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DATA EVALUATION RECORD

STUDY TYPE: Teratology - Rabbits (Guideline §83-3)

MRID NUMBER: 407171-02 Caswell No.: 640

TEST MATERIAL: Technical grade PCNB with a stated purity 96.0% was used.

SYNONYMS: Pentachloronitrobenzene; Terraclor

STUDY NUMBER(S): 399-070

SPONSOR: Uniroyal Chemical Co.

TESTING FACILITY: International Research and Development Corporation, Mattawan, MI

TITLE OF REPORT: Developmental Toxicity Study in New Zealnad White Rabbits

AUTHOR(S): Keller, K. A.

REPORT ISSUED: June 24, 1988

CONCLUSIONS: Groups of 16 pregnant New Zealand White rabbits were given daily doses of 0 (two groups), 6.25, 12.5, 125 (two groups), and 250 mg PCNB per kg body weight by gavage on gestation days 7 through 19. At the highest dose tested there was mortality, abortions, weight loss during gestation, and decreased food consumption. The only effects observed in the 125 mg/kg/day dose groups were decreased body weight and body weight gain. Group mean maternal body weight was statistically significantly less than control values only during the second of the two trials that were conducted at that dose level. Based on these results, a no-observable-effect level (NOEL) for maternal toxicity was established in the studyies at 12.5 mg/kg/day, and the lowest-effect level (LEL) was 125 mg/kg/day.

Based on statistically significantly decreased fetal weights reported in the highest dosed group, the LEL for developmental toxicity was established at 250 mg/kg/day, and the NOEL was found to be 125 mg/kg/day in rabbits.

Core classification: Minimum

I. PROTOCOL

A. Materials

1. Test species: Six-month old female New Zealand White strain rabbits were used. The day the animals were artificially inseminated was designated Day 0 of gestation.

B. Experimental procedures: The test substance was suspended in aqueous 0.2% carboxymethylcellulose and administered by gavage on Days 7 through 19 of gestation. The report stated that doses were selected on the basis of a preliminary range-finding study (see DER on MRID No. 407171-01). Doses originally selected for the study were 0 (A), 12.5, 125 (A), and 250 mg/kg/day, and because of results discussed below, a second set of doses (0 (B), 6.25, and 125 (B) mg/kg/day) were also tested. The design of the two experiments was described in the report as follows:

| Group number * | Dose (mg/kg/day) | Number of animals |
|---|---|---|
| 1 | Control A | 16 |
| 2 | Control B | 16 |
| 3 | 6.25 | 16 |
| 4 | 12.5 | 16 |
| 5 | 125 (A) | 16 |
| 6 | 125 (B) | 12 |
| 7 | 250 | 16 |

* For purposes of this review.

C. Maternal observations: Each doe was observed twice daily for occurrence of toxic signs and morbidity. Body weight determinations were made on days 0, 7, 13, 20, 24 and 29 of gestation, and food consumption was measured for days 7-13, 13-20, 7-20, 20-29, and 0-29 of gestation.

Surviving rabbits were weighed and sacrificed on day 29 of gestation. Internal organs were examined for gross lesions, and the gravid uterus was removed and weighed. The numbers of corpora lutea and implantation sites were noted.

Does dying prior to the end of the study were examined for gross pathological changes, and the pregnancy status of these animals was noted. Uteri from nongravid animals were stained with ammonium sulfide to detect implantations.

D. Litter observations: The number of implantation sites, live and dead fetuses, and resorptions were counted.

E. Fetal observations: Fetuses were individually weighed and examined for external abnormalities. The fetuses were then internally sexed, and their viscera were examined for variations and malformations. The brain was examined through a transverse section between the

E. Fetal observations (continued)

parietal and frontal bones of the unfixed fetal head. Fetuses were then fixed in ethanol and emaciated in potassium hydroxide. The skeletons were then stained with alizarin red S for examination.

F. Evaluation of observations: All external, visceral, and skeletal alterations were classified into two categories defined in the report as follows:

> Malformations are those structural anomalies that alter body conformity, disrupt or interfer with body function, or are generally thought to be incompatible with life. Specific examples of processes that result in maldevelopment include marked/severe mishapening, assymetry or irregularity of structure brought about by fusion, splitting, disarticulation, malalignment, hiatus, enlargement, lengthening, thickening, thinning, or branching. Absence (agenesis) of parts or whole structures is also considered a malformative process.
>
> Developmental variations are those alterations in anatomic structure that are considered to have no significant biological effect on animal health or body conformity, representing slight deviations from normal. Most examples of alterations placed in the variant category are minor variations in size and form of normally present ossification centers...Also included in this category of variations are slight mishapening or misalignment of structures, processes involving continued development (bilateral skeletal centers not yet fused, imcomplete maturation of renal papillae, presence of vestigial structures, etc) and development of extra ossification sites.

