8EHQ-0699-14492

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS:

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Clearly mark the confidential information with bracketing and check the box in the appropriate section (☐ *Contains CBI*). Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

1.0 SUBMISSION TYPE - *Contains CBI*

☐ 8(d) **X 8(e)** ☐ FYI ☐ 4 ☐ OTHER: Specify_____

- Intial Submission XX -Follow-up Submission ☐ Final Report Submission

Previous EPA Submission Number or Title if update or follow-up:

Supplementary to the enclosed Submission with Tracking Number 99-2-44 Docket Number, if any: #

☐ continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED
(may be required for 8(e): optional for §4, 8(d) & FYI)
X - YES ☐ NO

2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID
Cert# P 917006915
99-2-45

2.3 FOR EPA USE ONLY

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY -*Contains CBI*

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS#: 120983-64-4 2-(1-Chlorcyclopropyl)-1-(2-chlorphenyl) = -3-(1,2,4-triazol-1-yl)-propan-2-ol

Purity _____%

☐ - Single Ingredient

☐ Commerical/Tech Grade

☐-Mixture *Trade Name:* SXX 0665 *Common Name:* ___

CONTAINS NO CBI

4.0 REPORT/STUDY TITLE - *Contains CBI*

Supplementary Study to the Embryotoxicity Study (including Teratogenicity) with SXX 0665 Technical in the Rat, Part 1
RCC Project # 281518, Report # R5437

☐ Continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE): X ENVIRONMENTAL EFFECTS (EE):_____ ENVIRONMENTAL FATE (EF):_____

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY TYPE: TOX *Other:* ___ SUBJECT ORGANISM (HE, EE only): RATS Other: ___ ROUTE OF EXPOSURE (HE only): ___ *Other:* ___ VEHICLE OF EXPOSURE (HEonly) ___ *Other:* ___

6.0 REPORT/STUDY INFORMATION ☐ *Contains CBI* ☐ Study is GLP

Laboratory RCC Research & Consulting Company AG Report/Study Date: 12/6/91

Source of Data/Study Sponsor (if different than submitter) Bayer AG Number of pages : 193

☐ continuation sheet attached

7.0 SUBMITTER INFORMATION ☐ *Contains CBI*

Submitter: Donald W. Lamb, Ph.D Title: V. P., Prod. Safety & Reg. Affrs Phone: 412-777-7431

Company Name: Bayer Corporation Company Address: 100 Bayer Road

Pittsburgh, PA 15205-9741 Submitter Address (if different): ___

Technical Contact: Donald W. Lamb, Ph.D Phone: (412)777-7431

☐ continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS ☐ *Contains CBI*

SXX 0665 is a metabolite of toxicological concern for a compound (JAU 6476) which is under development as a fungicide.

☐ continuation sheet attached

RECEIVED OPPT NCIC 1999 JUN 30 AM 11:53

RECEIVED OPPT NCIC 99 JUL 29 AM 8:20

Submitter Signature: Donald W. Lamb **Date:** 6/23/99

8EHQ-99-14492

88990000211

9.0 CONTINUATION SHEET

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P917006915
99-2-45

CONTINUED FROM COVER SHEET SECTION #____2.1_____

TSCA 8(e) Evaluation

SXX 0665 is a compound which was under development as a potential fungicide, but development of this compound was ceased due to the toxicity profile of the compound. A related fungicide, JAU 6476 is presently under development, and it has been shown that JAU 6476 breaks down to SXX 0665, upon drying, after application to plants/seeds, and upon administration to test animals. (Note: The extent of breakdown varies considerably based on the plant/seed to which JAU 6476 is applied). However, as JAU 6476 has fungicide properties, and the development of JAU 6476 as a fungicide is not based on the conversion of JAU 6476 to SXX 0665, JAU 6476 is not considered to be a delivery system for applying SXX 0665 to plants/seeds. Therefore, although SXX 0665 does have fungicide activity and may be of toxicological concern for evaluating risk assessment and in determining RFD values for JAU 6476, SXX 0665 is strictly a metabolite of JAU 6476 and is not a compound which is being developed for commercial use. Thus, SXX 0665 is not regulated by TSCA 8(e) Adverse Effects Regulations. However, as SXX 0665 is a metabolite of toxicological concern, this report is being submitted as a supplementary developmental toxicity study to previously reported study with I.D. # 99-2-44 (6/23/99).

Abstract

The purpose of this supplementary study was to assess the effects of SXX 0665 on embryonic and fetal development in pregnant Wistar/HAN rats at lower dosages than in the previous study, in order to establish a NOAEL.

Each group consisted of 25 mated female rats. SXX 0665 was administered by gavage once daily from day 6 through to day 15 post coitus, at dose levels of:

Group 1: 0 mg/kg body weight/day
(vehicle control)
Group 2: 1 mg/kg body weight/day
Group 3: 3 mg/kg body weight/day

The dosages were based on the results of the previous study (RCC Project 236114) in which an increased incidence of supernumerary ribs was observed at 10 mg/kg body weight/day. A standard dose volume of 10 ml/kg body weight, with a daily adjustment to the actual body weight, was used. Control animals were dosed with the vehicle alone (bi-distilled water with 0.5 % Cremophor EL).

Females were sacrificed on day 21 post coitus and the fetuses were removed by Caesarean section. The examination of the dams and fetuses was performed in accordance with international recommendations.

CONTINUED FROM COVER SHEET SECTION #____2.1_____

The following results were obtained:

GENERAL TOLERABILITY IN DAMS

- There were no signs of reaction to treatment, no deaths during the study and no treatment-related macroscopic changes at terminal necropsy.

- Both food consumption and body weight gain of the dams were similar in all groups.

REPRODUCTION PARAMETERS OF THE DAMS

- None of the maternal reproduction parameters - overall pregnancy rate, total litter loss, pre- and post-implantation loss, number of implantations, and number of live fetuses - were adversely affected by the administration of SXX 0665.

FETAL PARAMETERS

- There was no evidence of an effect of the administration of SXX 0665 to the dams on the fetal parameters - fetal sex ratios, mean fetal body weights, or the incidences of abnormal findings observed during external, visceral or skeletal examination.

- At both 1 and 3 mg/kg, the incidences of skeletal variants, indicative of the stage of skeletal development, were generally lower than the concurrent Control values, but at 3 mg/kg, there was an increased incidence of fetuses with supernumerary ribs. Differences from the concurrent Control values attained statistical significance, but the incidences were comparable to Control incidences in the first study (RCC Project 236114).

CONCLUSION

In this supplementary study, SXX 0665 was administered orally, by gavage, to mated Wistar/HAN rats at dosages of 0, 1, or 3 mg/kg body weight/day from day 6 through to day 15 post coitus in order to determine a NOAEL for effects on embryonic/fetal development.

On the basis of the results obtained in this supplementary study, there were no adverse effects from the administration of SXX 0665 to the dams on any of the maternal parameters or on any of the fetal parameters up to and including 3 mg/kg body weight/day. An increased incidence of fetuses with supernumerary ribs at 3 mg/kg body weight/day was considered to be incidental, as the values obtained were comparable to Control incidences in the first study (RCC Project 236114).

SUPPLEMENTAL SUBMISSION TO AC NO. 108979

STUDY TITLE

Supplementary Study to the
Embryotoxicity Study (Including Teratogenicity)
with SXX 0665 Technical in the Rat
Report: Part I

DATA REQUIREMENT

108979-1

US EPA-FIFRA Guideline No. 83-3(a)

AUTHORS

Dr. H. Becker and Dr. K. Biedermann

FILE
8836

STUDY COMPLETION DATE

Original Report: December 11, 1991
Supplemental Report: December 6, 1991

99-2-45

PERFORMING LABORATORY

RCC
Research and Consulting Company AG
P. O. Box CH 4452 Itingen
Switzerland

SPONSOR

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

LABORATORY PROJECT ID

RCC Project No. 281518
Bayer AG Report No. R 5437

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: 4-21-99

GOOD LABORATORY PRACTICE STATEMENT

PROJECT NUMBER: 281518

TEST ARTICLE: SXX 0665 TECHNICAL

STUDY DIRECTOR: H. Becker

TITLE: Supplementary Study to the Embryotoxicity Study (Including Teratogenicity) in the Rat

This study conforms to the OECD Principles of Good Laboratory Practice (GLP), the Good Laboratory Practice Guidelines for Switzerland 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, Switzerland and FIFRA with regard to the authority granted Agency inspectors and certain record retention requirements.

