.462	0.179	2.653	2.204	6.823	4.543	1.322	1.953	3.236	2.611

* P < 0.05, ** P < 0.01, *** P < 0.001

Individ 1 Data: 17-1 SKELETAL FINDINGS IN FUSES

Rats Piroctone blamine 0 mg/kg (Control) s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
	1-1	1-2	1-3	2-1	2-2	2-3	2-4	3-1	3-2	3-3	3-4	3-5	3-6	4-1	4-2	4-3	4-4	5-1	5-2	5-3	5-4	6-1	6-2	6-3	6-4	6-5		
No. of fetuses examined	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
Nasal bone								1																				
Frontal bone									1																			
Parietal bone																												
Occipital bone																												
Lacrimal bone																												
Maxilla																												
Mandibule																												
Hyoid bone																												
Palatine bone	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
Odontoid process	8	6	6	9	4	7	7	7	0	8	8	9	6	10	6	9	4	8	6	7	7	8	7	6	4	7	174	90.2
Spina																												
Cervical vertebral bodies 1	0	1	0	0	1	0	5	0	0	1	1	1	0	1	0	0	3	3	4	4	0	0	0	0	1	0	26	13.5
2	0	1	0	0	0	0	4	1	0	1	2	4	0	4	0	2	3	3	3	5	0	0	0	0	0	1	34	17.6
3	0	1	0	0	0	0	5	2	0	1	2	3	0	6	0	4	3	4	5	4	0	0	0	0	0	2	42	21.8
4	0	2	1	0	0	0	6	3	0	3	2	5	0	6	0	4	2	4	6	4	0	0	2	1	1	1	53	27.5
5	0	4	1	1	0	0	6	3	0	3	5	5	0	6	0	5	2	5	6	5	1	0	1	1	1	3	64	33.2
6	1	4	3	0	0	0	7	4	0	4	5	5	2	7	1	4	3	5	7	6	1	0	1	2	1	5	78	40.4
7	4	8	6	6	5	0	7	7	0	6	7	7	5	9	2	8	5	7	8	7	4	6	5	5	5	7	146	75.7
Cervical vertebral arches 1-7	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
Thoracic vertebral bodies 1-																												
9																												
10																												
11																												
12																												
Splitting 13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0.5
Thoracic vertebral arches 1-13	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100.0

Individual Data: 17-2 SKELETAL FINDINGS IN FETUSES

Rats — Pirfenidone olamine — 0 mg/kg (Control) — s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Lumbar vertebral bodies & arches																												
1-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1-6	8	7	8	9	7	7	6	7	2	8	8	10	8	8	6	9	5	9	8	7	7	8	7	6	7	7	189	92.2
1-7	0	1	0	0	0	0	1	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	4	2.1
Sacral vertebral bodies & arches																												
1-4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
Coccygeal vertebra bodies																												
1	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
3	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
5	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	5	9	8	7	7	8	7	6	7	7	192	99.5
6	8	8	6	9	3	4	7	6	0	8	7	9	5	10	5	6	5	8	8	7	6	6	7	6	6	7	167	86.5
7	7	8	4	2	2	0	7	5	0	6	4	8	0	7	1	0	1	4	3	6	6	1	6	6	2	4	100	51.8
8	4	5	0	0	0	0	1	0	0	2	0	0	0	1	0	0	0	0	0	1	2	0	1	3	1	1	25	13.0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Average No. of ossified coccygeal vertebral bodies	7.38	7.63	6.25	6.22	5.71	5.57	7.57	6.57	5.00	7.00	6.38	6.60	5.63	6.80	6.00	5.67	6.20	6.33	6.38	7.00	7.00	5.88	7.00	7.50	6.27	6.71 $\bar{x}$	X	6.47
																											S	1.4877
																											S.D.	0.68
																											S.E.	0.13
Coccygeal vertebra arches																												
1	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
3	7	8	7	7	5	6	7	7	2	8	8	9	5	10	5	8	5	4	7	7	6	7	7	6	6	7	171	88.6
4	0	0	0	0	0	0	2	1	0	1	0	0	0	1	1	1	0	0	0	1	1	0	2	0	1	0	12	6.2
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Data: 17-3 SKELETAL FINDINGS IN FETUSES