Statistical comparisons were made between each treatment group and its appropriate concurrent control group (i.e., Control A was used with the 12.5, 125 (A), and 250 mg/kg/day groups and Control B was used with the 6.25 and 125 (B) mg/kg/day groups).

Differences were considered to be statistically significant at $p < 0.05$.

Statistical analyses were used in the report as follows:

| Observation | Test for Linear Trend | Between Groups |
|---|---|---|
| Male to female sex ratios | None | Chi square (2 X 2) with Yates' correction |
| Proportions of litters with malformations or variations | None | Fisher's Exact test |

F. Evaluation of observations (continued)

| Observation | Test for Linear Trend | Between Groups |
|---|---|---|
| Proportions of resorptions, dead fetuses, and postimplantation losses | None | Mann-Whitney U test |
| Means for numbers of: Corpora lutea, Total implantations, Live fetuses, Gravid uterine weights, Fetal body weights, Maternal food consumption | None | One-way classification of variance, Bartlett's test for homogeneity of variances, Dunnett's multiple comparison |

## II. REPORTED RESULTS

A. Maternal observations: Mortality and pregnancy status of the does is summarized as follows:

| | Dose (mg/kg/day) | | | | | | |
|---|---|---|---|---|---|---|---|
| | Study A | | | | Study B | | |
| Parameter | 0 | 12.5 | 125 | 250 | 0 | 6.25 | 125 |
| Number inseminated | 16 | 16 | 16 | 16 | 16 | 16 | 12 |
| Number not pregnant | 1 | 0 | 3 | 1 | 1 | 3 | 1 |
| Number pregnant | 15 | 16 | 13 | 15 | 15 | 13 | 11 |
| Deaths | 0 | 1 | 2 * | 5 | 0 | 0 | 0 |
| Abortions | 2 | 2 | 5 * | 5 ** | 0 | 0 | 1 |
| Total resorptions | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Delivered | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| Number of litters | 11 | 13 | 7 | 6 | 14 | 13 | 10 |

*Includes the two females that aborted and died.
**One of these also died after aborting.

The deaths occurred during days 19 through 28 of gestation. According to the report, gross necropsy findings (mucoid material in the intestinal tract or hemorrhage of the trachea with red discoloration and/or "consolidation" in the lungs) indicated that two deaths were the result of mucoid enteritis (125 (A) mg/kg/day dose group) and three resulted from pneumonia (250 mg/kg/day dose group). The remaining mortalities could not be associated by the investigators with a cause.

Abortions were noted during days 23 through 28 of gestation.

A. Maternal observations (continued)

The incidences of mucoid stool, absence of stool, and anogenital staining were the only signs noted in the report. The incidences of these observations is summarized as follows:

| | Dose (mg/kg/day) | | | | | | |
|---|---|---|---|---|---|---|---|
| | Study A | | | | Study B | | |
| Observation | 0 | 12.5 | 125 | 250 | 0 | 6.25 | 125 |
| Number examined | 16 | 16 | 16 | 16 | 16 | 16 | 12 |
| Mucoid stool | 0 | 0 | 1 | 6 * | 0 | 0 | 0 |
| Absence of stool | 4 | 3 | 8 | 11 * | 2 | 1 | 1 |
| Anogenital staining | 3 | 8 | 9 | 10 * | 2 | 3 | 3 |

* Statistically significantly different from control, $p<0.05$; Fisher's Exact test.

