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August 18, 1999



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U.S. EPA
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Dear Sir:

On June 23, 1999 we submitted several reports in German on the compound SXX 0665. The English version has just been received and as a follow up, we are submitting these reports. No 8(e) HQ numbers have been assigned as yet.

TRACKING		
I.D. NUMBER	STUDY NAME	STUDY NUMBER
99-2-46	Study for Acute Oral Toxicity in Rats,	Study # T9034877
99-2-47	Study for Acute Oral Toxicity in Mice	Study # T0034878
99-2-48	Embryotoxicity Study on Postnatal DevelopmentOf Supernumerary Ribs in Rats following Oral Administration	Study # T4039958
99-2-49	Study for Embryotoxic Effects in Rabbits Following Oral Administration	Study # T9037397
99-2-51	Study for Acute Intraperitoneal Toxicity in Rats	Study # T7034875

14496

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Please contact us if there are any questions.

Sincerely,

Donald W. Lamb
Donald W. Lamb, Ph.D

Vice President, Product Safety & Regulatory Affairs
412-777-7431 Phone

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STUDY TITLE

SXX 0665
Embryotoxicity Study on Postnatal Development of
Supernumerary Ribs in Rats Following Oral Administration

DATA REQUIREMENT

US EPA-OPPTS Guideline No. 870.3700

AUTHOR

Dr. B. Holzum

109269

FILE

8865

STUDY COMPLETION DATE

October 1, 1992

PERFORMING LABORATORY

BAYER AG
DEPARTMENT OF TOXICOLOGY
Friedrich-Ebert-Strasse 217-233
D-42096 Wuppertal
Germany

LABORATORY PROJECT ID

Bayer AG Report No. 21792
Bayer AG Study No. T 4039958

STATEMENT OF DATA CONFIDENTIALITY

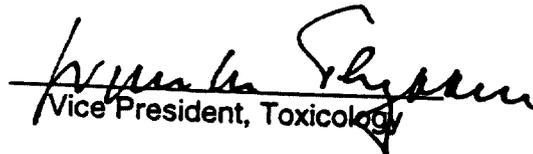
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The following statement supercedes the above statement of confidentiality that may occur elsewhere in this report:

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA Section 10(d)(1)(A), (B), or (C).

BAYER CORPORATION

Dr. J.H. Thyssen:


Vice President, Toxicology

Date:

Aug. 5-99

GLP Compliance Statement

This study was conducted in compliance with the OECD Principles of Good Laboratory Practice (GLP) (Bundesanzeiger No. 42a of March 2, 1983) and Bundesgesetzblatt, Part I of March 22, 1990 and meets the FIFRA Good Laboratory Practice Standards (40 CFR Part 160), with the exception that recognized differences exist between the GLP principles / standards of OECD and FIFRA (for instance, authority granted Agency inspectors and certain record retention requirements).

STUDY DIRECTOR

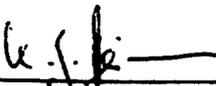
BAYER AG

for 
Dr. B. Holzum

12.3.1999
Date

SPONSOR

BAYER AG

for 
Dr. L. Mächemer

12.3.1999
Date

SUBMITTER

BAYER CORPORATION


Name: Dr. J.H. Thyssen
Vice President, Toxicology

Aug. 5. 99
Date

FLAGGING STATEMENT

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study meets or exceeds the criteria numbered 5.

SUBMITTER

BAYER CORPORATION

Dr. J.H. Thyssen: *J. H. Thyssen*
Vice President, Toxicology

Date: Aug. 5, 99

SPONSOR

AGRICULTURE DIVISION

Dr. J.H. Thyssen: *J. H. Thyssen*
Vice President, Toxicology

Date: Aug. 5, 99

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11. **Annex**

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1. STATEMENT OF QUALITY ASSURANCE UNIT

Study no. : T 4039958

Test substance : SXX 0665

This study was monitored by Quality Assurance on the dates given below. The results of the reviews and inspections were communicated in writing to the study director, and if necessary to the head of the institute or further affected persons as well.

Date of review or inspection	Forwarding date of inspection report
February 28, 1991 (study plan)	February 28, 1991
March 12, 1991	March 12, 1991
March 13, 1991	March 13, 1991
March ^t 25, 1991	March 25, 1991
April 02, 1991	April 02, 1991
May 15, 1991	May 15, 1991
October 01, 1991	October 01, 1991

The study results and methodology are accurately reflected by this report.

Quality Assurance/GLP, BAYER AG

Date: October 13, 1992

Responsible: _____
(Dr. H. Lehn)

SEE PAGE 170 FOR SIGNATURE

2. SIGNATURES

Study director:

(Dr. B. Holzum)

October 01, 1992
(Date)

Head of Institute:

(Dr. L. Macheimer)

October 14, 1992
(Date)



Dr.(USA) Robert Bashe
Translator
June 15, 1999

SEE PAGE 171 FOR SIGNATURE

3. SUMMARY

In an embryotoxicity study, administration of SXX 0665 to Wistar rats by the oral route led to an increase in the rate of fetuses exhibiting a 14th rib at daily doses of 10 mg/kg body weight and above [1,2]. The purpose of the present study was to investigate the postnatal development of prenatal supernumerary ribs. This involved daily oral administration of SXX 0665 to a group of 30 female Wistar rats at a dose of 0 mg/kg body weight, and to a group of 39 at a dose of 30 mg/kg body weight, from gestation day six to 15. About half of the animals were delivered by cesarian section on p.c. day 20. The remaining dams were allowed to give birth to their litters. After weaning, their pups were raised to an age of six weeks. The general toleration of the test substance by the dams and the effect on intrauterine and postnatal development were examined.

No evidence for maternal toxicity was observed at the daily 30 mg/kg body weight dose. The investigations for a test substance effect on intrauterine development showed that all 30 mg/kg group fetuses in the cesarian section group exhibited skeletal malformations (dysplasia of radius and ulna, isolated humeral dysplasia or cleft palate) and 14th ribs (punctiform, comma-shaped or more than half as long as the 13th rib). Isolated fetuses additionally displayed 15th and 16th punctiform ribs. Moreover, ossification of the skeletal system was retarded in most of the fetuses. The placental weight was markedly elevated in this group.

Excess dead pups were observed at birth in the rearing group at the daily 30 mg/kg body weight dose. Common emaciation, isolated cases of low body warmth and an increased rate of mortality were observed in the pups during rearing. In addition, the pups exhibited an increased incidence of 14th ribs (punctiform, comma-shaped or more than half as long as the 13th rib) at an age of six weeks.

Regarding the postnatal development of supernumerary ribs, it was found that a reduction in the number of pups with a punctiform or comma-shaped 14th rib to a magnitude comparable with that in the control group took place at the daily 30 mg/kg body weight dose during rearing. However, the number of affected six-week-old animals in the 30 mg/kg group was still higher than that in the controls. Postnatal persistence of 14th ribs that exhibit more than half the length of the 13th rib at the end of fetal development is likely. Punctiform 15th and 16th ribs such as those seen in isolated 30 mg/kg group fetuses were no longer found in six-week-old animals.

The 14th rib observed in fetuses following administration of SXX 0655 in a teratogenic dose range, 30 mg/kg body weight per day, thus represents an alteration that was not postnatally reversible in all cases. The results show that the length of the supernumerary (punctiform or comma-shaped) ribs in the fetus, rather than their location (14th, 15th or 16th rib), is the deciding factor governing reversibility during postnatal development.

4. INTRODUCTION

SXX 0665, an active ingredient exhibiting fungicidal properties, led to an increase in the rate of fetuses exhibiting a 14th rib when administered to rats in an embryotoxicity study at daily doses of 10 mg/kg body weight and above [1,2]. The purpose of the present study was to investigate the postnatal development of supernumerary ribs.

The study was performed during the period from March 05, 1991 to October 01, 1991 at the BAYER AG Fachbereich Toxikologie, Institute of Toxicology - Agrochemicals in D-5600 Wuppertal 1, Friedrich-Ebert-Strasse 217 - 333.

5. STUDY IDENTIFICATION AND RESPONSIBILITIES**5.1. Study number**

The study number was T 4039958.

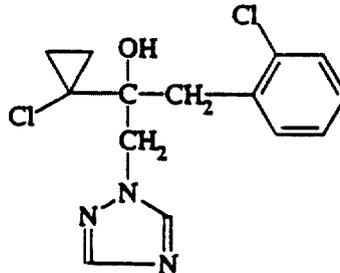
5.2. Responsibilities

Head of Institute	Dr. L. Machemer
Study director	Dr. B. Holzum
Active ingredient analyses	Dr. W. Gau, Dipl.Ing. K. Riegner
Quality Assurance	Dr. H. Lehn
Filing	Dr. E.A. Löbbecke

6. MATERIAL AND METHOD

6.1. Test substance and analysis for active ingredient in treatment formulations

Test substance name	: SXX 0665 techn.
Manufacturer	: BAYER AG
Batch no.	: 17005/89
Purity	: 93.9 % (analysis of December 18, 1990; cf. page 148 in annex)
Approval	: To June 17, 1991
Physical state	: Solid
Appearance	: Beige-brown powder
Test substance storage	: At ambient temperature
Common name	: --
Chemical name	: 2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1,2,4-triazol-1-yl)-propan-2-ol
CAS number	: --
Structural formula	:



Molar mass	: 312.0 g/mole
Empirical formula	: C ₁₄ H ₁₅ Cl ₂ N ₃ O

Deionized water containing 0.5 % Cremophor[®] EL (BASF) was used to prepare the treatment formulation suspensions. Cremophor[®] EL exerts no effect on the test parameters. The treatment formulations were stored at ambient temperature during the period of use. The stability of the active ingredient in the treatment formulations over the period of use (seven days) as well as the homogeneous distribution of the active ingredient throughout the treatment formulations were verified prior to study initiation in the oral embryotoxicity study with SXX 0665 in rabbits (T 9037397). Analyses for the active ingredient levels in the formulations performed in the second and fifth weeks of treatment showed no significant deviations from nominal (cf. analytical results on pp. 149 - 153 in the annex).

6.2. Experimental animals and maintenance

6.2.1. *Experimental animals*

The study was conducted with SPF-bred Wistar rats of the strain Bor:WISW (SPF Cpb) supplied by Winkelmann Experimental Animal Breeders in Borchen. Animals of this strain have been used for toxicologic studies at BAYER AG for years. The state of health of the breed is monitored and the animals routinely spot-checked for the main specific pathogens. The results of these tests are filed at BAYER AG.

Following receipt of the animals (on February 04, February 18 and March 04, 1991), those scheduled for this study were adapted to the animal room conditions for a period of at least seven days before treatment was initiated, and carefully observed for signs of illness during this period. No vaccinations or treatments with antiinfectives were carried out. Only healthy animals exhibiting no clinical signs were used for the study. The females were nulliparous and nongravid.

At the time of mating, the sexually mature male animals weighed more than 300 grams; the sexually mature females exhibited weights of 189 - 237 grams on p.c. day zero.

6.2.2. *Animal maintenance*

During the adaptation period, the female parent animals were kept in groups in Type III Makrolon® cages as described by A. Spiegel and R. Gönnert, *Zschr. Versuchstierkunde* 1, 38 (1961), and starting on p.c. day zero were individually accommodated, or kept together with their pups until termination of the three-week rearing period, in Type II Makrolon® cages on low-dust wood pellets supplied by Ssniff Spezialdiäten GmbH in Soest. After weaning, the pups of a litter were kept together in Type III Makrolon® cages until they were necropsied. The male parents were individually kept in Type III Makrolon® cages.

The wood pellets were spot-checked for contaminant levels; the records are filed at BAYER AG. The cages were exchanged for clean ones with fresh litter at least three times each week, or daily in the case of dams with pups.

All animals used in this study were housed in Animal Room 011 of Building 500.

6.2.3. Animal room conditions

The room climate in the animal rooms was standardized as follows.

Room temperature : 22° - 26°C (average 25°C)
Relative humidity : 23 - 60 % (average 37 %)
Light/dark cycles : Twelve hours; artificial lighting from 6 AM to 6 PM CET
Air exchanges : at least 10 times per hour

Occasional deviations from these standards took place, for example due to cleaning of the animal room. They had no apparent effect on animal maintenance.

6.2.4. Feeding

During the adaptation and study periods, the rations consisted of Altromin® 1324 - a standard diet produced by the Altromin company in Lage - and tap water, both of which were provided to the animals for *ad-libitum* consumption. The diet was furnished to the animals in food racks fitted in the cage covers. The water was provided in polycarbonate bottles with a capacity of 300 mL (Type II cages) or 700 mL (Type III cages) as described by A. Spiegel and R. Gönnert, *Zschr. Versuchstierkunde* 1, 38 (1961).

The nutritive composition and contaminant levels of the standard diet were routinely spot-checked by analysis (cf. pp. 154 - 156 in the annex for diet specification). The tap water met drinking water standards as specified in the German "Verordnung über Trinkwasser und über Wasser für Lebensmittelbetriebe" (Regulation on Drinking Water and on Water for Food Plants) of December 05, 1990 (*Bundesgesetzblatt* 1, 2613).