Rats — Piroctone olamine — 0 mg/kg (Control) — s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Ribs Normal	5	3	2	6	0	1	4	6	0	6	7	7	6	3	5	2	3	7	3	2	6	8	4	3	2	4	105	56.5
14th rib[a] Unilateral	2	0	1	2	3	1	1	1	0	2	1	3	1	3	1	1	1	1	1	1	0	0	1	2	4	1	35	18.7
Bilateral	1	5	5	1	4	5	2	0	2	0	0	0	1	4	0	6	1	1	4	4	1	0	2	1	1	2	53	28.5
Undeveloped 13th rib[a]																												
Waved rib[b]																												
Fused ribs[b]																												
Ossification centers of sternebrae 1	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	183	100
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	183	100
3	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	5	9	8	7	7	8	7	6	7	7	182	99.5
4	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	5	9	8	7	7	8	7	6	7	7	182	99.5
5	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	3	9	8	7	7	8	7	6	7	7	180	98.5
6	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	5	9	8	7	7	8	7	6	7	7	182	99.5
Hypoplasia																												
No. of fetuses	1	1	0	1	4	1	0	2	1	2	1	0	3	0	0	2	1	1	0	0	2	1	0	0	1	1	26	14.5
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	1	1	0	1	4	1	0	2	1	2	1	0	3	0	0	2	1	1	0	0	2	1	0	0	1	1	26	14.5
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Splitting																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

[a] Variation, [b] Abnormality

Individual Data: 1/14 SKELETAL FINDINGS FETUSES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Absence of one of the two parts																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	n.s
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	n.s
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Accessory sternebra[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Asymmetry[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	n.s
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	n.s
3	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	n.s
4	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	n.s
5	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	n.s
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fusion[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Clavicle																												
Scapula																												
Humerus																												
Radius	8	8	8	7	7	7	7	7	2	8	8	10	8	10	6	7	5	7	8	7	7	8	7	6	7	7	(83)	10
Ulna	8	8	8	7	7	7	7	7	2	8	8	10	8	10	6	7	5	7	8	7	7	8	7	6	7	7	(83)	10

[a] Variation, [b] Abnormality

Individual Data: 17-5 SKELETAL FINDINGS IN FETUSES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Metacarpals (bodies) 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
3	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
5	8	8	8	9	7	7	7	7	2	8	8	9	8	10	6	9	5	9	8	7	7	8	7	6	7	7	192	99.5
Phalanges of the forelimbs Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	8	6	7	7	6	7	7	7	1	8	7	8	5	9	6	9	5	8	7	7	5	8	7	6	7	7	175	90.7
3	8	8	8	9	7	7	7	7	1	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	192	99.5
4	8	8	8	9	7	7	7	7	1	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	192	99.5
5	7	4	7	7	6	7	7	7	0	8	6	7	5	9	6	9	5	8	7	7	5	8	7	6	7	7	168	87.6
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Distal 1	8	5	8	9	6	7	7	7	2	8	8	10	8	10	6	9	5	8	8	7	7	8	5	6	6	7	185	95.9
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
3	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
5	8	8	8	9	7	6	7	7	0	8	8	10	8	10	6	9	5	9	7	7	7	8	7	6	7	7	189	97.9
Ilium																												
Ischium																												
Pubis																												
Femur																												
Tibia																												
Fibula																												
Tarsus Astragalus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Calcaneus	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	3	46
Metatarsals (bodies) 1	7	7	5	1	3	7	7	7	0	8	6	9	7	9	5	7	5	8	7	7	6	8	7	6	6	6	161	83.4
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
3	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100
5	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	193	100

Individual Data: 17-6 SKELETAL FINDINGS FETUSES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Phalanges of the hind limb: Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	5	1	1	0	0	5	1	7	0	4	4	4	0	0	0	1	2	0	3	7	4	0	3	6	6	5	48	38.8
3	7	4	4	1	1	6	3	7	6	8	5	7	1	3	3	4	2	3	5	7	4	2	6	6	6	6	111	89.5
4	7	4	4	1	1	5	3	7	0	8	5	6	1	3	2	4	2	3	5	7	4	2	6	6	6	6	108	87.0
5	2	0	0	0	0	0	0	4	0	0	1	0	0	0	0	0	2	0	3	6	2	0	1	3	2	2	38	30.6
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Distal 1	8	8	8	9	7	7	7	7	0	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	121	97.6
2	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	123	100
3	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	123	100
4	8	8	8	9	7	7	7	7	2	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	123	100
5	8	8	8	9	7	7	7	7	0	8	8	10	8	10	6	9	5	9	8	7	7	8	7	6	7	7	121	97.6