Submitter: Bayer Corporation

Dr. J.H. Thyssen

.....

Date: 4-21-99

Study Director: H. Becker

.....

date: December 6, 1991

Sponsor: Bayer AG

Dr. L. Machemer

.....

date: Dec. 12, 1991

RCC PROJECT 281518
SXX 0665 TECHNICAL

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 83-3.

SUBMITTER

BAYER CORPORATION

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

Date: 4-21-99

SPONSOR

AGRICULTURE DIVISION

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

Date: 4-21-99

CONTENTS REPORT PART I

	PAGE
QUALITY ASSURANCE UNIT STATEMENT	7
PROJECT STAFF	8
PREFACE	9
GUIDELINES	10
SUMMARY	11
CONCLUSION	12
OBJECTIVE	13
MATERIALS AND METHODS	
Experimental Design	
Test System	13
Husbandry	14
Test Article	14
Procedures, Observations, Data Recording and Compilation	15
Data Processing	18
Terminology used in the Assessment of the Data	19
Statistical Methods	19
Archiving	20
RESULTS	21
FIGURES AND TABLES	
Food Consumption of Dams post coitum - Figure	25
Food Consumption of Dams post coitum - Tables	26
Differences in Food Consumption of Dams, Mean	29
Body Weights of Dams post coitum - Figure	30
Body Weights of Dams post coitum - Tables	31
Corrected Body Weight Gain of Dams	36
Differences in Body Weight Gain of Dams, Mean	39
Reproduction Data Summary	40
Reproduction Data (per Dam and Group)	42

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CONTENTS REPORT PART I (cont'd)

	PAGE
External Examination of Fetuses	45
Visceral Examination of Fetuses (Wilson Technique)	45
Skeletal Examination of Fetuses (Abnormal Findings)	46
Skeletal Examination of Fetuses (Stage of Development)	
- Summary on a Litter Basis	47
- Summary on a Fetus Basis	49
Body Weights of Live Fetuses - Summary per Dam	51
Distribution within Uterus: Implantations, Live Fetuses and Resorptions (plan view)	54
Contents of Uterus (plan view)	57
Mating/Necropsy Schedule and Individual Necropsy Findings	70
ATTACHMENTS	
Water Analyses - Bacteriological and Chemical Assays	74
Contaminant Analyses of Feed	77
Report of Determination of the Concentrations, the Homogeneity and Stability of SXX 0665 TECHNICAL in Bi-Distilled Water with 0.5 % CREMOPHOR EL	79
Historical Control Data and Spontaneous Abnormal Findings of Wistar Rats (SPF Quality) from 1987, 1988 and 1989	91

CONTENTS REPORT PART II

SKELETAL EXAMINATION OF FETUSES - INDIVIDUAL DATA	114

RCC PROJECT 281518
SXX 0665 TECHNICAL

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QUALITY ASSURANCE UNIT

R C C REGISTRATION & CONSULTING COMPANY AG
CH 4452 ITINGEN/SWITZERLAND

S T A T E M E N T

PROJECT NUMBER: 281518

TEST ARTICLE: SXX 0665 TECHNICAL

STUDY DIRECTOR: H. Becker

TITLE: Supplementary study to the embryotoxicity study (including teratogenicity) in the rat.

The conduct of this study was subjected to periodic inspections and the report audited by the Quality Assurance Unit. The dates are given below.

Dates of QAU Inspections / Audits	Dates of Reports to the Study Director and to Management
29.08.1990	29.08.1990
05.09.1990	05.09.1990
18.09.1990	18.09.1990
28.09.1990	28.09.1990
18.-20.11.1991	20.11.1991

Manager, Quality Assurance Unit K. Schneider

i.A. C. Arbeiter

Date: December 10, 1991

RCC PROJECT 281518
SXX 0665 TECHNICAL

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PROJECT STAFF

STUDY DIRECTOR H. Becker

.....
date: December 6, 1991

TECHNICAL COORDINATOR D. Frei

.....
date: May 22, 1991

ANALYTICAL CHEMISTRY K. Biedermann

.....
date: May 22, 1991

EDP AND STATISTICS Ch. Terrier

.....
date: May 22, 1991

MANAGING DIRECTOR Dr. K. Sachsse

.....
date: May 22, 1991

PREFACE

GENERAL

Title	Supplementary study to the embryotoxicity study (including teratogenicity) with SXX 0665 TECHNICAL in the rat
Sponsor	BAYER AG Institut für Toxikologie Landwirtschaft Friedrich-Ebert-Strasse 217 D-W-5600 Wuppertal 1
Study Monitor	Dr. B. Holzum
Testing Facilities	RCC, Research & Consulting Company AG and RCC Umweltchemie AG CH 4452 Itingen / Switzerland
RCC Project Number BAYER Project Number	281518 T 9034679
Test Article	SXX 0665 TECHNICAL
Test System	Rat

PROJECT STAFF

Study Director	H. Becker
Technical Coordinator	D. Frei
Analytical Chemistry	K. Biedermann
EDP and Statistics	TEC, Terrier EDV Consulting AG Hofackerstrasse 55 CH 4132 Muttenz / Switzerland

SCHEDULE

Delivery	August 24, 1990
Initiation (pairing)	September 5, 1990
Termination (last necropsy)	October 1, 1990

GUIDELINES

This study was conducted in compliance with:

Good Laboratory Practice (GLP) in Switzerland, Procedures and Principles. March 1986.

OECD Principles of Good Laboratory Practice, Paris, 1981.

Environmental Protection Agency; Good Laboratory Practice Standards; Final Rule, U.S.A. Federal Register, Vol. 48, No. 158, August 17, 1989.

"Teratogenicity", OECD Guidelines for the Testing of Chemicals, Section 4, Health Effects, No. 414, May 12, 1981.

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines - Subdivison F, Hazard Evaluation: Humans and Domestic Animals, Series 83-3 (Teratogenicity Study), revised edition, November 1984.

SUMMARY

The purpose of this supplementary study was to assess the effects of SXX 0665 TECHNICAL on embryonic and fetal development in pregnant Wistar/HAN rats at lower dosages than in the previous study in order to establish a NOAEL.

Each group consisted of 25 mated female rats. SXX 0665 TECHNICAL was administered orally by gavage once daily from day 6 through to day 15 post coitum, at dose levels of:

Group 1:	0 mg/kg body weight/day (vehicle control)
Group 2:	1 mg/kg body weight/day
Group 3:	3 mg/kg body weight/day

The dosages were based on the results of the previous study (RCC Project 236114) in which an increased incidence of supernumerary ribs was observed at 10 mg/kg body weight/day. A standard dose volume of 10 ml/kg body weight with a daily adjustment to the actual body weight was used. Control animals were dosed with the vehicle alone (bi-distilled water with 0.5 % Cremophor EL).

Females were sacrificed on day 21 post coitum and the fetuses were removed by Caesarean section. The examination of the dams and fetuses was performed in accordance with international recommendations.

The following results were obtained:

GENERAL TOLERABILITY IN DAMS

- There were no signs of reaction to treatment, no deaths during the study and no treatment-related macroscopic changes at terminal necropsy.
- Both food consumption and body weight gain of the dams were similar in all groups.

REPRODUCTION PARAMETERS OF THE DAMS

- None of the maternal reproduction parameters - overall pregnancy rate, total litter loss, pre- and post-implantation loss, number of implantations and number of live fetuses - were adversely affected by the administration of SXX 0665 TECHNICAL.