Records of the analyses to monitor compliance with the food and water specifications are filed at BAYER AG.

6.2.5. Identification of experimental animals

The dams were identified by cage cards listing the animal number, test substance, dose, study number and test introduction date (gestation day zero); and with ear tags supplied by the Hauptner company. After birth, the pups were marked with a black felt pen (Faber-Castell Marker 22) immediately after birth. As soon as they had developed sufficient fur, they were marked with saturated aqueous picric acid solution.

6.2.6. *Cleaning and disinfection*

The animal room was cleaned once each week using a disinfectant (Rapidosept[®] or Zephirol[®]). The animals were placed in clean cages with clean cage covers and water bottles at study initiation. The entire material of the cage was cleaned with hot water. A detergent was added to the last rinse, which only came into contact with the exterior walls of the cage.

6.3. **Mating, onset of gestation and lactation**

The animals were mated overnight by placing two female rats together with one male rat in a Type III cage. If spermatozoons were detected in the vaginal smear on the morning following mating, this day was considered gestation day zero (p.c. day zero). The day on which the pertinent dam bore all of its pups was considered lactation day zero (p.p. day zero).

6.4. **Active ingredient dosage, study groups and dose rationale**

The male animals were only used for mating and were not treated.

After insemination had been established, the females were allocated to two study groups, each of which was subdivided into cesarian section and rearing cohorts, according to a computer-generated randomizing plan (HP 3000 system random number generator; cf. pages 146 - 147 in the annex for randomizing list). Each of the two study groups consisted of 30 females (15 for cesarian section and 15 for rearing). In the 30 mg/kg group, nine additional females were introduced to the study (one for cesarian section and eight for rearing) because of the death of one animal in the cesarian section subgroup and the high pup mortality in the rearing subgroup.

The animals were treated each day from p.c. day 6 - 15 between 8 AM and 12 AM. The treatment formulations was orally administered to the animals using a stomach tube. The animals of both study groups were administered a uniform volume of 10 mL/kg body weight. The following doses, based on active ingredient and adjusted for the current body weight, were administered.

	Dose, mg/kg b.w	Concentration, mg/mL
Controls	0	0
Group 1	30	3

These doses were selected on the basis of results gained in a prior embryotoxicity study involving oral administration of SXX 0665 to rats [1,2]. In that study, administration of a daily 30 mg/kg body weight dose was tolerated without adverse effects to the dams. The animals exhibited an effect on the body weight gains and food intakes at a daily dose of 100 mg/kg body weight. In addition, the livers of the animals in this group displayed elevated weights and histopathologic alterations (centrilobular hypertrophy and centrilobular/periportal steatosis, increased rate of inflammatory cell clusters).

The daily 3 mg/kg body weight dose was tolerated without an embryotoxic effect. An increased rate of fetuses exhibiting a supernumerary (14th) rib was seen at daily doses of 10 mg/kg body weight and above. The resorption rate was elevated and ossification retarded at the daily 100 mg/kg body weight dose. In addition, three malformed fetuses in which a treatment effect could not be excluded were observed at this dose.

Since the rate of fetuses exhibiting supernumerary ribs in the 30 mg/kg group corresponded to that in the 100 mg/kg group, but the other uterine development parameters were unaffected at 30 mg/kg, daily doses of 0 mg/kg and 30 mg/kg body weight were selected in the present study for postnatal development of the supernumerary ribs.

6.5. Survey of examinations

6.5.1. General toleration of treatment by dams

The general toleration of the test substance by the dams was assessed on the basis of their appearance and behavior, food and water intakes, the appearance of the excretory products, the body weight gains and mortality of the animals, and on the basis of the gross pathology.

6.5.1.1 Appearance, behavior, food and water intakes, excretory products and mortality

The experimental animals were inspected twice daily (once daily on weekends and public holidays), and any observed findings recorded. Note was given to disturbances of the general condition, appearance or behavior; and to alterations in the excretory products.

The food intakes of the dams were determined over the gestation period intervals from p.c. day zero to six, six to eleven, 11 - 16 and 16 - 20 by weighing the amount of food provided and back-weighing the amount that remained unconsumed. No food intake determinations were made during the rearing period. The water intakes were assessed during the inspections by visual estimation of the remaining quantities.

6.5.1.2 Body weight gains

The body weights of the dams were determined on p.c. day zero, each day from p.c. day six to 15, on p.c. day 20, and in the rearing group animals additionally on p.p. days 0, 7, 14 and 21.

The corrected body weight gains of the cesarian section group dams were determined by subtracting the uterine weight from the p.c. day zero - 20 body weight gain.

6.5.1.3 Gross pathologic findings

The dams were sacrificed by cardiotomy under deep carbon dioxide anesthesia and examined for gross pathology at cesarian section on p.c. day 20, at termination of the three-week rearing period or after the death of all pups in the litter.

6.5.2. *Investigations during cesarian section*

The weight of the closed uterus was determined at cesarian section on p.c. day 20. Furthermore, the number of corpora lutea and implantations (if appropriate after staining [3]), the weights and outward appearance of the placentas, the numbers of viable and dead fetuses or embryos, and the sex and weight of all viable fetuses were determined. The fetuses were inspected for outwardly apparent malformations and miscellaneous abnormal findings during cesarian section. Alterations of the abdominal and thoracic organs were detected in subsequent evisceration of the fetuses. After all fetuses had been processed by the Dawson technique [4,5,6], the skeletal system was inspected for malformations, retardations (delayed ossification) and the presence and appearance of supernumerary (more than 13) ribs. The occurrence of 14th ribs was assessed as a variation because of the high spontaneous rate of fetuses exhibiting a 14th rib in the strain of rats used (up to 18 %), and the occurrence of more than 14 ribs as a malformation due to the rarity of this condition in control groups.

6.5.3. *Investigations during rearing*

6.5.3.1 Investigations of dams

In addition to the parameters listed in Section 6.5.1, the gestation period was determined, the process of birth (when possible) assessed and the lactation behavior observed in the dams selected for rearing. The number of implantation sites in the uterus was determined after staining [3] during necropsy of the dams at termination of the rearing period.

6.5.3.2 Investigations of pups

The numbers of viable and dead pups as well as the pup sexes (if possible those of dead pups as well) were determined shortly after birth (p.p. day zero). Up to an age of six weeks, the pups were daily evaluated with respect to their appearance, behavior, excretory products and mortality. The pup weights were determined on p.p. days zero, seven, 14, 21, 28, 35 and 42.

Standardization of the litter size was omitted in order to retain the largest possible number of pups for evaluation of the ribs.

On p.p. day 42 (+ 2), the pups were sacrificed by cardiomy under deep carbon dioxide anesthesia and examined for gross pathology after opening the body cavities. The thoraxes of the six-week-old animals subjected to scheduled sacrifice were removed and processed by the Dawson technique [4,6]. The number of ribs and the length of supernumerary ribs were assessed.

If autolysis and cannibalism did not render findings determination impossible, pups that died as well as those sacrificed in moribund condition were examined for gross pathology after opening the body cavities.

6.6. Statistics

The following methods were used for statistical significance testing.

a. The Wilcoxon non-parametric rank sum test (Wilcoxon-Mann-Whitney U-test) was used for the

- Weight gains of dams
- Number of corpora lutea per dam
- Number of implantations per dam (cesarian section groups)
- Number of fetuses per dam
- Number of resorptions per dam
- Fetal weight per dam
- Placental weight per dam
- Number of fetuses with minor skeletal deviations per dam
- Number of fetuses exhibiting malformations per dam
- Number of fetuses with a 14th rib per dam
- Litter size per dam
- Pup weight per dam

The Wilcoxon test calculations were performed with an IBM computer system at the BAYER AG Institute of Biometry, or with an HP Vectra PC, using an evaluation program developed for embryotoxicity studies. The reproduction parameters of the cesarian section groups were additionally evaluated on an individual pup or litter basis with the Chi² test, F-test, standard or Welch t-test using an HP-97 calculator or an HP Vectra PC. The statistical tests applied in each case are listed in the tables on pp. 55 - 59.

b. The Chi² test was used for the

- Number of fetuses or litters exhibiting malformations per group
- Number of fetuses or litters with supernumerary ribs per group
- Number of fetuses exhibiting retarded ossification per group
- Rearing index of dams
- Rate of survival of pups from p.p. day zero - 21
- Number of fetuses or litters with 14th rib per group

These calculations were performed using an HP-3000 computer system.

c. The F-test and the t-test were used for the

- Food intakes of dams
- Corrected body weight gains of dams
- Gestation period
- Numbers of pups on p.p. day zero and p.p. day 21

These calculations were performed using an HP-97 calculator or an HP Vectra PC.

c. The Welch t-test was used for the

- Number of implantations per dam (rearing groups)

These calculations were performed using an HP Vectra PC.

The tables in the annex list results rounded by the data processing system that was used; the means were calculated from unrounded raw data.

6.7. Compliance with GLP principles, filing

This study complied with the OECD principles of Good Laboratory Practice (GLP) as published in the **Bundesanzeiger** no. 42a of March 2, 1983 and **BGBl I** of March 22, 1990. Refer to page 3 for the GLP statement. In agreement with these principles, the study records (such as the study plan, report copy, raw data and fetuses as well as the thoraxes of the pups) are filed at the BAYER AG Fachbereich Toxikologie in Wuppertal.

7. RESULTS

7.1. General toleration of treatment by dams (cesarian section and rearing groups)

7.1.1 *Appearance, behavior and mortality*

No treatment-related clinical findings were made in the 30 mg/kg group dams.

One 30 mg/kg group animal died before treatment was initiated (on p.c. day three). Since no other animal died, there is no evidence for a treatment-related increase in mortality.

The clinical findings are listed together with the gross pathologic findings on pages 36 - 39 in the annex.

7.1.2 *Food and water intakes, excretory products*

The food and water intakes of the animals, and the appearance of their excretory products, underwent no treatment-related effect in the 30 mg/kg group.

The individual animal food intake data are listed together with the means on pages 40 - 45 in the annex.

7.1.3 *Body weight gains*

The weight gains of the 30 mg/kg group animals did not deviate significantly from those in the controls throughout gestation and the subsequent rearing period.

The individual animal body weights at the pertinent weighing dates are listed together with the means on pages 46 - 49 in the annex.

7.1.4 *Gross pathologic findings*

No toxicologically significant gross pathologic findings were made at necropsy of the animals during cesarian section or at termination of the rearing period. A comparable incidence of intestinal worms was found in multiple animals of both groups at necropsy. However, since no other gross pathologic or clinical alterations attributable to intestinal worm infestation were observed, it is unlikely that this intestinal worm infestation adversely affected the study assessment.

The findings at necropsy are listed together with the clinical findings on pages 36 - 39 in the annex.

7.2. Test substance effect on reproduction

7.2.1. Fertility index, gestation index and viability index (cesarian section and rearing groups)

The reproductive performance of the dams was assessed with the aid of the following indices:

$$\text{Fertility index (\%)} = \frac{\text{Number of females with implantations}}{\text{Number of fertilized females}} \times 100$$

$$\text{Gestation index (\%)} = \frac{\text{Number of females with fetuses/pups}}{\text{Number of females with implantations}} \times 100$$

Rearing groups only:

$$\text{Rearing index (\%)} = \frac{\text{Number of females that reared pups}}{\text{Number of females that bore pups}} \times 100$$

The 30 mg/kg cesarian section group animal that died (no. 4522) was not included in calculating the indices.

The index data are listed on page 51 in the annex.

The fertility and gestation indices in the 30 mg/kg group did not deviate significantly from the pertinent data in the control group. The rearing index was markedly depressed in the 30 mg/kg group. Four of the 21 litters in the 30 mg/kg group died within the first three days after birth, and one further litter within the first six days.

7.3. Reproduction data in cesarian section groups

Tables of means for the intrauterine development parameters listed in Sections 7.3.1 to 7.3.7 are located on pages 54 - 57 in the annex.

7.3.1. *Weights and outward appearance of placentas*

The mean placental weight was considerably elevated in the 30 mg/kg group. Moreover, engorged placentas were seen in two dams of this group, and placentas with a necrotic margin in six dams (one dam at 0 mg/kg).

The macroscopic findings made in the placentas are listed on page 119 in the annex.

7.3.2. *Resorption rate and number of fetuses*

The mean number of fetuses and the resorption rate in the 30 mg/kg group did not deviate significantly from the pertinent control group data, and were situated within the usual range of variation for this laboratory (cf. historical data on pages 162 - 163 in the annex).

The observed resorptions are differentiated into early and late resorptions on page 88 in the annex.

7.3.3. *Sex of fetuses*

The ratio of male to female fetuses in the 30 mg/kg group underwent no statistically significant change.

7.3.4. *Weight of fetuses*

The fetal weight in the 30 mg/kg group underwent no treatment-related adverse effect.

7.3.5. *Retardation of fetal skeletal development*

The mean number of pups per dam exhibiting skeletal deviations as a result of retarded ossification, and the percentage of these fetuses in the total number of viable fetuses per group, was considerably elevated in the 30 mg/kg group. The sternum, ribs and hyoid bone were affected.