Maxilla																												
Mandibule																												
Hyoid bone																												
Palatine bone	8	8	6	9	5	7	9	7	7		9		9	7	9	7	7	8	6	9	8	7	11	8				
Odontoid process	8	8	6	2	3	7	2	6	7		9		8	5	9	7	8	1	5	9	8	7	11	8				
Spine																												
Cervical vertebral bodies 1	1	0	4	1	1	2	0	3	1		3		0	2	3	4	4	2	2	0	0	0	3	0				
2	0	1	5	0	0	1	0	3	3		2		2	0	0	2	5	3	3	0	0	1	4	0				
3	1	1	6	0	3	4	1	3	6		4		2	3	3	3	6	6	4	1	0	1	4	0				
4	1	1	6	0	4	3	2	2	6		5		5	2	4	4	5	7	4	1	1	0	5	0				
5	2	1	5	1	4	3	2	4	5		6		3	2	4	4	7	7	4	0	0	2	7	0				
6	2	1	6	1	5	5	2	3	7		6		4	3	6	4	7	7	4	3	0	1	8	1				
7	8	4	6	3	6	7	8	7	7		8		8	3	9	6	9	8	6	6	4	9	10	7				
Cervical vertebral arches 1-7	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8				
Thoracic vertebral bodies 1-																												
9																												
10																												
11																												
Hypoplasia 12	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0				
Hypoplasia 13	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0				
Thoracic vertebral arches 1-13	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8				

* $p < 0.05$, *** $p < 0.001$

Individual Data: 18-2 SKELETAL FINDINGS - FETUSES

Rats Piroctone olamine 100 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	X
Lumbar vertebral bodies & arches																												
1-5																												
1-6	8	8	6	9	7	7	9	7	7		9		6	7	9	7	9	8	6	8	8	7	11	8			221	97.7
1-7	0	0	0	0	0	0	0	0	0		0		3	0	0	0	0	0	0	1	0	0	0	0			4	2.3
Hypoplasia 2-3	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.6
Sacral vertebral bodies & arches																												
1-4	8	7	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			226	99.4
Fusion of arches	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.6
Coccygeal vertebral bodies 1	8	7	6	8	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			222	98.3
2	8	7	6	8	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			222	98.3
3	8	7	6	8	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			222	98.3
4	8	7	6	8	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			222	98.3
5	8	7	6	8	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			222	98.3
6	6	5	6	7	6	6	9	7	7		9		9	7	8	6	8	7	6	9	7	7	11	8			207	92.0
7	1	1	5	5	4	4	7	6	6		7		6	6	3	2	7	5	6	6	3	4	11	8			162	71.6
8	0	0	2	1	1	1	1	5	1		2		1	4	0	0	6	2	4	0	1	2	3	6			43	19.6
9	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	1	0	0	0	0	1			3	1.3
10	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
11	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
12	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Defect of the tail	0	1	0	1	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			3	1.3
Average No. of ossified coccygeal vertebral bodies	5.88	5.13	7.17	5.89	6.57	6.57	6.87	7.57	7.00		7.00		6.78	7.43	6.22	6.14	6.89	6.75	7.67	6.67	6.38	6.89	7.27	7.88		$\bar{x}$	X	6.26
Fusion of sacral vertebral bodies & arches		1																									S	2.820
Absence of the sacral vertebrae 2-4		1																								S.D.	sd	1.68
Absence of the coccygeal vertebrae				1																						S.E.	se	0.47
Coccygeal vertebral arches 1	8	7	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			222	98.3
2	8	7	6	8	6	7	9	7	7		9		9	7	8	7	8	8	6	9	8	7	11	8			220	97.4
3	4	5	6	8	6	4	9	7	5		9		9	5	7	7	8	7	6	8	5	7	11	8			187	82.7
4	1	0	1	0	0	0	1	0	1		3		0	1	0	0	3	1	2	3	1	0	8	5			51	22.7
5	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
6	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
7	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0

* $P < 0.05$, ** < 0.01, *** $P < 0.001$

a Abnormality. One fetus did not have the last vertebral arch.

Individual Data: 18-3 SKELETAL FINDINGS IN FETUSES

Rats Piroctone olamine 100 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Ribs Normal	7	6	5	8	7	3	7	1	6		5		4	7	7	2	7	7	4	3	8	0	3	5			112	44.8
14th rib[a] Unilateral	0	2	1	0	0	2	1	4	0		3		0	0	2	2	1	1	1	1	0	6	1	2			30	12.1
Bilateral	1	0	0	1	0	2	1	2	1		1		5	0	0	3	0	0	1	5	0	1	7	1			33	13.2
Undeveloped 13th rib[a]	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Waved rib[b]	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Fused ribs[b]	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Fusion & bifurcation[b] of ribs	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.6
Ossification centers of sternebrae 1	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
2	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
4	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
5	7	7	6	9	6	6	9	7	6		8		9	7	8	7	9	7	6	9	8	7	11	8			167	95.4
6	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
Hypoplasia																												
No. of fetuses	3	0	0	1	4	2	1	0	1		1		0	1	1	0	1	5	1	0	5	0	2	1			30	12.1
1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
3	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
4	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
5	3	0	0	1	4	2	1	0	1		1		0	1	1	0	0	5	1	0	5	0	2	1			27	11.1
6	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.6
Splitting																												
No. of fetuses	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
3	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
4	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
5	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
6	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0