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SUMMARY (CONT')

FETAL PARAMETERS

- There was no evidence of an effect of the administration of SXX 0665 TECHNICAL to the dams on the fetal parameters - fetal sex ratios, mean fetal body weights or the incidences of abnormal findings observed during external, visceral or skeletal examination.

- At both 1 and 3 mg/kg, the incidences of skeletal variants indicative of the stage of skeletal development were generally lower than the concurrent Control values but at 3 mg/kg, there was an increased incidence of fetuses with supernumerary ribs. Differences from the concurrent Control values attained statistical significance but the incidences were comparable to Control incidences in the first study (RCC Project 236114).

CONCLUSION

In this supplementary study, SXX 0665 TECHNICAL was administered orally, by gavage, to mated Wistar/HAN rats at dosages of 0, 1 or 3 mg/kg body weight/day from day 6 through to day 15 post coitum in order to determine a NOAEL for effects on embryonic/fetal development.

On the basis of the results obtained in this supplementary study, there were no adverse effects of the administration of SXX 0665 TECHNICAL to the dams on any of the maternal parameters or on any of the fetal parameters up to and including 3 mg/kg body weight/day. An increased incidence of fetuses with supernumerary ribs at 3 mg/kg body weight/day was considered to be incidental as the values obtained were comparable to Control incidences in the first study (RCC Project 236114).

OBJECTIVE

PURPOSE —

The purpose of this study was to assess the effects of SXX 0665 TECHNICAL on embryonic and fetal development when administered orally by gavage once daily to mated female rats from day 6 through to day 15 post coitum.

This study should provide a rational basis for risk assessment in man.

MATERIALS AND METHODS

Experimental Design

TEST SYSTEM

Species	Wistar/HAN Rats (WIST, Outbred, SPF Quality)
Rationale	Specified by the international guidelines as a recommended test system
Source	BRL, Biological Research Laboratories Ltd. Wölferweg 4 CH 4414 Füllinsdorf / Switzerland
Acclimatization	7 days (minimum) prior to pairing, under test conditions, after veterinary examination
Number of animals	75 mated females, 25 per group
Age at pairing	11 weeks, minimum
Body weights (day 0 post coitum)	182 - 227 grams
Identification (day 0 post coitum)	Individual cage/animal number tattooed on the pinnae

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HUSBANDRY

Room Number: 128

Conditions

The animals were housed under standard laboratory conditions: air-conditioned with 10-15 air changes per hour; the environment monitored continuously with hourly recordings of temperature (range 22 +/- 3 degrees Centigrade) and relative humidity (range 40 - 70 %); 12 hours artificial fluorescent light/12 hours dark with background music (Schweizerischer Telefonrundspruch) played at a centrally defined low volume for at least 8 hours during the light period.

Accommodation

The animals were housed individually in Makrolon cages (type-3) with wire mesh tops and standardised granulated softwood bedding (Lignocel, Schill AG, CH 4132 Muttenz / Switzerland).

Diet

Pelleted standard Kliba 343 rat/mouse maintenance diet ("Kliba", Klingentalmuehle AG, CH 4303 Kaiseraugst/Switzerland) was available ad libitum (Batch no. 73/90). Results of analyses for contaminants are attached (pp. 77-78).

Water

Tap water was available ad libitum. Results of bacteriological, chemical and contaminant analyses are scheduled to be conducted at least once yearly by RCC (contaminant analyses only) and by the Official Chemist of the Kanton Basel-Landschaft (bacteriological and chemical analyses). Results are attached (pp. 74-76).

TEST ARTICLE

Identity	SXX 0665 TECHNICAL
Batch number	17005/89
Description	Light beige powder
Purity	94.7 % (according to analysis dated 13.6.90)
Storage	At room temperature, in the dark
Stability of the pure test article	December 13, 1990
Stability in the vehicle (bi-distilled water with 0.5 % Cremophor EL)	Stable for at least 2 hours
Safety precautions	Goggles and gloves

PROCEDURES, OBSERVATIONS, DATA RECORDING AND COMPILATION

PROCEDURES

MATING

After acclimatization, the females were paired overnight with sexually mature males, in the ratio of 1 male: 1 female. The day on which spermatozoa were found in the vaginal smear or a vaginal plug was observed was designated day 0 post coitum.

ALLOCATION OF MATED FEMALES TO THE TEST GROUPS

Group	Female Numbers	Dose* mg/kg body weight
1	1 - 25	0 (vehicle control)**
2	26 - 50	1
3	51 - 75	3

* = Dose levels were proposed by the Sponsor, based on the results of the previous study (RCC Project 236114) in which an increased incidence of supernumerary ribs was observed at 10 mg/kg body weight/day.
** = The vehicle control group was used also for RCC Project 281507 with the test article KWG 4168, which was running parallel for the same Sponsor.

METHOD OF ALLOCATION

Mated rats were assigned to the different groups using a computer-generated random algorithm.

ADMINISTRATION

The test article was administered orally, by gavage, once daily in the morning from day 6 through to day 15 post coitum. All groups received a dose volume of 10 ml/kg body weight, with a daily adjustment of the individual volume to the actual body weight. Control animals were similarly dosed with the vehicle alone.

RATIONALE

International guidelines recognize the efficacy of oral administration.

VEHICLE AND CONTROL ARTICLE

Bi-distilled water with 0.5 % Cremophor EL (BASF) was used as the vehicle for the test article in the dose groups and was administered as the control article to the females of the Control group.

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PREPARATION OF THE TEST ARTICLE/VEHICLE MIXTURES

The mixtures of the test article and vehicle were prepared daily before administration. SXX 0665 TECHNICAL was weighed into a glass beaker on a tared precision balance (Mettler PE 360) and the vehicle added (w/v). The mixtures were prepared using a homogenizer. During the daily administration period, homogeneity was maintained using a magnetic stirrer.

ANALYSES OF THE TEST ARTICLE/VEHICLE MIXTURES

Concentration, homogeneity and stability of the test article/vehicle mixtures were determined on one occasion during the dosing period of the study. Samples were taken immediately after preparation and again 2 hours later. Analyses were performed by the RCC Analytical Chemistry Laboratory using a method supplied by the Sponsor. Results of the analyses are attached (pp. 79 - 90).

OBSERVATIONS

MORTALITY RATE

The animals were checked at least twice daily for any mortalities.

Any female sacrificed or found dead during the study would have been subjected to macroscopic examination, with emphasis on the uterus and its contents. Specimens of abnormal tissue would have been fixed in neutral phosphate buffered 4 % formaldehyde solution.

SIGNS AND/OR SYMPTOMS

The animals were observed at least twice daily for signs of reaction to treatment and/or symptoms of ill health.

DATA RECORDING

FOOD CONSUMPTION

Food consumption was recorded on days 6, 11, 16 and 21 post coitum (see Data Compilation, next page / Data Processing, p. 18).

BODY WEIGHTS

Body weights were recorded daily from day 0 until day 21 post coitum (see Data Compilation, next page / Data Processing, p. 18).

TERMINATION OF THE STUDY

On day 21 post coitum, the females were killed by CO_2 asphyxiation and the fetuses were removed by Caesarean section.

CAESAREAN SECTION AND POST MORTEM EXAMINATION

Post mortem examination, including gross macroscopic examination of all internal organs, with emphasis on the uterus, uterine contents, position of fetuses in the uterus and number of corpora lutea, was performed and the data recorded. The fetuses were removed from the uterus, sexed, weighed individually, examined for gross external abnormalities and allocated to one of the following procedures:

1) Wilsons's slicing technique* for examination of the viscera and brain. One half of the live fetuses from each litter was fixed in a mixture of ethyl alcohol, formol and acetic acid. After examination, the sections were preserved in a solution of ethyl alcohol and glycerine (one fetus per container). Descriptions of any abnormalities were recorded.