The report noted that animals in the 125 (A), 125 (B), and 250 mg/kg/day dose groups exhibited weight losses during the dosing period. Overall weight loss results are summarized as follows:

| Dose (mg/kg/day) | Mean weight (kg) on gestation† Day 0 | Day 29†† | Weight change (kg) for Days 7-20 | Days 0-29 †† |
|---|---|---|---|---|
| | | Study A | | |
| 0 | 4502 | 4231 | -55 | -251 |
| 12.5 | 4452 | 4152 | 91 | -261 |
| 125 | 4449 | 4101 | -192 | -290 |
| 250 | 4432 | 3693 | -523 | -706 |
| | | Study B | | |
| 0 | 4356 | 4160 | 151 | -230 |
| 6.25 | 4226 | 3917 | 145 | -309 |
| 125 | 4182 | 3844 | -42 | -322 |

†The report did not include statistical analyses of these results.
††Body weights at day 29, corrected for gravid uterine weight.
†††These values were calculated from group mean body weights. No statistical analyses were conducted on these data.

Food consumption results are summarized as follows:

A. Maternal observations (continued)

| Dose (mg/kg/day) | Mean feed consumption (g/kg/day) 7-13 | 13-20 | 7-19 | 20-29 | 7-29 |
|---|---|---|---|---|---|
| | | Study A | | | |
| 0 | 30.2 | 23.7 | 26.5 | 18.7 | 24.6 |
| 12.5 | 31.8 | 26.0 | 27.6 | 18.3 | 25.7 |
| 125 | 31.5 | 19.2 | 25.3 | 22.4 | 29.2 |
| 250 | 22.1 | 5.9 ** | 14.6 * | 3.7 * | 14.2 |
| | | Study B | | | |
| 0 | 41.4 | 38.3 | 39.4 | 23.6 | 33.5 |
| 6.25 | 38.1 | 32.0 | 34.6 | 24.8 | 30.7 |
| 125 | 32.9 ** | 24.5 * | 28.7 ** | 27.0 | 28.9 |

* Statistically significantly different from control, $p<0.05$
** Statistically significantly different from Control, $p<0.01$

B. Litter observations: The report summarized these observations (means per litter) follows:

| Observation | Dose (mg/kg/day) Study A 0 | 12.5 | 125 | 250 | Study B 0 | 6.25 | 125 |
|---|---|---|---|---|---|---|---|
| Number of litters | 11 | 13 | 7 | 6 | 14 | 13 | 10 |
| Live fetuses | | | | | | | |
| Males* | 3.4 | 2.8 | 4.3 | 2.5 | 2.6 | 3.7 | 3.7 |
| Females* | 3.7 | 3.7 | 2.7 | 2.2 | 3.2 | 4.1 | 3.1 |
| Total** | 6.7 | 6.5 | 6.9 | 4.2 | 5.9 | 7.8 | 6.8 |
| Corpora lutea | 15.2 | 14.1 | 13.3 | 12.0 | 16.2 | 14.3 | 14.3 |
| Implantations | 7.2 | 7.4 | 7.9 | 6.0 | 7.8 | 8.7 | 7.2 |
| Postimplantation loss | 0.5 | 0.9 | 1.0 | 1.8 | 1.9 | 0.9 | 0.4 |
| Fetal weight (g) | | | | | | | |
| Both sexes combined | 41.4 | 39.1 | 40.3 | 28.4 † | 44.7 | 42.6 | 47.2 |
| Gravid uterine weight (g) | 441.6 | 358.7 | 433.9 | 235.7 | 358.0 | 487.4 | 429.3 |

* Calculated from the total number of male and female fetuses reported and the number of litters examined in the group.
** Listed here as reported.
† Statistically significantly different from control A, $p<0.05$.

C. Fetal observations: The report noted that there were no statistically significantly increased incidences of malformations in fetuses from treated groups. There were also no treatment-related incidences of developmental variations in fetuses examined in the study. The results as they were summarized in the report are included in Addenda A and B below.

## III. DISCUSSION

A. Investigators' conclusions: The report concluded:

> Excessive maternal toxicity, in terms of an increased incidence of mortality, abortion and certain stool abnormalities as well as adverse effect on weight gain and food consumption, was noted at the 250 mg/kg/day dosage level. These effects were also observed at the 125 mg/kg/day dosage level, but, with the exception of increased weight loss, did not occur consistently in the two groups that received this dosage level. Developmental toxicity (reduced fetal body weight) was present at the 250 mg/kg/day dosage level. There were no other effects on fetal development, including teratogenicity.
>
> In conclusion, the no observable effect level in regard to developmental toxicity was determined to be 125 mg/kg/day.