A survey of the minor skeletal system deviations determined in this study is located on page 115 in the annex.

The scheme for classifying skeletal findings as variations, retardations or malformations is shown in the list on pages 157 - 159 in the annex.

7.3.6. Supernumerary ribs in fetuses

The following Table 1 surveys the numbers of fetuses exhibiting a 14th rib (variation) or a 15th/16th rib (malformation), and the numbers of litters containing such fetuses. In this list, punctiform or comma-shaped ribs are termed "rudimentary" and complete or slightly shortened ribs exhibiting more than half the length of the 13th rib "extra" ribs. Fetuses exhibiting both a rudimentary and an extra rib were only included in the count of fetuses with extra ribs.

Table 1

Dose, mg/kg	Percentage of fetuses/litters including supernumerary ribs		
	Total	Rudimentary	Extra
14th Rib			
0	15.3/57.1	14.6/50.0	0.7/7.1
30	100 ^{***} /100 [*]	84.2 ^{***} /57.1	15.8 ^{***} /42.9
15th Rib			
0	0/0	0/0	0/0
30	3.0/14.3	3.0/14.3	0/0
16th Rib			
0	0/0	0/0	0/0
30	1.5/14.3	1.5/14.3	0/0

* Significant, $p < 0.05$

*** Significant, $p < 0.001$

As shown in the above table, the percentage of fetuses exhibiting supernumerary ribs was significantly elevated in the 30 mg/kg group. All 30 mg/kg group fetuses exhibited 14th ribs, a majority of which represented punctiform or comma-shaped ribs. The percentage of fetuses exhibiting a 15th or 16th rib was also elevated in the 30 mg/kg group; in all cases, the 15th or 16th rib was only developed as a punctiform structure.

7.3.7. Fetal malformations

The following incidence table (Table 2) lists the malformations that occurred in the viable fetuses. The numbers of fetuses exhibiting a 15th and 16th rib were already mentioned in Section 7.3.6, and are not included in Table 2. Since more than one malformation was determined in isolated fetuses, the sum of the malformations listed for the pertinent group does not correspond to the total number of fetuses exhibiting malformations.

A list of the malformations observed in the individual fetuses is located on page 118 in the annex.

Table 2

Malformation	Dose (mg/kg b.w. per day)			
	0		30	
	Fetuses	Litters	Fetuses	Litters
Total	0	0	133 (100 %) ^{***}	14 (100 %) ^{***}
Dysplasia of radius and ulna			133 (100 %) ^{***}	14 (100 %) ^{***}
Dysplasia of humerus			5 (3.8 %)	3 (21.4 %)
Cleft palate			10 (7.5 %) ^{**}	3 (21.4 %)
Inspected fetuses/litters	137	14	133	14

^{**} Significant, $p < 0.01$

^{***} Significant, $p < 0.001$

As shown in Table 2, all 30 mg/kg group fetuses exhibited skeletal malformations. In addition to the dysplasia of the radius and ulna observed in all fetuses of this group, isolated fetuses exhibited humeral dysplasia and/or cleft palate.

7.4. Reproduction data in rearing groups

7.4.1. Gestation period

The gestation period underwent no treatment-related effect in the 30 mg/kg group.

Individual data for the dams and group means are located on page 120 in the annex.

7.4.2. Birth process

The process of birth could only rarely be observed since the animals generally gave birth during the night. No evidence exists for an effect on the birth process at the 30 mg/kg dose.

7.4.3. Lactation behavior

Since isolated pups of four 30 mg/kg group dams were not suckled on p.p. day zero (no milk spot), an adverse effect on the lactation behavior of the dams cannot be excluded.

7.4.4. Litter size

The mean litter size (viable pups) at birth in the 30 mg/kg group was slightly smaller than that in the control group. The minor nature of the difference possibly results from the fact that the control group exhibited three very small litters of only three pups and thus a very small mean litter size at birth, one that was situated below the usual range of variation for Segment I studies in this laboratory, and was in the lower portion of the range for Segment III studies (cf. historical data on page 169 in the annex). The rate of dead pups at birth in the 30 mg/kg group (16.4 %) was significantly higher than in the control group (0 %).

Data on the litter sizes and rates of dead pups are located on pages 128 - 132 in the annex.

7.4.5. Sex of pups

The percentages of male and female pups at birth underwent no treatment-related effect in the 30 mg/kg group.

Data on the pup sexes are located on page 127 in the annex.

7.4.6. Clinical observations in pups

An increased incidence of emaciated pups, and isolated pups with depressed body temperatures was seen in the 30 mg/kg group. One pup in this group exhibited an abnormally shaped skull (very narrow, flat) at birth.

The clinical pup findings are listed together with the gross pathologic findings on pages 123 - 126 in the annex.

7.4.7. Body weight gains in pups

The body weights of the pups, at birth and up to an age of 42 days, underwent no treatment-related adverse effect. Individual pup results and group means are located on pages 135 - 143 in the annex.

7.4.8. Pup mortality

The pup mortality was elevated in the 30 mg/kg group. As mentioned in Section 7.2.1 on page 22, four of the 21 litters in the 30 mg/kg group died within the first three days after birth, and one further litter within the first six days. The other pups of this group that died during rearing did so within the first two weeks after birth. Two further pups died after weaning.

Data on the numbers of pups at the individual weighing dates up to p.p. day 42, and on the survival rate during the three-week rearing period, are located on pages 128 - 134 in the annex.

7.4.9. Gross pathologic findings in pups

Due to advanced autolysis or cannibalism, no macroscopic findings could be made in most of the pups that died. No significant gross pathologic findings were determined in the remaining pups.

A comparable incidence of intestinal worms was determined at necropsy of the 0 mg/kg and 30 mg/kg group animals at an age of six weeks. However, since no clinical or gross pathologic alterations attributable to intestinal worm infestation were observed in these animals, it is unlikely that this intestinal worm infestation had an effect on the study results.

The findings made in the pups at necropsy are located together with the clinical findings on pages 122 - 126 in the annex.

7.4.10. Supernumerary ribs in pups

The following Table 3 surveys the numbers of pups exhibiting supernumerary ribs at an age of six weeks, and the numbers of litters containing such pups.

Table 2

Dose, mg/kg	Percentage of pups/litters including supernumerary ribs		
	Total	Rudimentary	Extra
14th Rib			
0	3.7/15.4	3.7/15.4	0/0
30	31.9 ^{***} /75.0 [*]	13.4 ^{***} /18.8	18.5 ^{***} /56.3 [*]
15th/16th Rib			
0	0/0	0/0	0/0
30	0/0	0/0	0/0

^{*} Significant, $p < 0.05$

^{***} Significant, $p < 0.001$

The above table shows that the fraction of pups exhibiting a 14th rib was elevated in the 30 mg/kg group. In this group, the incidence at which exclusively punctiform or comma-shaped 14th ribs occurred was comparable to that of complete or nearly complete 14th ribs. In the control group, isolated pups were seen with a punctiform or comma-shaped 14th rib. Fifteenth or 16th ribs were not seen in either the controls or the 30 mg/kg group.

The individual pup findings for supernumerary ribs are listed on pages 144 - 145 in the annex.

8. ASSESSMENT

In an embryotoxicity study, administration of SXX 0665 to Wistar rats by the oral route led to an increase in the rate of fetuses exhibiting a 14th rib at daily doses of 10 mg/kg body weight and above [1,2]. The purpose of the present study was to investigate the postnatal development of prenatal supernumerary ribs. This involved daily oral administration of SXX 0665 to a group of 30 female Wistar rats at a dose of 0 mg/kg body weight, and to a group of 39 at 30 mg/kg body weight, from gestation day six to 15. About half of the animals were delivered by cesarian section on p.c. day 20. The remaining dams were allowed to give birth to their litters. After weaning, their pups were raised to an age of six weeks. The general toleration of the test substance by the dams and the effect on intrauterine and postnatal development were examined.

The appearance, behavior, mortality, food and water intakes, excretory products, body weight gains and findings at necropsy of the dams underwent no treatment-related effect at the daily 30 mg/kg body weight dose.

The investigations for a test substance effect on intrauterine development showed that the fertility index and gestation index underwent no adverse effect in the 30 mg/kg group.

In the 30 mg/kg cesarian section group, no evidence was seen for an effect on the resorption rate, fetal sex or fetal weight. All fetuses in this group exhibited skeletal malformations (dysplasia of radius and ulna, isolated humeral dysplasia and/or cleft palate) and a 14th rib (punctiform, comma-shaped or more than half as long as the 13th rib). Isolated fetuses also displayed punctiform 15th and/or 16th ribs. Ossification of the skeletal system was furthermore retarded in most of the fetuses. The placental weight was significantly elevated in this group.

In the rearing group, the gestation period, birth process, pup sex and pup weight were unaffected at the 30 mg/kg dose. The litter size at birth was depressed as a result of the increased number of dead pups at birth. An increased incidence of emaciated pups, and isolated pups with depressed body temperatures were seen in this group. The mortality of the pups during the first two weeks after birth was markedly elevated. Four of the 21 litters died within the first three days after birth, and one further litter within the first six days. No significant gross pathologic findings were made in the pups at necropsy. The 30 mg/kg group pups exhibited an increased incidence of 14th ribs (punctiform, comma-shaped or more than half as long as the 13th rib).

The following table lists the percentages of fetuses and pups exhibiting supernumerary ribs.

Table 4

	0 mg/kg		30 mg/kg	
	p.c. Day 20	p.p. Week 6	p.c. Day 20	p.p. Week 6
14th Rib (%)	15.3	3.7	100	31.9
- Rudimentary	14.6	3.7	84.2	13.4
- Extra	0.7	0	15.8	18.5
15th/16th Rib (%)	0	0	3.8	0
- Rudimentary	0	0	3.8	0
- Extra	0	0	0	0

The above table shows that the six-week-old 0 mg/kg group pups exhibited a reduction in the numbers of punctiform and comma-shaped 14th ribs relative to those in the fetuses (to 25 % of the initial levels). A significant decrease in punctiform and comma-shaped 14th ribs (to 16 % of the initial levels) was also seen in the 30 mg/kg group. However, the numbers of nearly complete or completely developed 14th ribs remained unchanged after the six-week rearing period. The punctiform 15th or 16th ribs seen in isolated 30 mg/kg group fetuses no longer occurred in the six-week-old animals.

At the daily 30 mg/kg body weight dose, a reduction in the numbers of pups exhibiting punctiform and comma-shaped 14th ribs of a magnitude comparable to that in the control group thus occurred during rearing. However, the numbers of affected six-week-old animals were still higher than those of affected control group animals. Postnatal persistence of 14th ribs that exhibit more than half the length of the 13th rib at the end of fetal development is likely.

Thus, complete postnatal reversibility of the 14th rib observed after oral administration of SXX 0655 in a teratogenic dose range, 30 mg/kg body weight per day, is not expected. The results show that the length of the supernumerary (punctiform or comma-shaped) ribs in the fetus, rather than their location (14th, 15th or 16th rib), is the deciding factor governing reversibility during postnatal development.

9. REFERENCES

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10. KEY TO ABBREVIATIONS

ABSOL.	absolute
Anim.	animal
ANZ., N.	number
B.w.g.	body weight gain
CONTR.	control
CORP.	Corpora
EINGES.	used, introduced to study
E/L	early / late
FEM, F	female
G	gross
g, G.	gram
GES.	total
GRP., GR.	group
IMPL., impl.	implantations
KGW	body weight
KNOCHENVERAENDER.	skeletal deviation(s)
LEB.	viable
LFD-Nr.	running number
LIV.	living, viable
MALE, male	male
MEZ	Central European Time (CET)
Mißb.	malformations
MITTELW., \bar{x} , M^T	mean
MNL., MAENNL., M	male
NO., nq., N, Nr.	number
o.b.	no pathologic findings, n.o.e.
p.	page
P.C., p.c.	post coitum
PLACENT.	placentas
p.p.	post partum
Präparat	formulation ^T
RAND-NO (NR)	random number
RESO.	resorptions
Retard.	retardation
S	skeletal
S.D., SD, s, st. dev.	standard deviation
SPEZ.	special
STANDARD-ABW.	standard deviation
THEOR.	theoretical
TOT.	total
TS 1%, TS 5%	test result at significance level of $\alpha = 1\%$ (5%) ^T
V	visceral
WBL., WEIBL.	female
Σ	Sum

Translator's note: Following German usage, a comma is used instead of a decimal point in the original tables. The sign "" (geographical minute, apostrophe) is sometimes used to indicate minutes of time. Days are abbreviated "d" and hours "h" in the original tables. The dates are specified in European order (dd.mm.yyyy. for example 28.10.1992 for October 28, 1992). In keeping with American usage and to avoid confusion with the numeral "1", the unit "liter" was abbreviated "L" in the translated text. Entries marked with a ^T are by translator.