2) The remaining fetuses were placed in a solution of potassium hydroxide for clearing and stained with alizarin red S (modified technique**). The skeletons were examined and all abnormalities were recorded. The specimens were preserved individually in plastic bags.

The uteri (and contents) of all females with live fetuses were weighed at necropsy on day 21 post coitum to enable the calculation of the corrected body weight gain (see Data Compilation / Processing, next page).

If no implantation sites were evident, the uterus was placed in an aqueous solution of ammonium sulfide*** to accentuate possible haemorrhagic areas of implantation sites.

All tissues and organs except fetuses removed from animals killed at scheduled necropsy were discarded.

Fetuses with abnormal findings were photographed.

DATA COMPILATION

Food consumption, body weight and Caesarean section data were recorded on-line and compiled by computer. Individual skeletal examination of fetuses data were recorded on data sheets, transferred to and compiled by computer.

All other data were recorded on data sheets and compiled manually.

Only externally malformed fetuses are included in the summary tables of reproduction data and in the tables of contents of uterus, because the data for these tables are recorded on-line during Caesarean section.

---

* = Wilson, J.G. (1965) in: Teratology, Principles and Techniques: J.G. Wilson and J. Warkany, Eds., The University of Chicago Press, Chicago and London, pp. 265-277.
** = Dawson, A.B. (1926) Stain Techniques 1, pp. 123-124
*** = Salewski, E. (1964) Arch. Exp. Path. Pharmak. 247, pp. 367-368.

DATA PROCESSING

Mean daily food consumption was calculated using the following formula:

$$\frac{\text{grams of food consumed per period}}{\text{days per period}} = \text{mean daily food consumption}$$

Body weight gains from days 0-6 p.c., 6-11 p.c., 11-16 p.c., 6-16 p.c., 16-21 p.c. and 6-21 p.c. were calculated.

Corrected body weight gain was calculated using the formula:

body weight on day 21 post coitum
- body weight on day 6 post coitum
- uterus weight at necropsy on day 21 post coitum

= corrected body weight gain.

For evaluation of the reproduction data, the following formulae were used:

- pre-implantation loss (%):

$$\frac{\text{number of corpora lutea} - \text{number of implantations}}{\text{number of corpora lutea}} \times 100$$

- post-implantation loss (%):

$$\frac{\text{number of implantations} - \text{number of live fetuses}}{\text{number of implantations}} \times 100$$

- sex ratio of males/females (%):

$$\frac{\text{number of males/females}}{\text{number of fetuses}} \times 100$$

For the reproduction data, group mean values were calculated both on a per dam basis and on a percentage per group basis. Only dams with live fetuses on day 21 post coitum were included in the calculations.

Mean fetal weights were calculated from the individual fetal weights both on a per group and on a per litter basis.

Computer-generated values in the tables represent the rounded-off results of calculations which used the exact raw data values.

TERMINOLOGY USED IN THE ASSESSMENT OF THE DATA

Empty implantation site	- very early resorption or aborted implantation
Embryonic resorption	- amorphous mass being resorbed
Fetal resorption	- clearly defined fetal body being resorbed
Dead fetus	- appearance of live fetus but without respiration or movement
Live fetus	- breathing and/or moving fetus
Runt	- small fetus <2.5 grams (weight of a normally developed fetus, mean over several years: 4.6 - 5.0 grams)
Abnormal finding	- malformation and/or anomaly
Skeletal variant	- variations in the number of ribs and degree of ossification of phalangeal nuclei and/or sternebrae

STATISTICAL METHODS

The following statistical methods were used to analyze body weights, food consumption, reproduction and skeletal examination data:

Univariate one-way analysis of variance was used to assess the significance of intergroup differences.

If the variables could be assumed to follow a normal distribution, the Dunnett-test (many-one t-test), based on a pooled variance estimate, was applied for the comparison between the treated groups and the Control group.

The Steel-test (many-one rank test) was applied when the data could not be assumed to follow a normal distribution.

Fisher's Exact test for 2x2 tables was applied if the variables could be dichotomized without loss of information.

Individual values, means, standard deviations and t-statistics were rounded off before printing.

References:

C. W. Dunnett, A Multiple Comparison Procedure for Comparing Several Treatments with a Control, J. Amer. Statist. Assoc. 50, 1096-121 (1955).

Rupert G. Miller, Simultaneous Statistical Inference, Springer Verlag, New York (1981).

Fisher, R.A. Statistical Methods for Research Workers, Oliver and Boyd, Edinburgh (1950).

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ARCHIVING

The following data and specimens will be archived by RCC, Research & Consulting Company AG, CH 4452 Itingen / Switzerland for at least 10 years:

protocol, report, duplicate of report, raw data of laboratory investigations, fetal sections, skeletal preparations of fetuses and test article reference sample.

RESULTS

SUMMARY OF PERFORMANCE OF MATED FEMALES

Group Dose (mg/kg)	1 (0)	2 (1)	3 (3)
No. of mated females	25	25	25
Female nos.	1-25	26-50	51-75
No. of non-pregnant females	0	1(A)	0
No. of females with total resorption	0	0	1(B)
No. of females with live fetuses at termination	25	24	24

(A) = Female no. 49 was non-pregnant.

(B) = Female no. 69 had only two implantation sites.

Only dams with live fetuses at termination on day 21 post coitum were included in the calculations of food consumption, body weight gain, corrected body weight gain and reproduction data.

MATERNAL DATA

SIGNS OF REACTION TO TREATMENT AND MORTALITIES :

There were no signs of reaction to treatment and no deaths occurred during the study.

FOOD CONSUMPTION (pp. 25-29):

Food consumption values were similar in all groups throughout the study. None of the differences from Control values attained statistical significance ($p>0.05$, Dunnett's test).

BODY WEIGHTS (pp. 30-39):

Body weight gain of the dams was similar in all groups throughout the study. None of the differences from Control values attained statistical significance ($p>0.05$, Dunnett's test).

Overall body weight gain corrected for uterus weight at termination was also similar in all groups.

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MATERNAL DATA (CONT'D)

NECROPSY FINDINGS (pp. 70-72):

No treatment-related macroscopic changes were noted at terminal necropsy of the dams.

REPRODUCTION DATA (pp. 21, 40-44, 54-69):

One female in group 2 (1 mg/kg) was non-pregnant and one female in group 3 (3 mg/kg) showed total litter loss - two implantation sites were detected when the uterus was stained with ammonium sulphide (Salewski technique). All other females were pregnant and had live fetuses at termination on day 21 post coitum.

None of the maternal reproduction parameters - pre- and post-implantation loss, number of implantations and number of live fetuses - were adversely affected by the administration of SXX 0665 TECHNICAL. The only differences from Control values to attain statistical significance (p. 40,) were for the lower incidence of post-implantation loss and consequently increased number of live fetuses at 3 mg/kg.

FETAL DATA

EXTERNAL EXAMINATION (p. 45):

No abnormal findings were observed during external examination of the fetuses.

SEX RATIOS (p. 40):

Fetal sex ratios were similar in all groups.

BODY WEIGHTS (Group mean p. 41; Litter mean pp. 51-53; Individual pp. 57-69):

At both 1 and 3 mg/kg, mean fetal body weights were slightly greater than the concurrent Control value. Although the differences from the concurrent Control value attained statistical significance (p. 41), all values were within the range of the historical Controls.

FETAL DATA (CONT'D)

VISCERAL EXAMINATION BY WILSON TECHNIQUE (p. 45):

No abnormal findings were observed during visceral examination of the fetuses.

SKELETAL EXAMINATION (ABNORMAL FINDINGS, p. 46):

The incidences of fetuses with abnormal findings observed during skeletal examination were as follows:

6/146 fetuses in 5/25 litters in the Control group,
6/133 fetuses in 4/24 litters at 1 mg/kg and
3/155 fetuses in 3/24 litters at 3 mg/kg.

With one exception, the abnormal findings observed were wavy ribs or dumbbell shaped thoracic vertebral centra. The one exception was a Control fetus with fused ribs, fused sternebrae and dumbbell shaped thoracic and lumbar vertebral centra.