[a] Variation, [b] Abnormality

* P < 0.05

Indiv[illegible] [illegible] Data: 18-4 SKELETAL FINDINGS I[illegible]ETUSES

Rats P[illegible]octone olamine 100 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Absence of one of the two parts																												
No. of fetuses	3	1	0	1	0	0	0	0	0		0		0	0	0	3	0	0	0	0	1	0	0	0			7	5.1
1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	0	1	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			1	0.6
3	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
4	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
5	3	0	0	1	0	0	0	0	0		0		0	0	0	3	0	0	0	0	1	0	0	0			8	4.6
6	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Accessory sternebra[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Asymmetry[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
3	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
4	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
5	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
6	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Fusion[b]	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.6
Clavicle																												
Scapula																												
Humerus																												
Radius	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			175	100
Ulna	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			174	99.4
Absence of manulna																	1											

[a] Variation, [b] Abnormality

* P < 0.05

Indivi al Data: 18-5 SKELETAL FINDINGS IN ETUSES

Rats Piroctone olamine 100 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	To-tal	%
Metacarpals (bodies) 1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
4	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
5	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
Phalanges of the forelimbs (proximal) 1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	7	7	6	6	6	7	9	6	6		8		9	7	8	7	7	8	6	9	8	7	10	8			123	98.4
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
4	8	7	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			123	98.4
5	4	7	6	6	6	7	9	6	6		8		9	7	7	7	7	8	6	9	8	7	10	8			118	94.4
Middle 1-5	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Distal 1	7	7	6	8	6	7	9	7	7		8		9	7	9	7	8	8	6	9	7	7	11	8			118	94.4
2	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			125	100
4	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
5	8	7	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			123	98.4
Oligodactyly	0	0	0	0	0	0	0	0	0		0		0	0	0	0	1	0	0	0	0	0	0	0			1	0.8
Ischium																												
Pubis																												
Femur																												
Tibia																												
Fibula																												
Tarsus Astragalus	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Calcaneus	0	1	2	0	0	1	0	0	0		0		0	0	0	0	1	0	3	0	0	3	0	0			11	8.8
Metatarsals (bodies) 1	4	8	6	2	3	6	4	7	6		6		9	7	9	6	8	5	6	9	2	7	10	8			105	78.7
2	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			125	100
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			125	100
4	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			125	100
5	8	8	6	9	7	7	9	7	7		9		9	7	9	7	9	8	6	9	8	7	11	8			125	100

** P < 0.01

Individual Data: 18-6 SKELETAL FINDINGS IN FETUSES

Rats Piroctone olamine 100 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Phalanges of the Hind Limbs																												
Proximal 1	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
2	0	3	3	1	2	4	0	0	4		2		6	7	0	5	5	4	6	0	2	5	5	5			19	38.4
3	2	6	4	2	3	5	2	0	4		5		8	7	1	6	7	5	6	1	3	6	7	5			25	54.3
4	2	6	3	2	3	5	1	0	4		4		8	7	1	6	7	5	6	1	3	6	7	5			22	52.4
5	0	1	0	0	1	1	0	0	0		1		1	1	0	1	1	3	5	0	2	1	1	1			21	12.0
Middle 1 5	0	0	0	0	0	0	0	0	0		0		0	0	0	0	0	0	0	0	0	0	0	0			0	0
Distal 1	8	8	6	9	6	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			123	98.9
2	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
3	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
4	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4
5	8	8	6	9	7	7	9	7	7		9		9	7	9	7	8	8	6	9	8	7	11	8			124	99.4

Individ . Data: 19-1 SKELETAL FINDINGS IN I USES

Rats . Piroctone dlamine 500 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
	1-7	1-8	1-9	2-9	2-11	2-12	2-13	2-14	3-13	3-14	3-15	3-16	4-9	4-10	4-11	4-12	5-9	5-10	5-11	6-11	6-14	6-15						
No. of fetuses examined	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Nasal bone																												
Frontal bone																												
Parietal bone																												
Occipital bone																												
Lacrimal bone																												
Maxilla																												
Mandibule																												
Hyoid bone																												
Palatine bone	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Odontoid process	8	5	6	6	8	3	4	8	8	6	4	6	5		7	8	5	8	7	10	7	9					138	84.2
Spina																												
Cervical vertebral bodies 1	3	2	0	0	2	0	1	2	2	2	2	4	3		0	2	5	0	1	7	3	2					43	26.2
2	3	1	0	2	3	0	0	3	1	3	1	1	3		1	0	4	0	1	6	2	1					36	22.0
3	5	4	0	4	2	3	3	3	2	6	0	1	4		3	0	7	2	1	7	6	1					64	39.0
4	4	4	0	3	3	4	3	4	3	4	0	2	3		4	2	7	4	1	7	5	2					69	42.1
5	6	5	0	4	4	4	3	4	3	5	1	2	4		4	1	7	6	1	7	6	2					79	48.2
6	8	5	0	4	4	4	3	6	3	5	2	2	4		5	1	7	5	2	7	7	2					86	52.4
7	8	5	3	6	10	7	4	6	9	6	7	6	6		6	5	7	8	3	8	8	3					131	79.9
Cervical vertebral arches 1-7	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Thoracic vertebral bodies 1-																	* P < 0.05, ** P < 0.01, *** P<0.001											
9																												
10																												
11																												
12																												
13																												
Thoracic vertebral arches 1-13	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100