B. Reviewer's discussion: The report did not include statistical analysis of maternal body weight results, so an analysis was independently conducted. The individual body weights were first analyzed by one-way analysis of variance and Bartlett's test for homogeneity of variance. The results of those analyses showed that the data required transformation, and a log transformation was used. An analysis of variance was conducted on the transformed data, and appropriate concurrent control groups were compared with each treatment group using a t test. Statistically significant differences are summarized with untransformed group means as follows:

| Dose (mg/kg/day) | Group mean body weight (g) * Day 13 | Day 20 | Day 24 | Day 29 | Day 29** |
|---|---|---|---|---|---|
| | | Experiment A | | | |
| 0 | 4586 | 4539 | 4649 | 4547 | 4231 |
| 12.5 | 4630 | 4609 | 4607 | 4510 | 4152 |
| 125 | 4564 | 4428 | 4433 | 4489 | 4101 |
| 250 | 4409 | 4034 †† | 4003 †† | 3929 †† | 3693 †† |
| | | Experiment B | | | |
| 0 | 4523 | 4591 | 4623 | 4518 | 4160 |
| 6.25 | 4372 | 4408 | 4465 | 4404 | 3917 |
| 125 | 4312 | 4248 † | 4343 | 4273 | 3844 † |

* Group means are not transformed.
** Adjusted by subtracting the weight of the gravid uterus.
† Statistically singnificantly different from controls ($p<0.05$). t test.
†† Statistically singnificantly different from controls ($p<0.01$). t test.

B. Reviewer's discussion (continued)

Because there were so few does and litters available for evaluation in the first study, results from the 125 mg/kg/day dose group can not be compared reliably with those from the 125 mg/kg dose group in the second experiment. The 125 mg/kg/day dose group in Experiment B indicated that body weight and food consumption were significantly reduced which suggested that 125 mg/kg/day is the lowest effect level for maternal toxicity. Based on body weight and food consumption results from both experiments, the no-observed-effect level (NOEL) for maternal toxicity is 12.5 mg/kg/day.

Fetal effects (reduced body weight) were observed only at the 250 mg/kg/day dose level (highest dose tested) along with excessive maternal toxicity (mortality, abortions, reduced body weight and decreased food consumption). The NOEL for fetal effects was 125 mg/kg/day. No increased incidences of teratogenic effects were observed in PCNB treated animals.

ADDENDUM A

Incidence of Malformations in
Fetuses from Rabbits Treated with
Pentachloronitrobenzene

TABLE 5. Summary of the Incidence of Fetal Malformations

| | PCNB (mg/kg/day) | | | |
|---|---|---|---|---|
| | 0 (Control A) | 0 (Control B) | 6.25 | 12.5 |
| No. of litters examined: | 12[a] | 15[a] | 13 | 13 |
| No. of fetuses examined externally: | 94[b] | 90[b] | 101 | 85[b] |
| No. of fetuses examined viscerally: | 94[b] | 90[b] | 101 | 85[b] |
| No. of fetuses examined skeletally: | 94[b] | 90[b] | 101 | 85[b] |
| **Malformations Observed:** | No. of fetuses (No. of litters) | | | |
| Microencephaly: | | 2 (1) | | |
| Encephalocele: | | 1 (1) | | |
| Spina bifida: | | 1 (1) | | |
| Gastroschisis: | 1 (1) | | | |
| Omphalocele: | | | 1 (1) | |
| Syndactyly: | | | | |
| Malformed brain: | | 2 (1) | | |
| Bulbous aortic arch: | 1 (1) | | 2 (2) | |
| Coarction of aortic arch: | 1 (1) | | | |
| Stenosis of aortic arch: | 1 (1) | | | |
| Stenosis of ascending aorta: | | | 2 (2) | |
| Bulbous pulmonary trunk: | 1 (1) | | | |
| Stenosis of pulmonary trunk: | 1 (1) | | 2 (2) | |
| Pulmonary hypoplasia: | | | 1 (1) | |
| Stenosis of ductus arteriosus: | | | 1 (1) | |
| Interventricular septal defect: | 1 (1) | | | |
| Right subclavian arises from pulmonary trunk: | | 1 (1) | | |
| Malformed heart: | | | 4 (2) | |
| Adrenal agenesis: | | | 1 (1) | |
| Distended intestines: | | | 1 (1) | |
| Malpositioned kidney: | | 1 (1) | 1 (1) | |
| Fused kidneys: | | 1 (1) | 1 (1) | |
| Gallbladder agenesis: | | | 1 (1) | |
| Fused skull bones: | | | 2 (2) | 1 (1) |
| Malformed skull bones: | | 3 (2) | | |
| Micrognathia: | | | | |
| Bent scapula: | 1 (1) | | | |
| Vertebral anomaly with or without associated rib anomalies: | 1 (1) | 1 (1) | 1 (1) | 1 (1) |
| Rib anomaly: | | | | |
| Interrupted ossification of rib: | 1 (1) | | | |
| Sternoschisis: | 1 (1) | | | |
| Total fetuses (litters) with malformations: | 4 (3) | 4 (3) | 9 (6) | 2 (2) |