Neither the types nor the incidences of abnormal findings indicated an effect of the administration of SXX 0665 TECHNICAL to the dams.

SKELETAL EXAMINATION (STAGE OF DEVELOPMENT, p. 47):

Correlating with the slightly increased mean fetal body weight mentioned above and indicating a slight increase in the stage of development at 1 and 3 mg/kg in comparison to the concurrent Control group, there was a slightly lower incidence of fetuses with incompletely ossified cranial bones and non-ossified cervical vertebrae 2-4, tali, metatarsals and proximal/distal phalanges of the fore and hind feet. Both on a per litter and on a per fetus basis, most of the differences from Control values attained statistical significance at 3 mg/kg and occasional differences from Control values attained statistical significance at 1 mg/kg.

In contrast to the lower incidences of non-ossified/incompletely ossified skeletal elements mentioned above, there was a statistically significant increase in the incidence of supernumerary rib(s) at 3 mg/kg. However, the incidences obtained (25 % left, 26 % right) were within the range of historical Control values obtained in rats of this strain, in this laboratory, in the previous two years and were similar to the Control incidences obtained in the first study with SXX 0665 TECHNICAL (RCC Project 236114), viz. 21 % left, 19 % right. At 1 mg/kg, the incidence of supernumerary rib(s) was similar to that of the concurrent Control group.

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FIGURES AND TABLES

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SXX 0665 TECHNICAL

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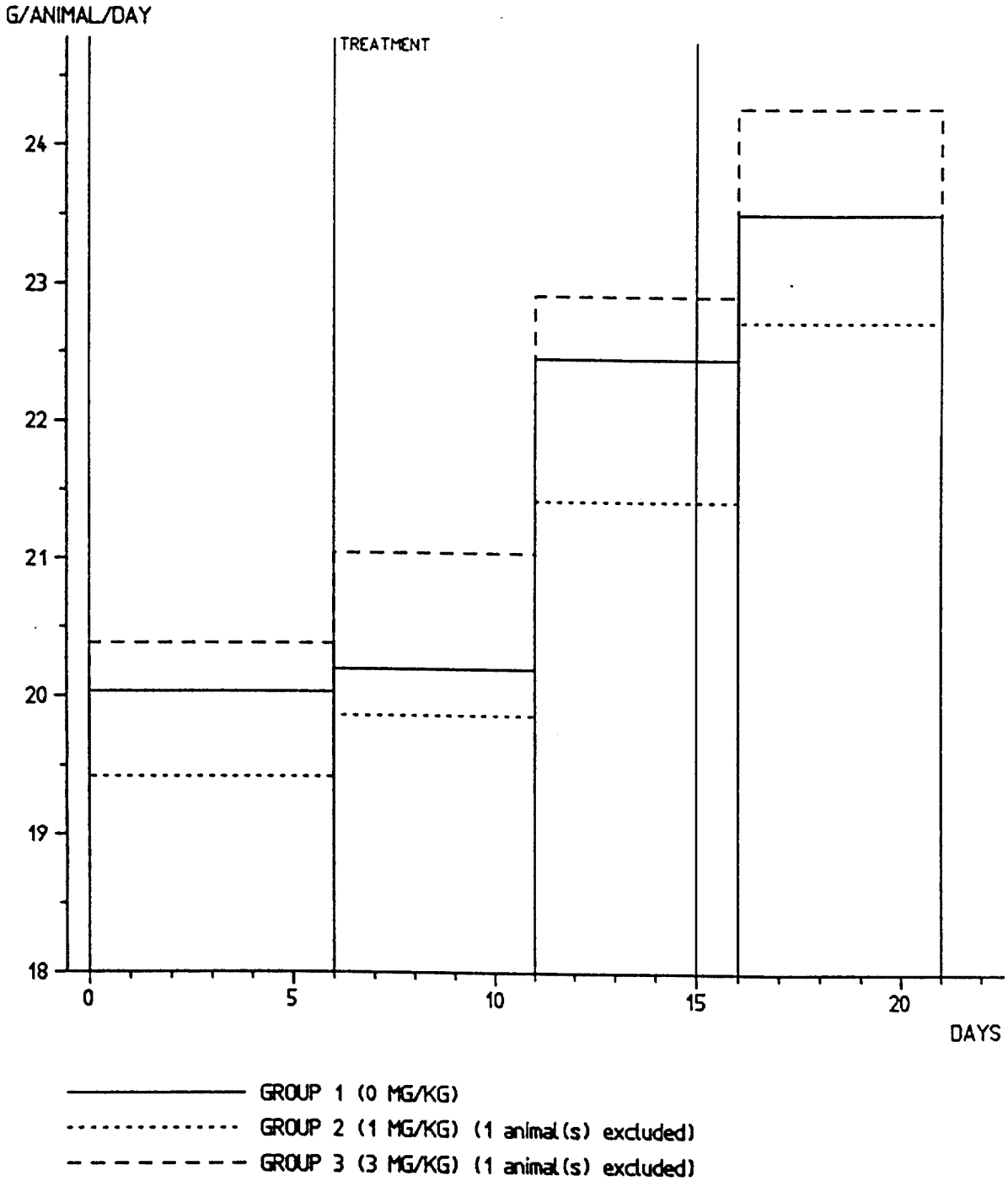
FOOD CONSUMPTION OF DAMS
POST COITUM



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FOOD CONSUMPTION OF DAMS SUMMARY (G/ANIMAL/DAY) POST COITUM

			GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
DAYS	0-6	MEAN	20.0	19.4	20.4
		ST.DEV.	1.6	1.8	2.0
		N	25	24	24
DAYS	6-11	MEAN	20.2	19.9	21.0
		ST.DEV.	1.4	1.8	2.4
		N	25	24	24
DAYS	11-16	MEAN	22.5	21.4	22.9
		ST.DEV.	1.9	1.9	2.2
		N	25	24	24
DAYS	16-21	MEAN	23.5	22.7	24.3
		ST.DEV.	2.4	2.2	2.3
		N	25	24	24
animal(s) excluded			0	1	1

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) OF DAMS POST COITUM

GROUP 1 (0 MG/KG)

DAYS ANIMAL	0-6	6-11	11-16	16-21
1	22.8	21.3	24.4	26.3
2	20.6	21.2	22.4	20.4
3	20.4	21.0	22.9	23.7
4	19.5	20.0	24.5	24.4
5	19.0	19.0	21.7	23.1
6	20.8	20.5	23.2	23.9
7	20.1	18.5	21.6	21.7
8	20.4	21.0	22.4	25.2
9	20.1	20.3	21.9	23.9
10	20.8	20.5	22.3	23.1
11	18.8	19.1	22.0	22.5
12	21.5	20.7	20.9	21.4
13	19.0	19.4	22.9	22.7
14	17.1	18.5	20.1	20.4
15	19.9	21.1	23.6	26.9
16	24.1	24.0	28.7	30.5
17	17.2	17.8	20.0	21.7
18	22.7	22.2	24.2	26.8
19	18.1	17.9	20.0	19.4
20	19.7	18.8	20.0	21.5
21	19.2	20.7	21.1	22.6
22	19.6	20.6	22.2	24.7
23	20.0	19.8	22.4	24.7
24	19.3	20.4	22.0	22.0
25	19.9	20.8	24.0	24.4

GROUP 2 (1 MG/KG)