Indivi[illegible] Data: 19-2 SKELETAL FINDINGS IN [illegible]USES

Rats Piroctone olamine 500 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Lumbar vertebral bodies & arches																												
1-5																												
1-6	8	5	8	6	11	7	7	8	9	8	8	7	6		7	8	7	8	7	9	8	9					161	98.2
1-7	0	0	0	0	0	0	1	0	0	0	0	0	1		0	0	0	0	0	1	0	0					3	1.8
Sacral vertebral bodies & arches																												
1-4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Coccygeal vertebral bodies 1	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
6	7	5	8	6	11	7	8	7	9	7	8	7	7		6	8	7	7	7	10	8	9					159	97.0 ***
7	7	5	5	6	8	7	5	2	4	4	7	4	2		2	4	7	4	6	10	6	9					114	69.5 ***
8	2	4	2	4	3	5	1	0	1	2	3	1	1		0	1	3	2	3	3	3	3					47	28.7 ***
9	0	3	0	1	1	4	0	0	0	0	0	0	0		0	0	0	1	2	1	0	0					13	7.9 ***
10	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	1	0	0					1	0.6
11	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Average No. of ossified coccygeal vertebral bodies	7.00	8.40	6.88	7.83	7.07	7.86	6.75	6.13	6.56	6.63	7.25	6.71	6.43		6.14	6.63	7.43	6.75	7.57	7.50	7.13	7.33				$\bar{X}$	X	** 7.05
																	** P < 0.01		*	** P < 0.001							S	4.507
																										S.D.	sd	0.558
																										S.E.	se	0.23
																										t	t	3.078
Coccygeal vertebral arches 1	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
2	8	5	8	6	11	7	8	7	9	8	8	7	7		7	8	7	8	7	10	8	9					163	99.4
3	6	5	7	6	10	7	8	1	9	7	8	7	7		7	6	7	7	6	10	8	9					148	90.2
4	1	4	0	2	2	5	1	0	1	1	0	3	4		2	1	4	1	1	5	3	1					42	25.6 ***
5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0

Individual Data: 19-3, SKELETAL FINDINGS IN FETUSES

Rats — Piroctone olamine — 500 mg/kg — s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Ribs Normal	4	2	5	3	0	1	7	6	4	4	1	0	2		6	1	6	6	3	2	2	3					65	41.5
14th rib[a] Unilateral	3	3	1	0	1	0	0	2	3	1	4	1	2		0	4	1	0	1	3	2	0					32	19.5
Bilateral	1	0	2	3	10	6	1	6	2	3	3	6	3		1	3	0	2	3	5	4	6					64	39.0
Undeveloped 13th rib[a]	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Waved rib[b]	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Fused ribs[b]	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Ossification centers of sternebrae 1	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	8	5	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					162	98.8
6	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Hypoplasia																												
No. of fetuses	1	1	3	0	3	2	0	5	0	0	0	0	0		4	2	3	1	1	0	0	0					26	15.9
1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
5	1	1	3	0	3	2	0	5	0	0	0	0	0		4	2	3	1	1	0	0	0					26	15.9
6	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	0	0					1	0.6
Splitting																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0

[a] Variation, [b] Abnormality

* $P < 0.05$

Individ[illegible] Data: 19-4 SKELETAL FINDINGS IN [illegible]USES

Rats . Piroctone olamine .500 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Absence of one of the two parts																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	1	0	0	0					2	1.2
1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	1	0	0	0					2	1.2
6	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Accessory sternebra[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Asymmetry[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	0	0					1	0.6
1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	0	0					1	0.6
3	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	0	0					1	0.6
4	0	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	0	0					1	0.6
5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Fusion[b]	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Clavicle																												
Scapula																												
Humerus																												
Radius	8	5	8	6	11	7	8	8	7	8	8	7	7		7	8	7	8	7	10	8	7					164	100
Ulna	8	5	8	6	11	7	8	8	7	8	8	7	7		7	8	7	8	7	10	8	7					164	100