11. ANNEX

Tables with findings; tables with individual animal data, means and statistics; randomization list; data on active ingredient analysis, diet specification and classification of fetal skeletal deviations; historical control data

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40	- 45	- Food intakes (individual animal data for dams with group means)
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52	- 59	- Weight gains during gestation and during the treatment period, corpora lutea, implantations, number of fetuses, losses, fetal weights, placental weights, skeletal deviations and malformations (individual animal data for dams and group means)
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Page	
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- 169 - Litter size at birth (Segment I and III studies)

Clinical signs and observations in dams

(Caesarian section groups)

Dose mg/kg	Animal No.	Clinical signs and observations	Observation (p.c. day)
0	4471	Intestinal worms	20 (necropsy)
	4474	Intestinal worms	20 (necropsy)
	4476	Intestinal worms	20 (necropsy)
	4478	Intestinal worms	20 (necropsy)
	4485	Intestinal worms	20 (necropsy)
	4509	Soft feces	10
	4515	Intestinal worms	20 (necropsy)
	4517	Intestinal worms	20 (necropsy)
	4518	Intestinal worms	20 (necropsy)
30	4479	Intestinal worms	20 (necropsy)
	4483	Intestinal worms	20 (necropsy)
	4490	Intestinal worms	20 (necropsy)
	4495	Intestinal worms	20 (necropsy)
	4507	Intestinal worms	20 (necropsy)
	4512	Intestinal worms	20 (necropsy)
	4513	Intestinal worms	20 (necropsy)
	4516	Intestinal worms	20 (necropsy)
	4522	Died	3
4524	Intestinal worms	20 (necropsy)	

Incidence table**Clinical signs and observations in dams from p.c. day six on**

(Cesarian section groups)

Clinical signs and observations	Dose in mg/kg b.w.	
	0	30
Intestinal worms	8	9
Soft feces	1	

Clinical signs and observations in dams

(Rearing groups)

Dose mg/kg	Animal No.	Clinical signs and observations	Observation day	
			p.c.	p.p
0	4473	Intestinal worms		21 (necropsy)
	4482	Intestinal worms		21 (necropsy)
	4488	Intestinal worms		21 (necropsy)
	4493	Intestinal worms		21 (necropsy)
	4501	Soft feces	10	
	4505	Soft feces	11	
	4506	Intestinal worms		21 (necropsy)
	4521	Intestinal worms		21 (necropsy)
30	4480	Head held obliquely		0-1
	4481	Intestinal worms		4 (necropsy)
	4487	Intestinal worms		3 (necropsy)
	4504	Intestinal worms		4 (necropsy)
	4523	Intestinal worms		22 (necropsy)
	4525	Intestinal worms		22 (necropsy)
	4526	Intestinal worms		22 (necropsy)
	4529	Intestinal worms		21 (necropsy)
	4048	Intestinal worms		21 (necropsy)
	4065	Intestinal worms	24	(necropsy)

Incidence table**Clinical signs and observations in dams from p.c. day six on****(Rearing groups)**

Clinical signs and observations	Dose in mg/kg b.w.	
	0	30
Intestinal worms	6	9
Soft feces	2	
Head held obliquely		1

FOOD CONSUMPTION (G/ANIMAL/DAY)

(Caesarean section group)

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Group: 0 mg/kg

Animal No.	Day p.c.				
	0-6	6-11	11-16	16-20	0-20
4471	13.7	14.4	16.8	19.8	15.9
4474	16.0	15.0	16.6	19.8	16.7
4476	14.7+	15.6+	14.2+	12.8+	14.4+
4478	16.7	17.2	19.6	19.0	18.0
4485	17.7	17.0	17.8	19.0	17.8
4496	16.5	16.2	17.6	18.5	17.1
4500	19.7	16.6	18.6	17.5	18.2
4503	18.8	17.0	17.8	20.8	18.5
4508	17.5	17.4	17.4	18.5	17.7
4509	17.7	16.6	17.6	19.0	17.7
4511	18.0	16.4	18.6	22.0	18.6
4515	17.8	17.0	18.8	18.0	17.9
4517	17.3	15.8	16.8	18.5	17.1
4518	18.3	16.6	18.6	18.8	18.1
4520	16.8	15.6	18.2	20.0	17.5
n :	14	14	14	14	14
Σ :	242.5	228.8	250.8	269.0	246.5
\bar{x} :	17.3	16.3	17.9	19.2	17.6
SD :	1.42	0.87	0.87	1.16	0.74

+ = not used for calculation

FOOD CONSUMPTION (G/ANIMAL/DAY)

(Cesarean section group)

Group: 30 mg/kg

Animal No.	Day p.c.				
	0-6	6-11	11-16	16-20	0-20
4472	15.8	14.8	17.2	18.0	16.4
4479	16.0	14.6	17.0	18.8	16.5
4483	18.7	17.2	19.4	19.5	18.7
4486	14.2+	13.4+	14.6+	13.3+	13.9+
4490	16.5	18.0	19.8	20.5	18.5
4495	18.7	19.0	19.4	19.5	19.1
4497	15.7	15.6	16.4	18.5	16.4
4499	18.2	15.4	17.8	17.8	17.3
4502	18.7	17.8	18.2	19.0	18.4
4507	16.7	16.4	17.4	19.0	17.3
4512	17.2	16.2	18.0	20.3	17.8
4513	17.5	16.0	17.2	21.0	17.8
4516	18.2	17.0	20.2	19.8	18.7
4522	-	-	-	-	-
4524	16.3	16.2	17.6	18.3	17.0
4046	15.7	14.2	17.0	17.8	16.1
n :	14	14	14	14	14
Σ :	239.7	228.4	252.6	267.5	245.7
\bar{x} :	17.1	16.3	18.0	19.1	17.5
SD :	1.17	1.38	1.19	1.03	1.01

+ = not used for calculation

- = no values

Food Consumption during Pregnancy

Mean Values (g/animal/day)

(Cesarean section groups)

Dose mg/kg		Day p.c.				
		0-6	6-11	11-16	16-20	0-20
0	n	14	14	14	14	14
	\bar{x}	17.3	16.3	17.9	19.2	17.6
	SD	1.42	0.87	0.87	1.16	0.74
30	n	14	14	14	14	14
	\bar{x}	17.1	16.3	18.0	19.1	17.5
	SD	1.17	1.38	1.19	1.03	1.01

FOOD CONSUMPTION (G/ANIMAL/DAY)

(Rearing group)

Group: 0 mg/kg

Animal No.	Day p.c.				
	0-6	6-11	11-16	16-20	0-20
4470	17.8	17.2	18.4	20.0	18.3
4473	18.0	18.4	19.8	20.8	19.1
4482	16.2	16.2	18.2	19.5	17.4
4484	16.2	16.4	18.6	21.0	17.8
4488	18.0	19.0	21.8	21.8	20.0
4489	16.5	16.6	18.6	19.0	17.6
4492	16.7	16.2	16.8	18.8	17.0
4493	15.3	14.6	16.2	16.8	15.7
4494	17.5	17.6	20.0	20.3	18.7
4501	19.2	17.4	19.2	20.0	18.9
4505	17.7	15.2	14.6	18.5	16.5
4506	18.5	18.0	19.0	21.0	19.0
4510	18.2+	15.8+	14.0+	14.3+	15.8+
4519	19.5	18.0	20.0	22.3	19.8
4521	18.0	16.2	14.2	19.0	16.8
n :	14	14	14	14	14
Σ :	245.0	237.0	255.4	278.5	252.3
\bar{x} :	17.5	16.9	18.2	19.9	18.0
SD :	1.20	1.24	2.13	1.45	1.29

+ = not used for calculation

FOOD CONSUMPTION (G/ANIMAL/DAY)

(Rearing group)

Group: 30 mg/kg

Animal No.	Day p.c.				
	0-6	6-11	11-16	16-20	0-20
4475	18.2	17.6	19.8	22.3	19.3
4477	16.3	17.6	18.8	20.0	18.0
4480	15.7	16.6	18.4	19.5	17.4
4481	17.5	17.8	19.0	20.5	18.6
4487	17.8	17.8	19.8	17.8	18.3
4491	17.7	17.0	19.6	18.3	18.1
4498	15.2	16.4	17.2	19.0	16.8
4504	17.7	16.0	18.0	17.0	17.2
4514	18.5	16.8	19.0	-	-
4523	17.8	15.0	-	18.8	-
4525	19.0	16.8	-	19.0	-
4526	18.7	15.4	-	19.8	-
4527	17.0	-	-	18.5	-
4528	17.7	16.4	-	17.5	-
4529	17.3	16.8	-	19.0	-
4047	-	15.4	18.4	20.5	-
4048	-	15.8	18.8	19.0	-
4049	-	15.2	18.4	19.0	-
4060	14.7+	17.0+	15.8+	-	-
4065	18.3+	14.8+	14.4+	-	-
4066	14.8	15.0	16.8	-	-
4072	16.5	16.8	17.0	-	-
4084	18.7	17.2	18.8	-	-
n :	18	20	15	17	8
Σ :	312.0	329.4	277.8	325.3	143.5
\bar{x} :	17.3	16.5	18.5	19.1	17.9
SD :	1.21	0.93	0.94	1.26	0.81

+ = not used for calculation
 - = no values

Food Consumption during Pregnancy

Mean Values (g/animal/day)

(Rearing groups)

Dose mg/kg		Day p.c.				
		0-6	6-11	11-16	16-20	0-20
0	n	14	14	14	14	14
	\bar{x}	17.5	16.9	18.2	19.9	18.0
	SD	1.20	1.24	2.13	1.45	1.29
30	n	18	20	15	17	8
	\bar{x}	17.3	16.5	18.5	19.1	17.9
	SD	1.21	0.93	0.94	1.26	0.81

BODY WEIGHT (G)

Group: 0 mg/kg SX 0605 T4039950
 (Caesarean section group)

Animal No.	Gestation day															
	0	6	7	8	9	10	11	12	13	14	15	20				
4471	210	227	227	228	232	236	238	241	242	243	250	292				
4474	216	232	227	229	229	240	239	235	238	240	247	294				
4476**	189	212	212	212	218	216	222	218	215	213	210	207				
4478	207	223	223	228	224	229	234	237	238	242	250	290				
4485	206	228	230	230	235	241	241	244	245	249	251	270				
4496	203	223	226	228	230	233	235	237	238	244	248	298				
4500	212	233	231	236	239	240	242	245	250	253	256	302				
4503	213	235	234	238	240	243	249	247	251	256	262	303				
4508	213	230	234	234	238	240	246	247	253	256	258	309				
4509	208	221	223	223	227	228	231	235	238	238	245	284				
4511	222	239	242	245	247	251	254	259	263	263	269	319				
4515	193	213	216	221	224	230	224	237	239	243	247	282				
4517	220	237	241	242	245	247	251	253	254	255	257	312				
4518	202	226	226	223	233	233	240	244	244	250	247	299				
4520	209	225	227	230	231	229	236	237	240	247	250	296				

N	16	16	14	14	14	14	14	14	14	14	14	14
Mean	209.6	228.0	229.1	231.1	233.9	237.1	240.0	242.7	245.2	248.5	252.6	296.4
SD	7.5	7.0	7.0	7.1	7.2	7.2	8.1	7.2	7.8	7.3	6.9	12.8

** not used for calculation - no implantations

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BODY WEIGHT (G)

16039958

SXX 0665

Group: 30 mg/kg

(Caesarean section group)

Animal No.	Gestation day															
	0	6	7	8	9	10	11	12	13	14	15	20				
4472	202	226	228	224	229	230	232	236	231	234	240	253				
4479	201	222	221	222	223	226	228	228	232	234	234	273				
4483	210	229	228	234	235	238	239	240	245	249	254	293				
4486**	205	202	205	202	208	207	208	206	204	207	208	207				
4490	203	230	237	236	243	241	245	244	245	251	247	281				
4495	208	231	234	237	238	243	248	245	247	256	257	318				
4497	204	217	219	220	228	229	230	230	231	238	241	301				
4499	200	221	224	220	225	226	231	236	239	235	244	292				
4502	208	230	232	234	233	232	245	248	246	251	258	317				
4507	204	223	225	227	223	229	237	237	236	241	243	269				
4512	201	225	234	230	233	235	237	242	245	249	251	294				
4513	199	220	227	224	230	232	237	241	244	246	251	314				
4516	193	224	226	226	231	239	240	243	249	249	258	302				
4522#	210	--	--	--	--	--	--	--	--	--	--	--				
4524	200	223	223	227	227	231	236	237	237	241	251	303				
4046	193	218	218	219	214	220	225	228	233	237	240	292				

N	14	14	14	14	14	14	14	14	14	14	14	14
Mean	201.9	224.2	226.9	227.1	229.4	232.2	236.4	238.2	240.0	243.6	247.8	293.0
SD	5.0	4.5	5.8	6.2	7.2	6.4	6.8	6.3	6.6	7.4	7.6	18.8

-- no value
** not used for calculation - no implantations
##

BODY WEIGHT (G)

14039950

SIX 0665

(Rearing group)