DAYS ANIMAL	0-6	6-11	11-16	16-21
26	17.3	16.0	20.0	21.4
27	21.2	20.1	20.2	22.8
28	19.6	20.0	18.7	23.3
29	17.6	18.3	20.3	21.7
30	19.3	20.1	22.3	21.8
31	20.7	21.0	22.3	22.8
32	17.5	16.4	19.3	21.9
33	21.6	21.9	25.3	27.3
34	19.7	19.7	22.7	22.5
35	19.8	18.9	21.3	22.4
36	18.2	18.7	22.2	25.7
37	18.0	19.8	23.5	26.3
38	20.6	20.5	21.2	22.5
39	18.9	19.4	20.8	23.7
40	21.9	21.4	24.8	25.6
41	21.8	22.3	23.7	23.9
42	18.5	23.0	20.3	19.4
43	21.3	19.8	20.7	21.8
44	22.7	23.4	23.6	24.6
45	18.8	20.5	21.8	21.0
46	19.6	19.3	21.0	22.8
47	18.5	20.4	21.0	22.3
48	16.9	17.7	18.9	20.5
49 (A)	20.2	22.1	17.9	15.5
50	16.4	18.1	18.4	17.6

(A) Non-pregnant
(I) Implant. sites only

FOOD CONSUMPTION (G/ANIMAL/DAY) OF DAMS POST COITUM

GROUP 3 (3 MG/KG)

DAYS ANIMAL	0-6	6-11	11-16	16-21
51	21.4	21.3	23.4	26.2
52	23.5	24.8	26.4	28.3
53	18.3	19.8	21.1	21.9
54	18.4	17.3	19.4	20.7
55	20.4	20.7	22.3	26.1
56	20.9	20.1	21.8	24.8
57	17.1	17.1	19.2	20.9
58	20.7	20.8	23.2	24.6
59	20.7	21.8	24.1	23.7
60	19.0	27.2	23.9	25.9
61	18.1	18.5	21.8	22.8
62	20.7	19.3	24.0	25.1
63	21.1	20.4	20.4	21.6
64	20.7	20.5	22.9	26.6
65	23.7	23.1	25.5	24.7
66	23.1	21.4	23.0	23.7
67	20.8	21.3	21.9	28.2
68	21.3	22.6	25.6	26.7
69 (I)	19.2	19.3	15.2	16.8
70	23.8	24.4	26.7	23.7
71	17.9	17.9	18.7	19.9
72	20.3	20.4	22.5	22.1
73	16.8	19.2	21.9	23.2
74	19.9	23.0	25.7	26.9
75	20.6	22.3	24.8	24.8

(A) Non-pregnant
(I) Implant. sites only

DIFFERENCES IN FOOD CONSUMPTION OF DAMS, MEAN (G/ANIMAL/DAY)

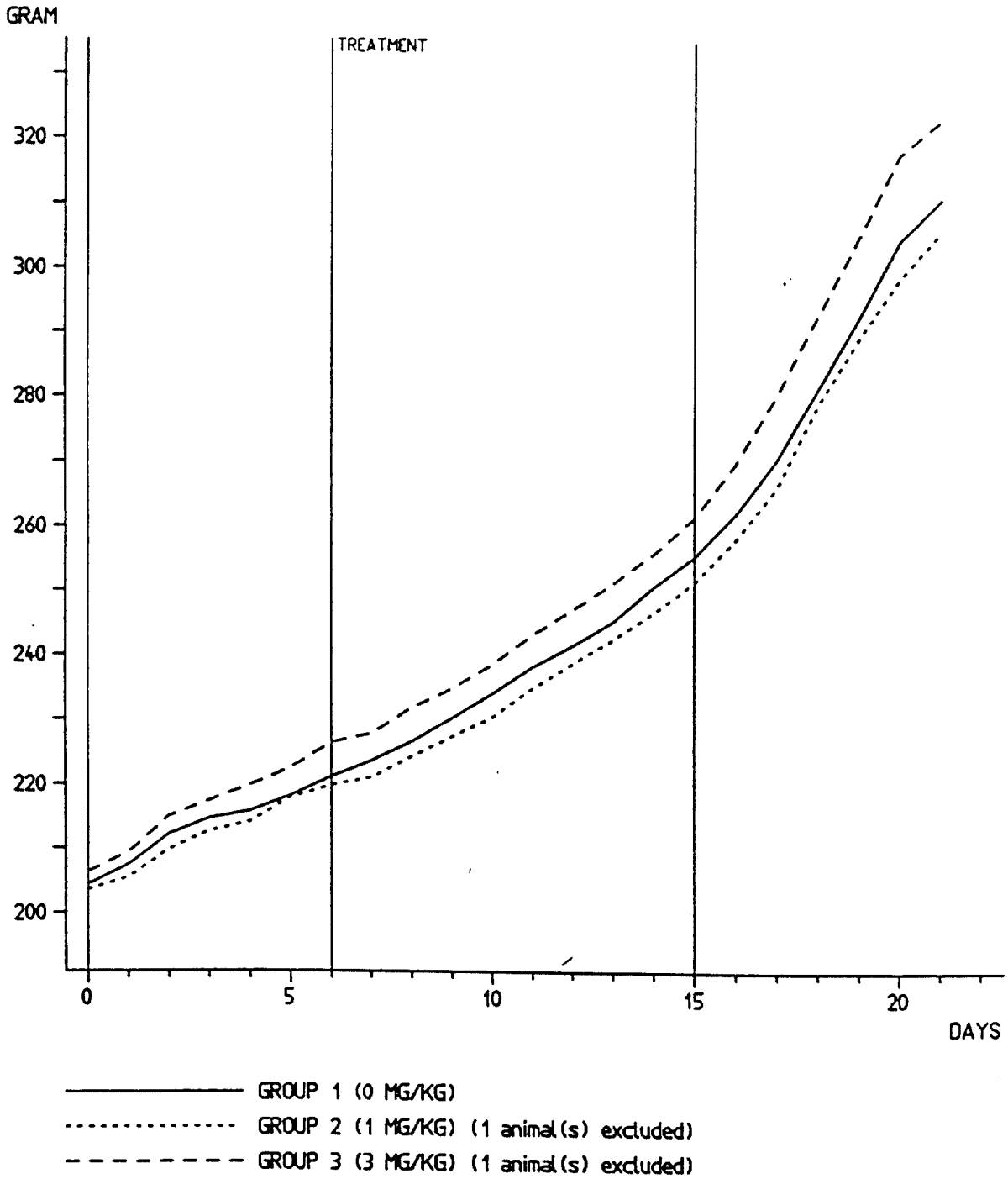
Group (mg/kg)	Days post coitum 0 - 6 g (%)*	6 - 11 g (%)*	11 - 16 g (%)*
1 (0)	20.0	20.2	22.5
2 (1)	19.4 (-3.0)	19.9 (-1.5)	21.4 (-4.9)
3 (3)	20.4 (+2.0)	21.0 (+4.0)	22.9 (+1.8)

Group (mg/kg)	Days post coitum 6 - 16** g (%)*	16 - 21 g (%)*
1 (0)	21.4	23.5
2 (1)	20.7 (-3.3)	22.7 (-3.4)
3 (3)	22.0 (+2.8)	24.3 (+3.4)

* = Percentages refer to the values of group 1.

** = The calculations of food consumption and body weight gain during the treatment period started on day 6 post coitum (immediately prior to the first administration) and ended on day 16 post coitum (approximately 24 hours after the last administration).