[a] Variation, [b] Abnormality

Individual Data: 19-5 SKELETAL FINDINGS IN FETUSES

Rats Piroctone olamine 500 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Metacarpals (bodies) 1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
Phalanges of the forelimb Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
2	8	5	7	5	11	7	8	6	9	7	8	7	6		7	8	7	7	6	10	7	9					155	94.5
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	7	5	11	7	7	6	9	7	8	7	6		7	8	7	6	6	10	7	9					153	93.3
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Distal 1	8	5	8	4	10	7	8	5	9	7	7	7	6		7	8	6	8	7	10	4	9					150	91.5
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	6	7	10	8	9					162	98.8
Ilium																												
Ischium																												
Pubis																												
Femur																												
Tibia																												
Fibula																												
Tarsus Astragalus	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0	0
Calcaneus	4	2	0	1	0	1	1	0	0	0	0	2	1		0	0	5	0	2	0	0	0					19	11.6
Metatarsals (bodies) 1	8	5	7	4	3	7	8	4	5	8	7	7	5		7	7	7	2	6	8	6	9					130	79.3
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100
5	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164	100

*** P < 0.001

Individual Data: 19-6 SKELETAL FINDINGS - FETUSES

Rats Piroctone olamine 500 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total
Phalanges of the hindlimbs																											
Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	2	0	0					2
2	5	4	4	3	1	7	1	0	2	2	5	2	0		6	0	4	2	3	4	2	1					58
3	6	4	5	3	1	7	3	0	2	2	5	2	1		6	2	6	2	5	5	3	1					71
4	6	4	5	3	1	7	3	0	2	2	5	3	1		6	2	4	2	5	5	3	1					70
5	0	3	2	2	0	1	0	0	0	1	3	0	0		2	0	1	1	0	1	0	0					17
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0					0
Distal 1	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164
2	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164
3	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164
4	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	8	7	10	8	9					164
5	8	5	8	6	11	7	8	8	9	8	8	7	7		7	8	7	7	7	10	8	9					163

* P < 0.05 ** P < 0.01

Individual Data: 20-1 SKELETAL FINDINGS IN FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
	1-11	1-12	1-13	1-14	2-15	2-16	2-17	2-18	3-17	3-18	3-19	3-20	3-21	3-22	4-14	4-15	4-16	5-13	5-14	5-15	5-17	6-16	6-17					
No. of fetuses examined	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				162	100
Nasal bone																												
Frontal bone																												
Parietal bone																												
Occipital bone																												
Lacrimal bone																												
Maxilla																												
Mandibule																												
Hyoid bone																												
Palatine bone	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				162	100
Odontoid process	0	6	6	7	7	7	4	8	4	7	8	8	7	5	3	4	8	3	6	5	8	8	8				137	84.1
Spina																												
Cervical vertebral bodies 1	5	1	2	2	2	0	0	5	3	6	2	1	5	3	0	0	2	1	3	4	3	0	0				50	28.6
2	2	1	0	2	1	0	0	4	3	3	2	2	5	3	0	0	4	2	0	0	0	0	0				24	20.1
3	3	1	3	2	1	1	1	6	3	6	3	4	5	5	0	1	2	1	2	2	0	0	0				32	20.3
4	3	1	0	4	2	0	0	6	3	7	4	5	6	5	0	1	3	2	2	3	0	0	0				37	23.2
5	3	0	4	6	2	2	2	7	3	7	5	6	8	5	0	1	4	3	3	3	1	1	1				72	44.8
6	4	1	5	3	3	2	4	7	3	7	5	6	8	6	0	1	6	3	4	4	1	2	1				86	53.2
7	6	3	7	7	7	7	7	8	4	7	8	8	8	6	4	2	9	4	7	6	6	8	6				145	89.8
Cervical vertebral arches 1-7	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				162	100
Thoracic vertebral bodies 1-																												
9																												
10																												
11																												
Fusion of a thoracic vertebral body & arch[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0				1	0.6
13																												
Thoracic vertebral arches 1-13	8	6	8	7	8		8	8	5	7	8	8	8	7	6		8	7	7	6	8	8	8				168	98.4