Group: 0 mg/kg

Animal No.	Gestation day														Day post partum				
	0	6	7	8	9	10	11	12	13	14	15	20	0	7	14	21			
4470	213	236	237	240	243	246	253	254	253	253	253	260	317	234	251	264	241		
4473	226	250	252	251	260	258	265	268	268	270	276	276	300	276	287	293	291		
4482	197	218	223	223	227	231	233	233	236	244	243	247	290	224	247	255	233		
4484	210	228	233	234	237	243	249	252	253	258	263	263	331	229	246	262	268		
4488	211	235	238	240	248	250	253	255	258	264	268	268	322	249	272	280	251		
4489	204	226	230	230	234	236	240	248	242	246	249	274	274	236	256	266	257		
4492	202	220	218	227	229	232	234	231	235	238	243	243	289	207	240	254	246		
4493	196	210	215	214	219	219	221	223	220	229	234	234	273	211	237	235	230		
4494	198	218	223	224	227	230	233	236	235	243	244	244	273	252	--	--	--		
4501	208	229	228	233	235	232	242	244	243	249	252	298	298	208	241	242	244		
4505	202	222	224	227	228	232	237	238	244	232	239	275	275	219	244	248	244		
4506	220	239	239	245	245	248	255	255	256	260	262	288	288	254	267	272	264		
4510	215#	237#	238#	239#	243#	242#	242#	235#	236#	236#	237#	237#	236#	--	--	--	--		
4519	206	230	231	233	238	239	248	248	250	251	256	322	322	232	267	267	257		
4521	215	236	235	238	238	239	247	239	239	243	248	295	295	230	250	260	254		

N	Mean														SD				
	14	14	14	14	14	14	14	14	14	14	14	14	14	14	13	13	13		
Mean	207.6	228.5	230.4	232.9	236.3	238.2	243.6	244.0	245.1	248.6	252.9	298.2	232.9	254.2	261.4	252.3			
SD	9.0	10.6	9.7	9.5	10.5	10.1	11.5	12.0	12.2	11.8	11.8	19.9	19.6	14.8	15.5	16.1			

-- no value
value not used for calculation

BODY WEIGHT (G)

14039950

SXK 0665

(Rearing group)

Group: 30 mg/kg

Animal No.	Gestation day										Day post partum					
	0	6	7	8	9	10	11	12	13	14	15	20	0	7	14	21
4475	209	245	249	244	248	251	257	258	261	259	273	337	229	252	257	237
4477	200	223	226	227	231	234	242	242	242	245	252	302	212	270	260	254
4480	198	223	226	222	233	234	239	241	244	246	249	298	216	--	--	--
4481	207	230	229	234	232	238	239	237	240	248	256	309	210	--	--	--
4487	207	237	237	238	246	247	250	254	254	265	269	316	225	--	--	--
4491	212	235	240	237	243	245	251	251	253	261	263	316	233	256	267	261
4498	202	224	228	230	231	237	238	236	243	242	249	304	230	266	258	253
4504	202	224	226	226	230	236	242	247	247	248	257	309	221	--	--	--
4514	190	211	215	215	219	224	228	231	233	236	241	280	192	220	229	234
4523	193	213	218	215	218	217	219	226	226	231	236	284	213	224	228	231
4525	202	226	226	226	232	229	233	237	239	246	252	305	227	226	262	245
4526	207	231	235	231	236	233	238	237	245	247	252	290	227	245	249	240
4527	216	236	236	241	238	240	244	246	250	254	257	299	242	--	--	--
4528	190	209	208	208	210	219	221	223	228	235	238	273	222	236	236	234
4529	214	234	231	237	236	242	248	248	254	256	261	294	241	262	273	256
4047	207	230	234	233	230	238	238	240	249	253	253	290	241	261	267	264
4048	198	217	221	221	224	226	231	234	245	244	248	295	216	243	260	262
4049	200	227	221	221	228	232	232	235	243	244	246	297	228	233	235	240
4060	217	260	247	250	247	248	251	254	258	261	252	242	--	--	--	--
4065	220	245	242	252	245	238	238	233	238	237	230	294	--	--	--	--
4066	201	220	223	225	222	226	230	230	235	238	243	299	198	232	241	228
4072	197	228	231	225	227	232	239	238	235	244	251	304	204	239	248	243
4084	215	247	250	249	249	253	260	264	269	273	275	334	239	276	282	273

N	Gestation day										Day post partum					
	21	21	21	21	21	21	21	21	21	21	21	21	21	16	16	16
Mean	203.2	227.1	229.0	229.0	231.6	234.9	239.0	240.7	244.5	248.3	253.4	301.7	222.2	246.3	253.2	247.2
SD	7.6	10.1	10.3	10.2	10.0	9.6	10.4	10.3	10.4	10.3	10.5	15.4	14.0	17.5	16.0	13.5

-- no value
value not used for calculation

Body Weight Gain (Corrected) during Pregnancy (Day 0-20 p.c.)

Individual Values and Means

(Cesarean section groups)

0 mg/kg		30 mg/kg	
Anim. no.	B.w.g. g	Anim. no.	B.w.g. g
4471	32	4472	36
4474	27	4479	32
4476+	17	4483	25
4478	19	4486+	-2
4485	39	4490	51
4496	29	4495	38
4500	28	4497	26
4503	36	4499	26
4508	29	4502	30
4509	25	4507	33
4511	37	4512	36
4515	36	4513	44
4517	29	4516	46
4518	37	4522++	-
4520	33	4524	31
		4046	30
n	14		14
\bar{x}	31.1		34.6
s	5.60		7.88

+ not used for calculation - no implantation sites

++ Exitus

Fertility index, gestation index and rearing index

Dose, mg/kg b.w. per day	Inseminated animals n	Fertility index %	Gestation index %	Rearing index %
Cesarian section				
0	15	93.3	100	--
30	16	93.3	100	--
Rearing				
0	15	93.3	100	92.9
30	23	91.3	100	76.2

Cesarean Section Group / Schnittentbindung Gruppe

INDIVIDUAL VALUES / EINZELWERTE
 EFFECT OF SXX 0665 WIRKUNG VON SXX 0665
 ON PREGNANT RATS AND THEIR FOETUSES AN TRAECHTIGEN RATTEN UND DEREN FETEN
 10 DAILY TREATMENTS PER OS 10 TAEGLICHE BEHANDLUNG PER OS
 FROM DAY 6 TO 15 OF PREGNANCY VOM 6. BIS 15. TAG DER TRAECHTIGKEIT
 CONTROL GR. 0.5% AQUEOUS CREMOPHOR EMULSION 0.5%IGE WASSERIGE CREMOPHOREMULSION
 KONTROLLOR.

ANIMAL NO.	TIER-NR.	WEIGHT GAIN (G) DURING PREGNANCY	GEWICHTSZUNAHME WAEREND DER TRAECHTIGKEIT	NUMBER (CORP.)	ANZAHL (KORP.)	PER DAM (FOETUSES)	PRO MUTTERTIER (FETEN)	OF LOSS (SUM)	VERLUSTE (GES.)	MEAN WEIGHT IN GRAMS (FOETUS)	DURCHSCHNITTL. GEWICHT IN GRAMM (FETEN)	NO. OF FOETUSES EXAMINED BY WILSON	ANZAHL DER FETEN BEURTEILT NACH WILSON	FEETEM WITH MINOR SKELETAL DEVIATIONS	GERINGEN KNOCHENVERAENDER.	14th rib
4471	82	23	23	14	9	4	5	9	0	3.51	0.60	0	9	4	0	2
4474	78	15	15	14	9	5	4	9	0	3.63	0.59	0	9	2	0	0
4476	18	27	27	12	12	7	4	11	1	3.78	0.57	0	11	7	0	0
4478	83	23	23	14	11	2	2	4	0	3.66	0.72	0	4	2	0	0
4485	64	25	25	12	11	7	4	11	0	3.70	0.69	0	11	2	0	1
4496	95	23	23	13	12	5	6	11	1	3.63	0.60	0	11	4	0	2
4500	90	27	27	13	9	5	4	9	0	3.88	0.64	0	9	0	0	3
4503	90	27	27	12	12	4	8	12	0	3.67	0.57	0	12	7	0	4
4508	96	24	24	13	9	4	5	9	0	3.65	0.62	0	9	8	0	0
4511	97	30	30	12	12	8	2	10	2	3.79	0.66	0	10	6	0	0
4515	89	34	34	12	11	2	8	10	0	3.47	0.52	0	10	1	0	3
4517	92	20	20	13	13	6	5	11	2	3.81	0.58	0	11	3	0	3
4518	97	21	21	13	12	5	6	11	1	3.44	0.53	0	11	7	0	0
4520	87	25	25	11	11	3	7	10	1	3.45	0.64	0	10	3	0	3

MEAN MITTEL 86.9 24.6 12.7 10.5 4.8 5.0 9.8 0.7 3.65 0.61 0.0 9.79 4.00 0.0 1.50

x) NOT USED FOR CALCULATION OF MEAN VALUE / NICHT ZUR ERRECHNUNG DER MITTELWERTE VERWENDET

Cesarean Sectio. Group / Schnittentbindungsgrup.

INDIVIDUAL VALUES / EINZELWERTE

STUDY NO. / STUDIEN-NR. 1403958
 EFFECT OF SXX 0665 ON PREGNANT RATS AND THEIR FOETUSES
 WIRKUNG VON SXX 0665 AN TRAECHTIGEN RATTEN UND DEREN FETEN
 10 DAILY TREATMENTS PER OS FROM DAY 6 TO 15 OF PREGNANCY
 10 TAEIGIGE BEHANDLUNG PER OS VOM 6. BIS 15. TAG DER TRAECHTIGKEIT
 DOSE GROUP / DOSISGRUPPE 30 MG/KO
 30 MG/KO

ANIMAL NO.	WEIGHT DURING PREGNANCY (G)	WEIGHT GAIN (G)	NUMBER OF PREGNANT RATS	NUMBER OF FOETUSES	LOSS	MEAN IN GRAMS	NO. OF FOETUSES EXAMINED BY WILSON	NO. OF FOETUSES WITH MALFORMATIONS	14th rib					
TIER-NR.	TRAECHTIGKEIT (LUNGSZEIT)	WAEHREND DER BEHANDLUNG (LUNGSZEIT)	ZAHL (PRO MUTTERTIER) FETEN	(PER DAM) FETES	MALE FEM.	FOETUS PLACENT.	DAWSON	FETEN MIT GERINGEN KNOCHENVERAENDER.	14. Rippe					
4046	99	22	14	9	4	13	1	13	13					
4472	51	14	13	2	0	2	0	2	2					
4479	72	12	6	5	1	6	0	6	6					
4483	83	25	14	4	6	10	3	10	10					
4486	2 *	6 *	0x											
4490	17	17	5	1	3	4	1	4	4					
4495	110	26	13	8	4	12	0	12	12					
4497	97	24	12	7	5	12	0	12	12					
4499	92	23	13	8	3	11	1	11	11					
4502	109	28	13	7	6	13	0	13	13					
4507	65	20	11	5	0	5	5	5	5					
4512	93	26	13	3	7	10	2	10	10					
4513	115	31	13	8	4	12	1	12	12					
4516	109	34	11	3	7	10	0	10	10					
4522	- x	- x	MOTHER ANIMAL NOT EVALUATED											
4524	103	28	15	7	6	13	1	13	13					
MEAN	91.1	23.6	12.7	10.6	5.5	4.0	9.5	1.1	3.71	0.77	0.0	9.50	7.64	9.50

x) NOT USED FOR CALCULATION OF MEAN VALUE / NICHT ZUR ERRECHNUNG DER MITTELWERTE VERWENDET

SUMMARY OF REPRODUCTION DATA

- Cesarean Section Group -

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Group (mg/kg)	0	30	
Number of dams with implantations (a)	14	14	Stat. Test
with viable fetuses (b)	14	14	

Corpora lutea per group	178	178	
per dam: mean	12.7	12.7	F
st. dev.	0.91	1.20	
n (a)	14	14	

Corpora lutea per group	178	178	
per dam: mean	12.7	12.7	F
st. dev.	0.91	1.20	
n (b)	14	14	

Implantations per group	147	148	
% of Corp. lutea	82.6	83.1	
per dam: mean	10.5	10.6	F
st. dev.	2.10	3.67	
n (a)	14	14	

Implantations per group	147	148	
% of Corp. lutea	82.6	83.1	
per dam: mean	10.5	10.6	F
st. dev.	2.10	3.67	
n (b)	14	14	

Preimplantation Loss per group	31	30	
% of Corp. lutea	17.4	16.9	
per dam: mean	2.2	2.1	C
st. dev.	2.75	3.23	
No. of dams affected	9	10	
n (a)	14	14	

Chi-Square C
F-, t-Test F

SUMMARY OF REPRODUCTION DATA

Group (mg/kg)	- Cesarean Section Group -		Stat. Test
	0	30	
<hr/>			
Number of dams			
with implantations (a)	14	14	
with viable fetuses (b)	14	14	
<hr/>			
Preimplantation Loss			
per group	31	30	
% of Corp. lutea	17.4	16.9	
per dam: mean	2.2	2.1	C
st. dev.	2.75	3.23	
No. of dams affected	9	10	
n (b)	14	14	
Live Fetuses			
per group	137	133	
per dam: mean	9.8	9.5	F
st. dev.	1.93	3.70	
n (b)	14	14	
% of Implantations			
per group	93.2	89.9	
per dam: mean	93.2	90.0	F
st. dev.	7.02	13.98	
n (b)	14	14	
Sex Ratio of Fetuses			
per group			
males	67	77	
% males	48.9	57.9	C
females	70	56	
% females	51.1	42.1	
litter mean			
% males: mean	49.0	60.7	F
st. dev.	15.24	24.14	
% females: mean	51.0	39.3	F
st. dev.	15.24	24.14	
n (b)	14	14	