Values from the treated groups did not differ significantly from those of the concurrent control group; $p>0.05$

[a] Includes litter(s) that delivered, aborted or died on gestation day 28 or 29

[b] Includes nonviable fetus(es)

TABLE 5. Cont. Summary of the Incidence of Fetal Malformations

| | PCNB (mg/kg/day) | | |
|---|---|---|---|
| | 125(A) | 125(B) | 250 |
| No. of litters examined: | 10[a] | 10 | 6 |
| No. of fetuses examined externally: | 73[b] | 68 | 28[b] |
| No. of fetuses examined viscerally: | 73[b] | 68 | 28[b] |
| No. of fetuses examined skeletally: | 73[b] | 68 | 28[b] |
| **Malformations Observed:** | No. of fetuses (No. of litters) | | |
| Microencephaly: | | | |
| Encephalocele: | | | |
| Spina bifida: | | | |
| Gastroschisis: | | | |
| Omphalocele: | | | |
| Syndactyly: | 1 (1) | | |
| Malformed brain: | | | |
| Bulbous aortic arch: | | | |
| Coarction of aortic arch: | | | |
| Stenosis of aortic arch: | | | |
| Stenosis of ascending aorta: | | | |
| Bulbous pulmonary trunk: | | | |
| Stenosis of pulmonary trunk: | | | |
| Pulmonary hypoplasia: | | | |
| Stenosis of ductus arteriosus: | | | |
| Interventricular septal defect: | | | |
| Right subclavian arises from pulmonary trunk: | | | |
| Malformed heart: | | | |
| Adrenal agenesis: | | | |
| Distended intestines: | | | |
| Malpositioned kidney: | | | |
| Fused kidneys: | | | |
| Gallbladder agenesis: | | | |
| Fused skull bones: | 1 (1) | | |
| Malformed skull bones: | | | |
| Micrognathia: | | 1 (1) | |
| Bent scapula: | | | |
| Vertebral anomaly with or without associated rib anomalies: | | | |
| Rib anomaly: | | 1 (1) | |
| Interrupted ossification of rib: | 1 (1) | 1 (1) | |
| Sternoschisis: | | | |
| Total fetuses (litters) with malformations: | 3 (3) | 2 (2) | 0 (0) |

Values from the treated groups did not differ significantly from those of the concurrent control group; $p>0.05$

[a] Includes litter(s) that delivered, aborted or died on gestation day 28 or 29

[b] Includes nonviable fetus(es)

ADDENDUM B

Incidence of Variations in
Fetuses from Rabbits Treated with
Pentachloronitrobenzene