BODY WEIGHTS OF DAMS
POST COITUM



BODY WEIGHTS (GRAM) OF DAMS SUMMARY POST COITUM

			GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
DAY	0	MEAN	204	204	206
		ST.DEV.	10.0	10.6	11.1
		N	25	24	24
DAY	1	MEAN	207	205	209
		ST.DEV.	10.4	10.8	12.3
		N	25	24	24
DAY	2	MEAN	212	210	215
		ST.DEV.	10.5	11.9	12.8
		N	25	24	24
DAY	3	MEAN	215	213	217
		ST.DEV.	10.9	11.8	12.9
		N	25	24	24
DAY	4	MEAN	216	214	220
		ST.DEV.	10.9	11.3	13.4
		N	25	24	24
DAY	5	MEAN	218	218	222
		ST.DEV.	10.8	11.8	13.1
		N	25	24	24
DAY	6	MEAN	221	220	226
		ST.DEV.	11.9	12.2	14.3
		N	25	24	24
DAY	7	MEAN	224	221	228
		ST.DEV.	11.2	12.4	14.1
		N	25	24	24
DAY	8	MEAN	227	224	232
		ST.DEV.	11.2	13.5	14.4
		N	25	24	24
DAY	9	MEAN	230	227	235
		ST.DEV.	11.5	13.0	14.4
		N	25	24	24
DAY	10	MEAN	234	230	239
		ST.DEV.	12.3	12.9	15.0
		N	25	24	24
DAY	11	MEAN	238	235	243
		ST.DEV.	13.1	13.8	16.5
		N	25	24	24
DAY	12	MEAN	242	239	247
		ST.DEV.	11.9	13.5	16.8
		N	25	24	24
DAY	13	MEAN	245	243	251
		ST.DEV.	12.4	14.1	16.3
		N	25	24	24
DAY	14	MEAN	251	247	256
		ST.DEV.	13.0	15.1	17.4
		N	25	24	24
DAY	15	MEAN	255	251	262
		ST.DEV.	14.1	15.0	18.5
		N	25	24	24
DAY	16	MEAN	262	258	270
		ST.DEV.	15.4	15.0	19.2
		N	25	24	24
animal(s) excluded			0	1	1

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF DAMS SUMMARY POST COITUM

			GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
DAY	17	MEAN	271	266	281
		ST.DEV.	15.6	15.8	20.5
		N	25	24	24
DAY	18	MEAN	282	279	293
		ST.DEV.	17.8	17.3	21.8
		N	25	24	24
DAY	19	MEAN	293	289	305
		ST.DEV.	20.3	19.1	23.1
		N	25	24	24
DAY	20	MEAN	305	299	318
		ST.DEV.	22.4	20.4	24.1
		N	25	24	24
DAY	21	MEAN	311	306	323
		ST.DEV.	21.9	21.7	22.5
		N	25	24	24

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animal(s) excluded	0	1	1

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF DAMS POST COITUM

GROUP 1 (0 MG/KG)

DAYS / ANIMAL	0	1	2	3	4	5	6	7	8	9	10
1	199	204	211	218	219	222	221	225	226	234	233
2	194	202	207	208	211	213	215	220	225	224	236
3	185	187	195	199	200	200	205	208	212	219	217
4	198	202	204	211	207	212	216	218	221	224	228
5	200	203	204	209	211	213	212	217	220	226	230
6	201	203	206	209	213	213	217	220	221	225	232
7	191	190	193	197	195	197	202	204	203	205	208
8	205	213	216	220	219	220	226	228	232	239	240
9	208	209	215	221	220	219	220	223	227	234	234
10	204	206	210	216	214	218	218	224	227	231	235
11	208	207	214	219	214	217	218	222	227	231	235
12	221	225	231	227	235	236	240	242	247	249	248
13	214	219	220	223	228	228	231	234	235	241	247
14	201	202	209	200	205	209	213	213	219	219	225
15	219	217	221	226	226	220	228	229	235	237	240
16	222	227	229	237	237	242	249	249	247	252	266
17	203	206	212	212	210	215	214	219	223	226	231
18	219	226	234	235	233	238	244	244	248	250	253
19	197	197	202	203	206	211	212	213	216	215	221
20	198	202	206	205	209	212	214	217	218	222	223
21	209	214	217	219	218	223	228	227	231	235	238
22	195	198	203	202	207	212	210	216	219	223	226
23	210	213	222	223	226	226	232	235	235	241	244
24	194	200	203	207	205	210	211	212	214	217	221
25	214	215	220	219	224	228	231	234	236	237	240

DAYS / ANIMAL	11	12	13	14	15	16	17	18	19	20	21
1	240	238	246	250	256	259	270	278	289	303	312
2	232	244	244	254	258	265	271	287	298	306	316
3	224	229	232	235	244	249	256	264	280	290	289
4	233	238	245	246	255	261	275	281	301	315	318
5	236	241	242	248	256	256	266	278	289	304	311
6	233	240	242	247	257	260	275	287	292	309	321
7	212	217	220	225	228	238	243	251	259	272	282
8	247	246	255	258	261	267	273	285	296	304	316
9	243	245	244	249	257	256	267	275	282	300	307
10	238	241	245	253	255	261	269	282	292	304	312
11	233	240	246	249	254	262	269	281	293	308	310
12	257	255	259	270	270	281	287	304	319	336	334
13	254	253	260	263	275	285	292	307	323	339	335
14	228	232	235	244	244	253	263	268	280	292	296
15	248	246	252	260	259	265	278	290	303	313	327
16	266	271	275	279	290	299	310	326	339	354	361
17	230	234	239	246	251	258	269	279	297	307	306
18	259	262	265	274	279	288	296	313	326	341	350
19	225	227	231	237	239	247	253	264	270	279	279
20	227	225	233	237	240	243	252	262	271	281	293
21	247	246	247	256	257	268	274	283	302	313	322
22	226	236	237	243	240	245	252	261	270	274	277
23	248	250	254	256	258	269	269	278	285	290	297
24	222	230	230	229	235	240	248	258	257	264	274
25	247	253	255	260	267	280	287	297	307	318	327

(A) Non-pregnant
(I) Implant. sites only

BODY WEIGHTS (GRAM) OF DAMS POST COITUM

GROUP 2 (1 MG/KG)

DAYS ANIMAL	0	1	2	3	4	5	6	7	8	9	10
26	182	183	184	190	188	191	194	194	195	201	203
27	199	202	206	212	210	215	215	220	220	224	225
28	219	222	226	231	232	232	237	239	241	248	249
29	197	198	203	203	206	209	208	211	210	215	218
30	192	196	201	206	209	212	211	214	216	221	228
31	207	211	215	218	221	225	227	230	234	234	240
32	198	197	201	201	204	208	210	209	208	211	216
33	220	219	226	230	229	236	233	234	239	244	248
34	215	217	220	222	223	228	230	228	231	235	235
35	214	217	222	222	225	230	235	238	244	242	244
36	202	201	204	208	211	214	215	215	219	224	233
37	215	212	217	218	218	222	228	227	233	236	240
38	201	203	210	211	211	216	222	223	225	226	233
39	204	206	210	211	210	217	214	214	216	221	222
40	220	223	233	235	233	239	245	245	250	253	252
41	197	202	207	215	214	220	224	223	229	227	237
42	190	193	195	199	202	206	208	209	216	218	221
43	198	203	207	208	208	212	215	216	222	223	225
44	213	218	221	225	226	230	229	231	238	241	241
45	196	201	201	205	210	213	215	216	220	223	227
46	213	217	220	223	223	228	229	232	230	232	235
47	206	205	214	216	221	220	220	226	230	234	234
48	195	197	198	199	204	205	205	206	207	212	212
49 (A)	215	220	220	227	225	234	236	235	241	243	247
50	191	190	195	195	199	201	206	205	208	211	212

DAYS ANIMAL	11	12	13	14	15	16	17	18	19	20	21
26	205	211	213	215	221	228	233	247	257	272	272
27	229	234	235	240	245	248	263	274	284	296	297
28	256	259	257	258	260	272	274	288	296	305	322
29	225	226	233	236	236	243	251	264	271	280	292
30	230	233	240	237	245	253	255	267	277	287	297
31	241	247	248	253	256	261	271	281	289	295	293
32	218	223	220	231	231	234	243	251	256	263	269
33	252	262	263	271	276	278	293	303	323	337	348
34	243	248	252	252	259	267	273	294	306	314	320
35	251	251	258	264	267	274	281	291	298	306	315
36	234	239	246	251	257	266	274	288	300	311	323
37	242	249	254	261	267	267	275	286	297	302	312
38	236	241	243	251	255	265	273	289	301	315	322
39	227	230	234	238	242	247	260	274	288	294	305
40	262	262	270	276	282	287	297	315	324	342	350
41	243	239	248	255	260	267	284	302	316	324	324
42	224	227	233	235	241	245	253	264	272	274	280
43	228	233	237	238	240	250	257	271	284	292	292
44	248	252	255	262	267	274	277	294	304	315	321
45	232	236	240	241	248	256	261	271	279	290	290
46	239	246	250	253	256	267	273	283	296	300	305
47	237	242	246	254	255	264	274	287	299	311	325
48	217	219	221	224	232	238	247	256	264	273	283
49 (A)	247	245	239	238	237	244	240	237	237	240	238
50	218	223	227	228	237	245	248	260	266	274	286