Chi-Square C
F-, t-Test F

SUMMARY OF REPRODUCTION DATA

Group (mg/kg)	- Cesarean Section Group -		Stat. Test
	0	30	
<u>Number of dams</u>			
with implantations (a)	14	14	
with viable fetuses (b)	14	14	
Resorptions			
total per group	10	15	
% of implantations	6.8	10.1	
per dam: mean	0.7	1.1	C
st. dev.	0.73	1.44	
No. of dams affected	8	8	
n (a)	14	14	
Resorptions			
total per group	10	15	
% of implantations	6.8	10.1	
per dam: mean	0.7	1.1	C
st. dev.	0.73	1.44	
No. of dams affected	8	8	
n (b)	14	14	
Early Resorptions			
per group	1	1	
% of implantations	0.7	0.7	
per dam: mean	0.1	0.1	C
st. dev.	0.27	0.27	
No. of dams affected	1	1	
n (a)	14	14	
Early Resorptions			
per group	1	1	
% of implantations	0.7	0.7	
per dam: mean	0.1	0.1	C
st. dev.	0.27	0.27	
No. of dams affected	1	1	
n (b)	14	14	

Chi-Square C

SUMMARY OF REPRODUCTION DATA

Group (mg/kg)	- Cesarean Section Data -		Stat. Test
	0	30	
<hr/>			
<u>Number of dams</u>			
with implantations (a)	14	14	
with viable fetuses (b)	14	14	
<hr/>			
Late Resorptions			
per group	9	14	
% of implantations	6.1	9.5	
per dam: mean	0.6	1.0	C
st. dev.	0.74	1.24	
No. of dams affected	7	8	
n (a)	14	14	
Late Resorptions			
per group	9	14	
% of implantations	6.1	9.5	
per dam: mean	0.6	1.0	C
st. dev.	0.74	1.24	
No. of dams affected	7	8	
n (b)	14	14	
Weight of Live Fetuses			
Litter Basis			
total fetuses			
n (litters)	14	14	
mean	3.65	3.71	F,T
st. dev.	0.139	0.273	
male fetuses			
n (litters)	14	14	
mean	3.73	3.75	F,T
st. dev.	0.154	0.249	
female fetuses			
n (litters)	14	12	
mean	3.54	3.59	F,T
st. dev.	0.155	0.317	

Chi-Square C
F-, t-Test F
t-Test (Welch) T

SUMMARY OF REPRODUCTION DATA

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Group (mg/kg)	- Cesarean Section Group -		Stat.
	0	30	
<u>Number of dams</u>			
with implantations (a)	14	14	Test
with viable fetuses (b)	14	14	

Weight of Live Fetuses

Individual Basis

total fetuses

n (fetuses)	137	133	
mean	3.65	3.65	F,T
st. dev.	0.242	0.343	

male fetuses

n (fetuses)	67	77	
mean	3.76	3.70	F,T
st. dev.	0.214	0.325	

female fetuses

n (fetuses)	70	56	
mean	3.54	3.57	F,T
st. dev.	0.215	0.355	

Placental Weight

Litter Basis

n (litters)	14	14	
mean	0.61	0.77***	F,T
st. dev.	0.056	0.089	

Placental Weight

Individual Basis

n (placentas)	137	133	
mean	0.60	0.74***	F,T
st. dev.	0.073	0.110	

*** p < 0.001

F-, t-Test F
t-Test (Welch) T

INDIVIDUAL ANIMAL DATA

Dam No. 4471 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1				X	1	3.10	0.56			
2			X		2	3.80	0.61			
3				X	3	3.54	0.54			
4			X		4	3.52	0.61			
5				X	5	3.02	0.46			
6			X		6	3.76	0.63			
7			X		7	3.82	0.72			
8				X	8	3.65	0.61			
9				X	9	3.38	0.70			
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{4}{9}$	$\frac{5}{9}$		$\frac{31.59}{9}$	$\frac{5.44}{9}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{0}{9}$
%	0	0	44	56				0	0	0
\bar{x}						3.51	0.60			
SD						0.29	0.08			

Uterus weight: 50 g

Corpora lutea (right/left): 6/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4474 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right				X	10	3.38	0.56			
2			X		11	3.90	0.69			
3			X		12	3.82	0.56			
4 left			X		13	3.58	0.61			
5				X	14	3.39	0.49			
6			X		15	3.77	0.64			
7			X		16	3.90	0.58			
8				X	17	3.66	0.56			
9				X	18	3.31	0.59			
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{5}{9}$	$\frac{4}{9}$		$\frac{32.71}{9}$	$\frac{5.28}{9}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{0}{9}$
%	0	0	56	44				0	0	0
\bar{x}						3.63	0.59			
SD						0.23	0.06			

Uterus weight: 51 g

Corpora lutea (right/left): 6/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4478 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1	right		X							
2			X		19	3.51	0.51			
3				X	20	3.65	0.62			
4				X	21	3.61	0.49			
5			X		22	3.89	0.62			
6				X	23	3.75	0.55			
7				X	24	3.85	0.56			
8			X		25	3.91	0.57			
9			X		26	3.77	0.55			
10	left		X		27	4.11	0.64			
11			X		28	3.73	0.54			
12			X		29	3.75	0.63			
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{1}{12}$	$\frac{0}{12}$	$\frac{7}{11}$	$\frac{4}{11}$		$\frac{41.53}{11}$	$\frac{6.28}{11}$	$\frac{0}{11}$	$\frac{0}{0}$	$\frac{0}{11}$
%	8	0	64	36				0	0	0
\bar{x}						3.78	0.57			
SD						0.16	0.05			

Uterus weight: 64 g

Corpora lutea (right/left): 9/ 3

INDIVIDUAL ANIMAL DATA

Dam No. 4485 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation			
	E	L	M	F				G	V	S	
1	left			X	48	3.77	0.75				
2				X	49	3.67	0.70				
3			X		50	3.52	0.70				
4		X									
5				X	51	3.70	0.72				
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
Total		$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$		$\frac{0}{5}$	$\frac{1}{5}$	$\frac{2}{4}$	$\frac{2}{4}$		$\frac{14.66}{4}$	$\frac{2.87}{4}$	$\frac{0}{4}$	$\frac{0}{0}$	$\frac{0}{4}$
%		0	20	50	50				0	0	0
\bar{x}							3.66	0.72			
SD							0.11	0.02			

Uterus weight: 25 g

Corpora lutea (right/left): 9/ 5

INDIVIDUAL ANIMAL DATA

Dam No. 4496 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1			X		52	4.18	0.73			
2			X		53	3.47	0.60			
3				X	54	3.69	0.68			
4			X		55	3.60	0.81			
5			X		56	3.74	0.62			
6				X	57	3.54	0.73			
7				X	58	3.56	0.63			
8			X		59	3.58	0.70			
9				X	60	3.84	0.59			
10			X		61	3.89	0.82			
11			X		62	3.66	0.64			
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{11}$	$\frac{0}{11}$	$\frac{7}{11}$	$\frac{4}{11}$		$\frac{40.75}{11}$	$\frac{7.55}{11}$	$\frac{0}{11}$	$\frac{0}{11}$	$\frac{0}{11}$
%	0	0	64	36				0	0	0
\bar{x}						3.70	0.69			
SD						0.20	0.08			

Uterus weight: 66 g

Corpora lutea (right/left): 4/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4500 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1				X	91	3.61	0.56			
2				X	92	3.58	0.59			
3		X								
4				X	93	3.50	0.58			
5			X		94	3.69	0.64			
6				X	95	3.61	0.60			
7				X	96	3.46	0.60			
8			X		97	3.77	0.59			
9			X		98	3.89	0.65			
10			X		99	3.61	0.57			
11			X		100	3.71	0.68			
12				X	101	3.45	0.59			
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{1}{12}$	$\frac{5}{11}$	$\frac{6}{11}$		$\frac{39.88}{11}$	$\frac{6.65}{11}$	$\frac{0}{11}$	$\frac{0}{11}$	$\frac{0}{11}$
%	0	8	45	55				0	0	0
\bar{x}						3.63	0.60			
SD						0.13	0.04			

Uterus weight: 62 g

Corpora lutea (right/left): 5/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4503 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1			X		113	3.78	0.65			
2			X		114	4.14	0.78			
3				X	115	3.46	0.53			
4			X		116	4.01	0.61			
5				X	117	3.86	0.63			
6			X		118	3.91	0.65			
7			X		119	4.24	0.66			
8				X	120	3.89	0.55			
9				X	121	3.59	0.68			
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{5}{9}$	$\frac{4}{9}$		$\frac{34.88}{9}$	$\frac{5.74}{9}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{0}{9}$
%	0	0	56	44				0	0	0
\bar{x}						3.88	0.64			
SD						0.25	0.07			

Uterus weight: 54 g

Corpora lutea (right/left): 5/ 8

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INDIVIDUAL ANIMAL DATA

Dam No. 4508 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		122	3.74	0.65			
2				X	123	3.70	0.62			
3				X	124	3.61	0.60			
4 left				X	125	3.78	0.55			
5				X	126	3.67	0.53			
6				X	127	3.55	0.56			
7				X	128	3.72	0.50			
8			X		129	3.68	0.52			
9				X	130	3.53	0.60			
10			X		131	3.83	0.56			
11				X	132	3.49	0.53			
12			X		133	3.69	0.61			
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{0}{12}$	$\frac{4}{12}$	$\frac{8}{12}$		$\frac{43.99}{12}$	$\frac{6.83}{12}$	$\frac{0}{12}$	$\frac{0}{12}$	$\frac{0}{12}$
%	0	0	33	67				0	0	0
\bar{x}						3.67	0.57			
SD						0.10	0.05			

Uterus weight: 67 g

Corpora lutea (right/left): 3/ 9

INDIVIDUAL ANIMAL DATA

Dam No. 4509 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right				X	134	3.55	0.60			
2			X		135	3.81	0.67			
3				X	136	3.79	0.58			
4 left				X	137	3.78	0.65			
5			X		138	3.75	0.64			
6				X	139	3.61	0.66			
7				X	140	3.63	0.58			
8			X		141	3.91	0.57			
9			X		142	3.06	0.64			
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{4}{9}$	$\frac{5}{9}$		$\frac{32.89}{9}$	$\frac{5.59}{9}$	$\frac{0}{9}$	$\frac{0}{9}$	$\frac{0}{9}$
%	0	0	44	56				0	0	0
\bar{x}						3.65	0.62			
SD						0.25	0.04			

Uterus weight: 51 g

Corpora lutea (right/left): 5/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4511 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1		X								
2				X	161	3.59	0.71			
3			X		162	4.01	0.74			
4			X		163	3.86	0.64			
5			X		164	3.89	0.67			
6			X		165	3.97	0.74			
7			X		166	3.96	0.60			
8			X		167	3.99	0.66			
9		X								
10			X		168	3.79	0.62			
11			X		169	3.86	0.59			
12				X	170	3.02	0.65			
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{2}{12}$	$\frac{8}{10}$	$\frac{2}{10}$		$\frac{37.94}{10}$	$\frac{6.62}{10}$	$\frac{0}{10}$	$\frac{0}{10}$	$\frac{0}{10}$
%	0	17	80	20				0	0	0
\bar{x}						3.79	0.66			
SD						0.30	0.05			

Uterus weight: 60 g

Corpora lutea (right/left): 5/ 7

INDIVIDUAL ANIMAL DATA

Dam No. 4515 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right				X	171	3.40	0.55			
2			X		172	3.68	0.51			
3		X								
4				X	173	3.67	0.50			
5				X	174	3.58	0.55			
6			X		175	3.28	0.45			
7 left				X	176	3.69	0.54			
8				X	177	3.45	0.47			
9				X	178	3.20	0.59			
10				X	179	3.24	0.52			
11				X	180	3.55	0.54			
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$	$\frac{0}{11}$	$\frac{1}{11}$	$\frac{2}{10}$	$\frac{8}{10}$		$\frac{34.74}{10}$	$\frac{5.22}{10}$	$\frac{0}{10}$	$\frac{0}{0}$	$\frac{0}{10}$
%	0	9	20	80				0	0	0
\bar{x}						3.47	0.52			
SD						0.19	0.04			