TABLE 6. Summary of the Incidence of Fetal Developmental Variations

| | PCNB (mg/kg/day) | | | |
|---|---|---|---|---|
| | 0 (Control A) | 0 (Control B) | 6.25 | 12.5 |
| No. of litters examined: | 12[a] | 15[a] | 13 | 13 |
| No. of fetuses examined externally: | 94[b] | 90[b] | 101 | 85[b] |
| No. of fetuses examined viscerally: | 94[b] | 90[b] | 101 | 85[b] |
| No. of fetuses examined skeletally: | 94[b] | 90[b] | 101 | 85[b] |
| **Developmental Variations Observed:** | **No. of fetuses (No. of litters)** | | | |
| Thickened body: | | | | |
| Carpal flexure: | | | 1 (1) | |
| Tarsal flexure: | | | 1 (1) | |
| Short tail: | | | | |
| Hemorrhagic iris: | 1 (1) | 1 (1) | | |
| Left carotid arises from the innominate: | 3 (2) | 2 (1) | 8 (5) | 11 (3) |
| Azygous lobe of lung absent: | 3 (2) | 3 (3) | 3 (2) | 2 (1) |
| Retroesophageal aortic arch: | | 1 (1) | | |
| Gallbladder smaller than normal: | 1 (1) | 1 (1) | 1 (1) | 2 (1) |
| Bent hyoid arch(es): | | 3 (2) | 4 (3) | 8 (5) |
| Hyoid body unossified: | 1 (1) | | | 5 (3) |
| Misshapen skull bones: | 2 (1) | 1 (1) | | |
| Accessory skull bones: | | | 2 (2) | |
| Supraoccipital reduced in ossification: | | 1 (1) | | |
| 27 presacral vertebrae: | 35 (7) | 18 (6) | 31 (9) | 23 (9) |
| 24 presacral vertebrae: | | 1 (1) | | |
| 13th rudimentary rib(s): | 9 (6) | 15 (9) | 25 (10) | 11 (8) |
| Greater than 12 pairs of full ribs: | 55 (8) | 36 (10) | 46 (13) | 47 (12) |
| 7th cervical rib: | 1 (1) | 2 (1) | 5 (3) | 2 (2) |
| Spherical enlargement of rib(s): | 1 (1) | 1 (1) | 1 (1) | 1 (1) |
| Misshapen ribs: | | | | |
| Sternebra(e) #5 and/or #6 unossified: | 10 (5) | 3 (2) | 23 (8) | 21 (7) |
| Fused and/or misaligned sternebrae: | 3 (3) | 2 (2) | 1 (1) | 2 (2) |
| Extra sternebral site of ossification: | | 1 (1) | | |
| Pubic bones unossified: | | | | 1 (1) |
| Tail unossified: | | | | 4 (3) |
| Total fetuses (litters) with variations: | 74 (12) | 59 (14) | 82 (13) | 68 (13) |

[a]Includes litter(s) that delivered, aborted or died on gestation day 28 or 29
[b]Includes nonviable fetus(es)

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TABLE 6. Cont. Summary of the Incidence of Fetal Developmental Variations

| | PCNB (mg/kg/day) | | |
|---|---|---|---|
| | 125(A) | 125(B) | 250 |
| No. of litters examined: | 10[a] | 10 | 6 |
| No. of fetuses examined externally: | 73[b] | 68 | 28[b] |
| No. of fetuses examined viscerally: | 73[b] | 68 | 28[b] |
| No. of fetuses examined skeletally: | 73[b] | 68 | 28[b] |

| Developmental Variations Observed: | No. of fetuses (No. of litters) | | |
|---|---|---|---|
| Thickened body: | | 1 (1) | |
| Carpal flexure: | | | |
| Tarsal flexure: | 1 (1) | | |
| Short tail: | | 1 (1) | |
| Hemorrhagic iris: | | | |
| Left carotid arises from the innominate: | 2 (1) | 2 (2) | 2 (2) |
| Azygous lobe of lung absent: | 2 (2) | | 2 (2) |
| Retroesophageal aortic arch: | | | |
| Gallbladder smaller than normal: | 2 (1) | 1 (1) | 2 (1) |
| Bent hyoid arch(es): | 4 (2) | 2 (1) | |
| Hyoid body unossified: | 5 (4) | | 3 (2) |
| Misshapen skull bones: | 1 (1) | | |
| Accessory skull bones: | | | |
| Supraoccipital reduced in ossification: | | | |
| 27 presacral vertebrae: | 14 (4) | 20 (5) | 5 (4) |
| 24 presacral vertebrae: | | | |
| 13th rudimentary rib(s): | 14 (8) | 13 (5) | 4 (4) |
| Greater than 12 pairs of full ribs: | 31 (8) | 37 (7) | 13 (5) |
| 7th cervical rib: | 1 (1) | 1 (1) | |
| Spherical enlargement of rib(s): | | | |
| Misshapen ribs: | | 1 (1) | |
| Sternebra(e) #5 and/or #6 unossified: | 15 (6) | 5 (2) | 11 (5) |
| Fused and/or misaligned sternebrae: | | 1 (1) | |
| Extra sternebral site of ossification: | | | |
| Pubic bones unossified: | 11 (2) | | 2 (1) |
| Tail unossified: | 18 (4) | | 1 (1) |
| Total fetuses (litters) with variations: | 59 (10) | 54 (8) | 24 (6) |

[a] Includes litter(s) that delivered, aborted or died on gestation day 28 or 29
[b] Includes nonviable fetus(es)