[a] Abnormality

* P < 0.05 ** P < 0.01 *** P < 0.001

Indiv al Data: 20-2 SKELETAL FINDINGS ETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	X
Lumbar vertebral bodies & arches																												
1-5																												
1-6	8	6	8	7	8	8	8	8	5	7	8	8	8	5	6	6	8	7	7	5	8	8	8				165	97.6
1-7	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	1	0	0	0				3	1.8
Sacral vertebral bodies & arches																												
1-4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
Fusion of bodies[a]	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				1	0.6
Coccygeal vertebral bodies 1	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
5	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
6	8	5	8	7	8	7	7	8	5	7	8	7	8	7	5	5	7	6	7	6	8	6	7				157	92.9
7	8	2	5	7	7	5	3	8	2	7	7	5	8	7	0	2	2	0	7	5	6	1	5				109	64.5
8	6	0	2	4	3	2	1	0	1	6	3	3	4	5	0	0	0	0	4	3	1	0	0				48	28.4
9	2	0	1	1	1	0	1	0	0	1	0	1	0	1	0	0	0	0	0	1	1	0	0				11	6.5
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
Defect of the tail	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0				1	0.6
Absence of the thoracic vertebrae 11-13[a]																	1										1	0.6
Average No. of ossified coccygeal vertebral bodies	8.00	6.17	7.00	7.71	7.38	6.75	6.50	7.00	6.60	8.00	7.25	7.00	7.50	7.75	5.83	6.17	5.44	5.86	7.57	7.50	7.00	5.88	6.50			$\bar{x}$	X	$\bar{x}$ 6.82
																											S	2.35
																	[a]	Abnormality								S.D.	sd	0.25
																	*	P < 0.05;		**	P<0.001					S.E.	se	0.06
																										t	t	2.82
Coccygeal vertebral arches 1	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	8	7	7	6	8	8	8				168	99.4
2	8	6	8	7	8	8	7	8	5	7	8	8	8	7	6	6	8	6	7	6	8	8	8				166	98.2
3	8	4	7	7	8	7	6	8	1	7	8	7	7	7	3	4	4	3	7	5	7	7	7				138	81.3
4	3	0	0	1	6	0	1	2	1	7	2	5	1	7	0	0	0	0	2	0	1	0	0				37	22.1
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0

Individual Data: 20-3 SKELETAL FINDINGS / FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Ribs Normal	1	3	8	4	3	1	5	3	5	2	3	4	1	1	4	3	5	6	3	1	6	7	3				82	[illegible]
14th rib[a] Unilateral	1	1	0	2	2	3	2	1	0	2	4	2	4	0	1	0	1	0	0	1	0	0	4				31	[illegible]
Bilateral	6	2	0	1	3	4	1	4	0	3	1	2	3	6	1	3	2	0	4	4	2	1	1				54	[illegible]
Undeveloped 13th rib[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0				1	0.6
Waved rib[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Fused ribs[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Absence of the ribs 11-13[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0				1	0.6
Ossification centers of sternebrae 1	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				168	[illegible]
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				168	[illegible]
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				168	[illegible]
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				168	[illegible]
5	8	4	7	6	8	8	6	8	4	7	8	8	8	7	6	5	6	6	6	6	7	8	8				155	[illegible]
6	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				168	[illegible]
Hypoplasia																												
No. of fetuses	0	3	3	2	2	0	3	0	1	0	1	0	1	0	1	1	4	6	0	0	4	3	3				38	22
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0				1	0.6
5	0	3	3	2	2	0	3	0	1	0	1	0	1	0	1	1	4	6	0	0	4	3	3				38	22
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0				1	0.6
Splitting																												
No. of fetuses	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				1	0.6
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
3	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				1	0.6
4	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				1	0.6
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
6	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				1	0.6

a Variation, b Abnormality

* P < 0.05, ** P < 0.01

Individual Data: 2014 SKELETAL FINDINGS FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Absence of one of the two parts																												
No. of fetuses	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0				4	2.4
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
5	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0				4	2.4
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Accessory sternebra[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Asymmetry[a]																												
No. of fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Fusion[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Clavicle																												
Scapula																												
Humerus																												
Radius	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				142	100
Ulna	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				142	100

[a] Variation, [b] Abnormality

Individual Data: 20-5 SKELETAL FINDINGS : FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Metacarpals (bodies) 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
5	8	6	8	7	8	8	8	8	5	7	8	8	8	7	5	6	9	7	7	6	8	8	8				169	100
Phalanges of the forelimbs Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
2	8	1	8	7	8	8	8	8	4	7	8	7	8	7	4	4	7	7	7	6	8	7	8				155	91
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
5	8	1	8	7	8	8	8	8	4	7	8	7	8	7	4	4	7	7	7	6	8	7	8				155	91
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
Distal 1	8	3	8	7	7	8	8	8	4	7	8	8	8	6	3	6	9	4	7	6	8	8	6				155	91
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	6	8	8	8				169	100
5	8	6	8	7	8	8	8	8	5	7	8	8	8	7	5	4	9	7	7	6	8	5	8				163	96
Ilium																												
Ischium																												
Pubis																												
Femur																												
Tibia																												
Fibula																												
Tarsus Astragalus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	
Calcaneus	0	1	5	2	5	0	0	1	2	7	3	1	0	0	0	0	0	3	0	3	2	0	0				35	20
Metatarsals (bodies) 1	6	2	6	7	7	6	4	8	3	7	8	7	6	7	3	2	2	1	7	5	6	5	3				118	69
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99
5	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99