Uterus weight: 53 g

Corpora lutea (right/left): 7/ 5

INDIVIDUAL ANIMAL DATA

Dam No. 4517 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1				X	213	3.61	0.47			
2		X								
3				X	214	3.60	0.56			
4			X		215	4.02	0.58			
5			X		216	3.65	0.57			
6			X		217	3.96	0.59			
7				X	218	4.07	0.65			
8		X								
9				X	219	3.69	0.61			
10			X		220	3.80	0.71			
11			X		221	3.87	0.60			
12				X	222	3.57	0.51			
13			X		223	4.05	0.53			
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{13}$	$\frac{2}{13}$	$\frac{6}{11}$	$\frac{5}{11}$		$\frac{41.89}{11}$	$\frac{6.38}{11}$	$\frac{0}{11}$	$\frac{0}{0}$	$\frac{0}{11}$
%	0	15	55	45				0	0	0
\bar{x}						3.81	0.58			
SD						0.19	0.07			

Uterus weight: 63 g

Corpora lutea (right/left): 6/7

INDIVIDUAL ANIMAL DATA

Dam No. 4518 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		224	3.69	0.52			
2				X	225	3.66	0.51			
3			X		226	3.48	0.56			
4				X	227	3.62	0.53			
5			X		228	3.53	0.59			
6				X	229	3.05	0.50			
7 left			X		230	3.59	0.56			
8		X								
9				X	231	3.22	0.55			
10				X	232	3.44	0.45			
11				X	233	3.05	0.52			
12			X		234	3.52	0.57			
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{1}{12}$	$\frac{5}{11}$	$\frac{6}{11}$		$\frac{37.85}{11}$	$\frac{5.86}{11}$	$\frac{0}{11}$	$\frac{0}{11}$	$\frac{0}{11}$
%	0	8	45	55				0	0	0
X						3.44	0.53			
SD						0.23	0.04			

Uterus weight: 60 g

Corpora lutea (right/left): 7/ 6

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INDIVIDUAL ANIMAL DATA

Dam No. 4520 Group: Control

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placen- tal Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right		X								
2			X		235	3.31	0.54			
3				X	236	3.61	0.69			
4			X		237	3.80	0.59			
5				X	238	3.68	0.64			
6				X	239	3.35	0.62			
7 left			X		240	3.43	0.68			
8				X	241	3.41	0.58			
9				X	242	3.34	0.71			
10				X	243	3.24	0.60			
11				X	244	3.31	0.71			
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{11}$	$\frac{1}{11}$	$\frac{3}{10}$	$\frac{7}{10}$		$\frac{34.48}{10}$	$\frac{6.36}{10}$	$\frac{0}{10}$	$\frac{0}{0}$	$\frac{0}{10}$
%	0	9	30	70				0	0	0
\bar{x}						3.45	0.64			
SD						0.19	0.06			

Uterus weight: 54 g

Corpora lutea (right/left): 6/ 5

INDIVIDUAL ANIMAL DATA

Dam No. 4472 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation			
	E	L	M	F				G	V	S	
1	left			X	30	3.67	0.92			X	
2				X	31	3.92	0.97			X	
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
Total		$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$		$\frac{0}{2}$	$\frac{0}{2}$	$\frac{2}{2}$	$\frac{0}{2}$		$\frac{7.59}{2}$	$\frac{1.89}{2}$	$\frac{0}{2}$	$\frac{0}{0}$	$\frac{2}{2}$
%		0	0	100	0				0	0	100
\bar{x}							3.80	0.94			
SD							0.18	0.04			

Uterus weight: 15 g

Corpora lutea (right/left): 8/ 5

INDIVIDUAL ANIMAL DATA

Dam No. 4479 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		32	3.67	0.73			X
2			X		33	4.00	1.15			X
3			X		34	4.31	0.90			X
4			X		35	4.42	0.91			X
5 left			X		36	4.13	0.79			X
6				X	37	3.71	0.91			X
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$		$\frac{N1}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$		
	$\frac{0}{6}$	$\frac{0}{6}$	$\frac{5}{6}$	$\frac{1}{6}$		$\frac{24.24}{6}$	$\frac{5.39}{6}$	$\frac{0}{6}$	$\frac{0}{6}$	$\frac{6}{6}$
%	0	0	83	17				0	0	100
\bar{x}						4.04	0.90			
SD						0.31	0.14			

Uterus weight: 40 g

Corpora lutea (right/left): 4/ 8

INDIVIDUAL ANIMAL DATA

Dam No. 4483 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		38	3.77	0.56			X
2				X	39	3.79	0.59			X
3		X								
4		X								
5		X								
6				X	40	3.89	0.62	X		X
7				X	41	3.80	0.61			X
8 left			X		42	4.03	0.65			X
9			X		43	3.79	0.60	X		X
10				X	44	4.14	0.64			X
11				X	45	3.50	0.68			X
12			X		46	3.98	0.71			X
13				X	47	3.62	0.57	X		X
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{13}$	$\frac{3}{13}$	$\frac{4}{10}$	$\frac{6}{10}$		$\frac{38.31}{10}$	$\frac{6.23}{10}$	$\frac{3}{10}$	$\frac{0}{0}$	$\frac{10}{10}$
%	0	23	40	60				30	0	100
\bar{x}						3.83	0.62			
SD						0.19	0.05			

Uterus weight: 58 g

Corpora lutea (right/left): 8/ 6

INDIVIDUAL ANIMAL DATA

Dam No. 4490 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1				X	63	4.08	0.60			X
2			X		64	3.79	0.82			X
3		X								
4				X	65	4.35	1.00			X
5				X	66	4.31	0.83			X
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$		$\frac{N1}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{5}$	$\frac{1}{5}$	$\frac{1}{4}$	$\frac{3}{4}$		$\frac{16.53}{4}$	$\frac{3.25}{4}$	$\frac{0}{4}$	$\frac{0}{0}$	$\frac{4}{4}$
%	0	20	25	75				0	0	100
\bar{x}						4.13	0.81			
SD						0.26	0.16			

Uterus weight: 27 g

Corpora lutea (right/left): 7/ 4

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INDIVIDUAL ANIMAL DATA

Dam No. 4495 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso..		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		67	3.87	0.87			X
2			X		68	3.69	0.76			X
3				X	69	3.26	0.77			X
4			X		70	3.57	0.75			X
5				X	71	3.56	0.64			X
6				X	72	3.55	0.72			X
7			X		73	3.64	0.95			X
8 left			X		74	3.69	0.92			X
9			X		75	3.85	0.70			X
10				X	76	3.75	0.80			X
11			X		77	3.84	0.79			X
12			X		78	3.60	0.89			X
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N} \quad \frac{N2}{N}$		$\frac{N1}{N} \quad \frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N} \quad \frac{N2}{N} \quad \frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{0}{12}$	$\frac{8}{12}$	$\frac{4}{12}$		$\frac{43.87}{12}$	$\frac{9.56}{12}$	$\frac{0}{12}$	$\frac{0}{0}$	$\frac{12}{12}$
%	0	0	67	33				0	0	100
\bar{x}						3.66	0.80			
SD						0.17	0.09			

Uterus weight: 72 g

Corpora lutea (right/left): 7/ 6

INDIVIDUAL ANIMAL DATA

Dam No. 4497 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		79	4.08	0.84			X
2				X	80	3.58	0.81			X
3				X	81	3.75	0.87			X
4			X		82	3.69	0.74			X
5			X		83	4.03	0.79			X
6				X	84	3.70	0.73			X
7 left				X	85	3.56	0.64			X
8			X		86	3.98	0.67			X
9			X		87	4.10	0.87			X
10			X		88	3.58	0.70			X
11			X		89	3.17	0.71			X
12				X	90	3.16	0.80			X
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$		$\frac{N1}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{0}{12}$	$\frac{7}{12}$	$\frac{5}{12}$		$\frac{44.38}{12}$	$\frac{9.17}{12}$	$\frac{0}{12}$	$\frac{0}{12}$	$\frac{12}{12}$
X	0	0	58	42				0	0	100
X						3.70	0.76			
SD						0.32	0.08			

Uterus weight: 71 g

Corpora lutea (right/left): 6/ 6

INDIVIDUAL ANIMAL DATA

Dam No. 4499 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		102	3.74	0.69			X
2			X		103	4.09	0.66			X
3			X		104	4.01	0.69			X
4				X	105	3.69	0.70			X
5			X		106	4.03	0.65			X
6			X		107	3.39	0.83			X
7 left				X	108	3.41	0.77			X
8				X	109	3.55	0.82			X
9			X		110	3.99	0.86			X
10			X		111	3.65	0.82			X
11			X		112	3.65	0.85			X
12		X								
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$		$\frac{N1}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	0	1	8	3		$\frac{41.20}{11}$	$\frac{8.34}{11}$	0	0	11
%	0	8	73	27				0	0	100
\bar{x}						3.75	0.76			
SD						0.25	0.08			

Uterus weight: 66 g

Corpora lutea (right/left): 6/ 7

INDIVIDUAL ANIMAL DATA

Dam No. 4502 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1	right			X	143	3.52	0.83			X
2			X		144	3.82	0.90			X
3				X	145	3.49	0.77			X
4			X		146	3.91	0.71			X
5			X		147	3.70	0.71			X
6			X		148	4.09	0.72			X
7				X	149	3.68	0.78			X
8			X		150	3.60	0.84			X
9	left		X		151	3.96	0.63			X
10				X	152	3.35	0.72			X
11				X	153	3.54	0.68			X
12				X	154	3.51	0.75			X
13			X		155	3.78	0.96			X
14										
15										
16										
17										
18										
19										
20										
Total		$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$		$\frac{0}{13}$	$\frac{0}{13}$	$\frac{7}{13}$	$\frac{6}{13}$	$\frac{47.95}{13}$	$\frac{10.00}{13}$	$\frac{0}{13}$	$\frac{0}{13}$	$\frac{13}{13}$
%		0	0	54	46			0	0	100
\bar{x}						3.69	0.77			
SD						0.21	0.09			

Uterus weight: 79 g

Corpora lutea (right/left): 8/ 5

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INDIVIDUAL ANIMAL DATA

Dam No. 4507 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right	X									
2			X		156	3.75	0.80	X		X
3		X								
4			X		157	3.74	0.95			X
5 left		X								
6		X								
7		X								
8			X		158	3.85	0.69			X
9			X		159	3.88	0.75	X		X
10			X		160	3.59	0.89			X
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{1}{10}$	$\frac{4}{10}$	$\frac{5}{5}$	$\frac{0}{5}$		$\frac{18.81}{5}$	$\frac{4.08}{5}$	$\frac{2}{5}$	$\frac{0}{0}$	$\frac{5}{5}$
%	10	40	100	0				40	0	100
\bar{x}						3.76	0.82			
SD						0.11	0.10			

Uterus weight: 32 g

Corpora lutea (right/left): 5/ 6

INDIVIDUAL ANIMAL DATA

Dam No. 4512 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right		X								
2			X		181	3.82	0.89			X
3				X	182	3.26	0.70	X		X
4				X	183	3.75	0.79	X		X
5 left				X	184	3.59	0.78	X		X
6			X		185	3.69	0.70	X		X
7				X	186	2.98	0.69			X
8				X	187	3.37	0.66			X
9				X	188	3.57	0.78			X
10			X		189	3.85	0.71	X		X
11				X	190	3.31	0.62			X
12		X								
13										
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{12}$	$\frac{2}{12}$	$\frac{3}{10}$	$\frac{7}{10}$		$\frac{35.19}{10}$	$\frac{7.32}{10}$	$\frac{5}{10}$	$\frac{0}{0}$	$\frac{10}{10}$
%	0	17	30	70				50	0	100
\bar{x}						3.52	0.73			
SD						0.28	0.08			

Uterus weight: 57 g

Corpora lutea (right/left): 4/ 9

INDIVIDUAL ANIMAL DATA

Dam No. 4513 Group: 30 mg/kg

SXX 0665

T4039953

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right			X		191	3.60	0.62			X
2			X		192	3.64	0.60			X
3			X		193	3.73	0.68			X
4			X		194	3.67	0.62			X
5				X	195	3.81	0.71			X
6			X		196	3.75	0.83			X
7 left				X	197	3.87	0.76			X
8			X		198	4.12	0.59			X
9			X		199	3.84	0.60			X
10			X		200	3.82	0.71			X
11				X	201	3.55	0.60			X
12		X								
13				X	202	3.61	0.65			X
14										
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$ $\frac{N2}{N}$		$\frac{N1}{N}$ $\frac{N2}{N}$			$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$ $\frac{N2}{N}$ $\frac{N3}{N}$		
$\frac{\Sigma}{N}$	$\frac{0}{13}$	$\frac{1}{13}$	$\frac{8}{12}$	$\frac{4}{12}$		$\frac{45.01}{12}$	$\frac{7.97}{12}$	$\frac{0}{12}$	$\frac{0}{0}$	$\frac{12}{12}$
%	0	8	67	33				0	0	100
\bar{x}						3.75	0.66			
SD						0.16	0.08			