*** P < 0.001

Indi dual Data: 20-6 SKELETAL FINDINGS I FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	Total	%
Phalanges of the hindlimbs																												
Proximal 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
2	2	1	2	4	5	0	2	0	1	7	4	5	1	7	1	0	0	1	4	3	2	1	1				54	32.0
3	2	1	4	5	5	0	2	0	1	7	7	5	3	7	1	0	0	4	4	3	3	1	2				67	39.6
4	2	1	4	5	5	0	2	0	1	7	7	5	3	7	1	0	0	4	4	3	3	1	1				66	39.1
5	0	1	1	3	2	0	1	0	1	6	2	1	1	6	0	0	0	0	2	2	1	0	0				30	17.8
Middle 1-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0	0
Distal 1	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99.4
2	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99.4
3	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99.4
4	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99.4
5	8	6	8	7	8	8	8	8	5	7	8	8	8	7	6	6	9	7	7	5	8	8	8				168	99.4
Left hindlimb																												
Absence of the tarsus, metatarsus & phalanges[a]																				1							1	0.6
Right hindlimb																												
Tarsus																				0								
Metatarsals (bodies) 1-5																				1								
Phalanges Proximal 1,5																				0								
2,3																				1								
Middle 1-5																				0								
Distal 1-5																				1								

** P < 0.01 *** P < 0.001

[a] Abnormality

Individual Data: 21 VISCERAL FINDINGS IN FETUSES

Rats Piroctone olamine 0 mg/kg (Control) s.c.

Dam No.	No. of fetuses examined	Cleft palate	Sinistroposition of the heart			Dilatation of the renal pelvis			
1-1	8								
1-2	6								
1-3	8								
2-1	8	1							
2-2	6								
2-3	7								
2-4	6								
3-1	6								
3-2	2								
3-3	7								
3-4	8								
4-1	9								
4-2	8								
4-3	7								
4-4	6								
4-5	8								
4-6	5								
5-1	8								
5-2	8								
5-3	7								
5-4	6								
6-1	7								
6-2	7								
6-3	6								
6-4	6								
6-5	6								
26									
Total	178	1							
%		0.56							

No. of litters examined (26)

No. of fetuses examined (178)

No. of litters with abnormalities (1 : 3.85 %)

No. of fetuses with abnormalities (1 : 0.56 %)

Individual Data: 22 VISCERAL FINDINGS IN FETUSES

Rats Piroctone olamine 100 mg/kg s.c.

Dam No.	No. of fetuses examined	Cleft palate	Sinistroposition of the heart			Dilatation of the renal pelvis			
1-4	8		1						
1-5	8								
1-6	6								
2-5	9								
2-6	7								
2-7	7								
2-9	9								
2-8	7								
2-10	7								
3-11									
3-12	8								
4-5									
4-6	7								
4-7	7								
4-8	9								
5-6	6								
5-8	9								
5-9	8								
5-10	5								
6-6	9								
6-7	7								
6-8	7								
6-9	11								
6-10	7		1						
22									
Total	168		2						
%			1.19						

No. of litters examined (22)
No. of fetuses examined (168)
No. of litters with abnormalities (2 : 9.09%)
No. of fetuses with abnormalities (2 : 1.19%)

Individual Data: 23 VISCERAL FINDINGS IN FETUSES

Rats Piroctone olamine 500 mg/kg s.c.

Dam No.	No. of fetuses examined	Cleft palate	Situs inversus of the heart			Dilatation of the renal pelvis			
1-7	8								
1-8	5								
1-9	8								
2-9	6								
2-11	11								
2-12	6								
2-13	7								
2-16	7								
2-17	9								
2-18	7								
3-8	8								
3-11	7								
4-9	8								
4-10									
4-11	6								
4-12	8								
5-9	7								
5-10	7								
5-11	6								
5-11	9								
5-16	7								
5-18	8								
21									
Total	155								
%									

No. of litters examined (21)

No. of fetuses examined (153)

No. of litters with abnormalities (0 : 0 %)

No. of fetuses with abnormalities (0 : 0 %)

Individual Data: 24 VISCERAL FINDINGS IN FETUSES

Rats Piroctone olamine 2000 mg/kg s.c.

Dam No.	No. of fetuses examined	Cleft palate	Sinistroposition of the heart			Dilatation of the renal pelvis			
1-11	7								
1-12	7					1			
1-14	5								
2-15	7					1			
2-16	7								
2-17	6								
2-18	8								
3-17	6								
3-18	7								
3-19	7								
3-20	7								
3-21	7								
3-22	7								
4-14	6								
4-15	5								
4-16	9								
5-13	7					1			
5-14	6								
5-15	5								
5-17	8								
6-16	8								
6-17	7						1		
22		1							
Total	147					3			
						2.0 (%)			

No. of litters examined (22)
No. of fetuses examined (147)
No. of litters with abnormalities (3 : 13.6(%))
No. of fetuses with abnormalities (3 : 2.0(%))