Uterus weight: 71 g

Corpora lutea (right/left): 6/ 7

INDIVIDUAL ANIMAL DATA

Dam No. 4516 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1	right			X	203	3.75	0.58			X
2				X	204	4.15	0.79			X
3			X		205	4.23	0.72			X
4				X	206	3.70	0.77			X
5				X	207	3.37	0.80			X
6			X		208	4.06	0.87			X
7	left		X		209	3.81	0.79			X
8				X	210	4.07	0.94			X
9				X	211	4.25	0.81			X
10				X	212	3.79	0.74			X
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total		$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$		$\frac{0}{10}$	$\frac{0}{10}$	$\frac{3}{10}$	$\frac{7}{10}$	$\frac{39.18}{10}$	$\frac{7.81}{10}$	$\frac{0}{10}$	$\frac{0}{10}$	$\frac{10}{10}$
%		0	0	30	70			0	0	100
\bar{x}						3.92	0.78			
SD						0.28	0.09			

Uterus weight: 63 g

Corpora lutea (right/left): 7/ 4

INDIVIDUAL ANIMAL DATA

Dam No. 4524 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation			
	E	L	M	F				G	V	S	
1	right			X	245	3.03	0.76			X	
2			X								
3			X		246	3.15	0.76			X	
4				X	247	2.96	0.70			X	
5			X		248	3.29	0.71			X	
6			X		249	3.45	0.71			X	
7				X	250	3.39	0.73			X	
8			X		251	3.11	0.65			X	
9	left		X		252	3.51	0.69			X	
10			X		253	3.34	0.74			X	
11				X	254	3.28	0.71			X	
12				X	255	3.20	0.61			X	
13				X	256	3.36	0.77			X	
14				X	257	2.83	0.80			X	
15											
16											
17											
18											
19											
20											
Total		$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$		$\frac{0}{14}$	$\frac{1}{14}$	$\frac{7}{13}$	$\frac{6}{13}$		$\frac{41.90}{13}$	$\frac{9.34}{13}$	$\frac{0}{13}$	$\frac{0}{0}$	$\frac{13}{13}$
%		0	7	54	46				0	0	100
\bar{x}							3.22	0.72			
SD							0.20	0.05			

Uterus weight: 72 g

Corpora lutea (right/left): 8/ 7

INDIVIDUAL ANIMAL DATA

Dam No. 4046 Group: 30 mg/kg

SXX 0665

T4039958

Impl. No.	Reso.		Sex		Fetus No.	Fetus Weight (g)	Placental Weight (g)	Malformation		
	E	L	M	F				G	V	S
1 right				X	258	3.11	0.62			X
2			X		259	2.95	0.65			X
3			X		260	2.96	0.52			X
4		X								
5			X		261	3.20	0.74			X
6			X		262	3.16	0.65			X
7			X		263	3.17	0.50			X
8			X		264	3.37	0.63			X
9 left				X	265	3.39	0.71			X
10				X	266	2.85	0.86			X
11			X		267	3.32	0.73			X
12			X		268	3.31	0.67			X
13				X	269	2.80	0.56			X
14			X		270	3.17	0.63			X
15										
16										
17										
18										
19										
20										
Total	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$		$\frac{\Sigma}{N}$	$\frac{\Sigma}{N}$	$\frac{N1}{N}$	$\frac{N2}{N}$	$\frac{N3}{N}$
$\frac{\Sigma}{N}$	$\frac{0}{14}$	$\frac{1}{14}$	$\frac{9}{13}$	$\frac{4}{13}$		$\frac{40.76}{13}$	$\frac{8.47}{13}$	$\frac{0}{13}$	$\frac{0}{0}$	$\frac{13}{13}$
%	0	7	69	31				0	0	100
\bar{x}						3.14	0.65			
SD						0.19	0.10			

Uterus weight: 69 g

Corpora lutea (right/left): 8/ 6

Früh-/Spätresorptionen
Early/Late resorptions

0 mg/kg		30 mg/kg	
No.	E/L	No.	E/L
4471	0/ 0	4472	0/ 0
4474	0/ 0	4479	0/ 0
4478	1/ 0	4483	0/ 3
4485	0/ 1	4490	0/ 1
4496	0/ 0	4495	0/ 0
4500	0/ 1	4497	0/ 0
4503	0/ 0	4499	0/ 1
4508	0/ 0	4502	0/ 0
4509	0/ 0	4507	1/ 4
4511	0/ 2	4512	0/ 2
4515	0/ 1	4513	0/ 1
4517	0/ 2	4516	0/ 0
4518	0/ 1	4524	0/ 1
4520	0/ 1	4046	0/ 1

Tote Feten werden als Spätresorptionen gewertet
Dead foetuses were counted as late resorptions

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Confidential

Dose: $\bar{0}$ mg/kg

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Dam no.: 4471

Type of retardation	Running no. of fetus								
	1	2	3	4	5	6	7	8	9
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded								
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification								
	Enlarged fontanel								
Hyoid bone missing									
Fourteenth rib (variation)	right								P
	p-punctiform s-shortened								
	k-comma-shape c-complete								P
left									

Dam no.: 4474

Type of retardation	Running no. of fetus									
	10	11	12	13	14	15	16	17	18	
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded									
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	right									
	p-punctiform s-shortened									
	k-comma-shape c-complete									
left										

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\bar{0}$ mg/kg

Dam no.: 4478		Running no. of fetus									
Type of retardation		19	20	21	22	23	24	25	26	27	
Sternum	Missing osseous centers										
	Slight cleft										
Spine	Vertebral body retarded	X	X	X		X		X		X	
	Vertebral arch retarded										
Ribs	Thirteenth rib retarded										
	Eminences										
Pelvis	Missing osseous centers										
	Metatarsals/metacarpals < 3										
Palate	Slight cleft										
Skull	Retarded ossification										
	Enlarged fontanel										
	Hyoid bone missing										
	Fourteenth rib (variation) right										
	p-punctiform s-shortened										
	k-comma-shape c-complete left										

Dam no.: 4478		Running no. of fetus									
Type of retardation		28	29								
Sternum	Missing osseous centers										
	Slight cleft										
Spine	Vertebral body retarded		X								
	Vertebral arch retarded										
Ribs	Thirteenth rib retarded										
	Eminences										
Pelvis	Missing osseous centers										
	Metatarsals/metacarpals < 3										
Palate	Slight cleft										
Skull	Retarded ossification										
	Enlarged fontanel										
	Hyoid bone missing		X								
	Fourteenth rib (variation) right										
	p-punctiform s-shortened										
	k-comma-shape c-complete left										

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: 0 mg/kg

Dam no.: 4485		Running no. of fetus							
Type of retardation		48	49	50	51				
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded								
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification		X						
	Enlarged fontanel			X					
Hyoid bone missing									
Fourteenth rib (variation)	p-punctiform								
	s-shortened								
	k-comma-shape								
	c-complete								
	right								
	left								

Dam no.: 4496		Running no. of fetus								
Type of retardation		52	53	54	55	56	57	58	59	60
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded					X				
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	p-punctiform									
	s-shortened									
	k-comma-shape									
	c-complete									
	right								P	
	left									

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\bar{0}$ mg/kg

Dam no.: 4496		Running no. of fetus							
Type of retardation		61	62						
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded								
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification	X							
	Enlarged fontanel								
Hyoid bone missing									
Fourteenth rib (variation)	p-punctiform								
	s-shortened								
	k-comma-shape								
	c-complete								
	right								
	left								

Dam no.: 4500		Running no. of fetus								
Type of retardation		91	92	93	94	95	96	97	98	99
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded					X			X	
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	p-punctiform									
	s-shortened									
	k-comma-shape									
	c-complete									
	right								P	
	left									

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: 0 mg/kg

Dam no.: 4500		Running no. of fetus							
Type of retardation		100	101						
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded	X	X						
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification								
	Enlarged fontanel								
Hyoid bone missing									
Fourteenth rib (variation)	p-punctiform								
	s-shortened								
	k-comma-shape								
	right		p						
	left		k						

Dam no.: 4503		Running no. of fetus								
Type of retardation		113	114	115	116	117	118	119	120	121
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded									
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	p-punctiform									
	s-shortened									
	k-comma-shape									
	right		p							
	left		p			p	p			

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Confidential

Dose: 0 mg/kg

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Dam no.: 4508

Type of retardation	Running no. of fetus									
	122	123	124	125	126	127	128	129	130	
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded									
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	right									
	p-punctiform	s-shortened								
	k-comma-shape	c-complete	left	p	p	p				

Dam no.: 4508

Type of retardation	Running no. of fetus									
	131	132	133							
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded									
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	right									
	p-punctiform	s-shortened								
	k-comma-shape	c-complete	left	p						

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\bar{0}$ mg/kg

Dam no.: 4509		Running no. of fetus								
Type of retardation		134	135	136	137	138	139	140	141	142
Sternum	Missing osseous centers									X
	Slight cleft									
Spine	Vertebral body retarded		X		X	X		X		
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences					X				
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										X
Palate	Slight cleft									
Skull	Retarded ossification	X			X		X	X	X	X
	Enlarged fontanel									
Hyoid bone missing		X			X			X	X	X
Fourteenth rib (variation)										
p-punctiform s-shortened										
k-comma-shape c-complete										

Dam no.: 4511		Running no. of fetus								
Type of retardation		161	162	163	164	165	166	167	168	169
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded		X			X		X	X	
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing					X				X	
Fourteenth rib (variation)										
p-punctiform s-shortened										
k-comma-shape c-complete										

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: 0 mg/kg

Dam no.: 4511

Type of retardation		Running no. of fetus								
		170								
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded									
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification	X								
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)										
p-punctiform	s-shortened	right								
k-comma-shape	c-complete	left								

Dam no.: 4515

Type of retardation		Running no. of fetus								
		171	172	173	174	175	176	177	178	179
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded								X	
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)										
p-punctiform	s-shortened	right			P					
k-comma-shape	c-complete	left							P	

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\frac{0}{0}$ mg/kg

Dam no.: 4515		Running no. of fetus							
Type of retardation		180							
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded								
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification								
	Enlarged fontanel								
Hyoid bone missing									
Fourteenth rib (variation)	p-punctiform s-shortened right	p							
	k-comma-shape c-complete left								

Dam no.: 4517		Running no. of fetus								
Type of retardation		213	214	215	216	217	218	219	220	221
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded	X							X	
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences									
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification									
	Enlarged fontanel									
Hyoid bone missing						X				
Fourteenth rib (variation)	p-punctiform s-shortened right				k					
	k-comma-shape c-complete left				k					P

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\bar{0}$ mg/kg

Type of retardation		Running no. of fetus									
		222	223								
Sternum	Missing osseous centers										
	Slight cleft										
Spine	Vertebral body retarded										
	Vertebral arch retarded										
Ribs	Thirteenth rib retarded										
	Eminences										
Pelvis	Missing osseous centers										
Metatarsals/metacarpals < 3											
Palate	Slight cleft										
Skull	Retarded ossification										
	Enlarged fontanel										
Hyoid bone missing											
Fourteenth rib (variation)	right	k									
	p-punctiform	s-shortened									
	k-comma-shape	c-complete	c								
	left										

Type of retardation		Running no. of fetus									
		224	225	226	227	228	229	230	231	232	
Sternum	Missing osseous centers										
	Slight cleft										
Spine	Vertebral body retarded			X		X	X				X
	Vertebral arch retarded										
Ribs	Thirteenth rib retarded										
	Eminences										
Pelvis	Missing osseous centers										
Metatarsals/metacarpals < 3											
Palate	Slight cleft										
Skull	Retarded ossification										
	Enlarged fontanel							X			
Hyoid bone missing		X		X							
Fourteenth rib (variation)	right										
	p-punctiform	s-shortened									
	k-comma-shape	c-complete									
	left										

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\bar{0}$ mg/kg

Type of retardation		Running no. of fetus							
		233	234						
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded	X							
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification	X	X						
	Enlarged fontanel								
Hyoid bone missing		X	X						
Fourteenth rib (variation)	p-punctiform								
	s-shortened								
	k-comma-shape								
	c-complete								

Type of retardation		Running no. of fetus								
		235	236	237	238	239	240	241	242	243
Sternum	Missing osseous centers									
	Slight cleft									
Spine	Vertebral body retarded	X								
	Vertebral arch retarded									
Ribs	Thirteenth rib retarded									
	Eminences						X			
Pelvis	Missing osseous centers									
Metatarsals/metacarpals < 3										
Palate	Slight cleft									
Skull	Retarded ossification		X				X			
	Enlarged fontanel									
Hyoid bone missing										
Fourteenth rib (variation)	p-punctiform				P					
	s-shortened									
	k-comma-shape				k		P		P	
	c-complete									

X = Type of retardation observed

Individual assessment of fetuses exhibiting osseous retardations;
incidence of fourteenth rib (variation)

Dose: $\frac{0}{0}$ mg/kg

Dam no.: 4520		Running no. of fetus							
Type of retardation		244							
Sternum	Missing osseous centers								
	Slight cleft								
Spine	Vertebral body retarded								
	Vertebral arch retarded								
Ribs	Thirteenth rib retarded								
	Eminences								
Pelvis	Missing osseous centers								
Metatarsals/metacarpals < 3									
Palate	Slight cleft								
Skull	Retarded ossification								
	Enlarged fontanel								
Hyoid bone missing									
Fourteenth rib (variation)	p-punctiform	right							
	k-comma-shape	left							
	e-shortened								
	c-complete								

X = Type of retardation observed