(A) Non-pregnant
(I) Implant. sites only

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BODY WEIGHTS (GRAM) OF DAMS POST COITUM

GROUP 3 (3 MG/KG)

DAYS / ANIMAL	0	1	2	3	4	5	6	7	8	9	10
51	209	215	217	223	224	225	229	230	233	239	243
52	217	223	225	236	238	241	249	249	252	259	266
53	195	195	199	203	203	205	207	210	215	220	224
54	202	202	207	211	214	212	219	217	221	222	226
55	189	195	201	204	202	208	210	214	215	219	217
56	210	212	220	221	219	225	225	227	235	238	240
57	189	190	198	197	200	203	206	208	210	214	217
58	201	203	211	213	216	218	223	224	230	237	238
59	212	215	223	226	230	230	236	237	242	246	250
60	205	206	212	213	218	221	224	224	231	231	236
61	191	189	192	198	203	203	203	205	209	211	216
62	216	217	224	224	225	228	233	236	240	238	238
63	206	209	216	213	219	220	222	226	231	234	238
64	197	201	207	205	206	212	214	217	222	224	229
65	219	221	230	231	239	241	242	244	253	254	258
66	213	222	224	225	229	229	236	237	240	245	248
67	210	212	225	224	225	231	236	235	242	238	243
68	217	221	227	229	231	234	238	239	244	247	253
69 (I)	207	209	218	219	219	223	224	227	228	231	231
70	227	235	242	242	245	246	253	254	256	262	267
71	190	193	196	197	199	204	207	204	207	213	217
72	217	221	223	229	229	235	239	241	244	247	249
73	193	195	200	203	206	209	211	214	216	219	225
74	211	212	215	219	221	225	231	233	233	237	243
75	217	220	226	228	232	232	238	240	239	241	246

DAYS / ANIMAL	11	12	13	14	15	16	17	18	19	20	21
51	246	247	249	258	265	268	277	279	285	300	307
52	276	272	277	282	296	309	316	330	346	363	370
53	226	226	232	241	241	252	257	266	278	288	300
54	227	228	233	237	244	249	256	267	281	291	296
55	225	229	231	237	242	251	266	277	293	304	318
56	243	251	251	256	262	269	276	290	299	309	317
57	219	222	227	229	234	242	253	266	276	289	291
58	238	247	253	256	262	269	280	289	306	320	321
59	257	263	264	273	283	287	304	319	333	343	351
60	246	248	252	253	258	266	278	289	306	315	326
61	218	223	230	232	237	245	253	267	277	288	290
62	246	254	259	264	269	281	290	310	319	332	338
63	239	243	248	248	249	262	268	283	292	310	316
64	236	240	242	248	251	259	273	284	297	315	317
65	263	271	275	282	284	295	307	317	337	350	350
66	251	253	259	263	266	275	284	295	309	320	325
67	251	248	255	259	261	272	289	302	316	330	347
68	261	266	271	278	284	295	310	326	338	356	350
69 (I)	228	225	225	225	225	224	227	229	228	227	231
70	274	279	282	289	295	303	317	336	346	358	353
71	218	220	226	225	231	238	245	256	266	274	284
72	252	258	260	263	271	282	295	304	321	332	324
73	228	234	239	245	252	258	270	286	298	308	316
74	246	252	255	261	270	278	283	297	303	315	332
75	251	257	259	264	271	277	289	301	307	324	320

(A) Non-pregnant
(I) Implant. sites only

CORRECTED BODY WEIGHT GAIN OF DAMS
GROUP 1 (0 MG/KG)

FEMALE	WEIGHT ON DAY 6 P.C.	WEIGHT ON DAY OF SECTION	WEIGHT OF UTERUS	CORRECTED WEIGHT GAIN GRAM<1>	CORRECTED WEIGHT GAIN PERCENT<2>
1	220.9	311.6	67.5	23.2	10.5
2	214.7	315.7	82.3	18.7	8.7
3	205.3	288.8	64.4	19.1	9.3
4	215.8	318.5	82.4	20.3	9.4
5	212.3	311.0	74.4	24.3	11.5
6	217.2	321.3	87.1	16.9	7.8
7	201.6	282.5	66.4	14.4	7.2
8	226.1	316.3	51.8	38.4	17.0
9	219.9	307.4	58.0	29.5	13.4
10	217.6	311.6	72.0	22.0	10.1
11	218.3	310.4	80.0	12.1	5.5
12	239.7	333.9	92.5	1.7	0.7
13	231.2	335.3	88.1	16.0	6.9
14	212.9	296.0	73.6	9.5	4.5
15	228.3	326.8	71.8	26.8	11.7
16	249.2	361.5	91.6	20.7	8.3
17	213.8	306.2	81.1	11.3	5.3
18	244.2	349.7	88.0	17.6	7.2
19	211.9	279.5	58.4	9.2	4.3
20	214.2	293.2	56.8	22.1	10.3
21	228.5	322.4	87.3	6.7	2.9
22	210.0	277.5	31.8	35.7	17.0
23	231.7	297.4	37.3	28.3	12.2
24	211.3	274.3	46.4	16.6	7.8
25	231.0	327.1	75.1	21.0	9.1
		N	25	25	25
		MEAN	70.6	19.3	8.7
		ST.DEV.	16.7	8.6	3.9

<1> : (Weight on Day of Section) - (Weight on Day 6 P.C.) - (Weight Uterus)
<2> : Corrected Weight Gain in Percent of Weight on Day 6 P.C.
*/** : Dunnett-Test based on pooled variance significant at level 5% (*) or 1% (**)

CORRECTED BODY WEIGHT GAIN OF DAMS
GROUP 2 (1 MG/KG)

FEMALE	WEIGHT ON DAY 6 P.C.	WEIGHT ON DAY OF SECTION	WEIGHT OF UTERUS	CORRECTED WEIGHT GAIN GRAM<1>	CORRECTED WEIGHT GAIN PERCENT<2>
26	194.4	271.6	69.1	8.1	4.2
27	214.7	296.9	69.9	12.3	5.7
28	237.0	322.5	59.9	25.6	10.8
29	208.1	292.1	61.1	22.9	11.0
30	211.0	296.6	67.5	18.0	8.5
31	227.3	293.3	65.4	0.6	0.3
32	209.9	269.1	38.2	21.0	10.0
33	233.4	348.5	87.8	27.4	11.7
34	230.0	319.9	81.6	8.4	3.6
35	234.8	315.3	70.6	9.9	4.2
36	215.2	323.0	83.3	24.5	11.4
37	227.5	312.3	52.7	32.1	14.1
38	222.3	321.9	89.0	10.6	4.8
39	214.5	305.5	82.3	8.8	4.1
40	244.9	349.8	87.1	17.7	7.2
41	223.8	323.5	93.2	6.5	2.9
42	208.0	280.3	61.7	10.6	5.1
43	215.3	291.9	76.9	-0.4	-0.2
44	229.2	320.8	74.5	17.1	7.5
45	214.9	290.3	61.6	13.7	6.4
46	229.4	304.7	60.4	14.9	6.5
47	219.6	325.3	80.7	25.1	11.4
48	204.5	283.0	58.1	20.4	10.0
49 <NP>	236.1	237.6			
50	205.8	285.6	68.6	11.1	5.4
		N	24	24	24
		MEAN	70.9	15.3	6.9
		ST.DEV.	13.2	8.4	3.8

<1> : (Weight on Day of Section) - (Weight on Day 6 P.C.) - (Weight Uterus)
<2> : Corrected Weight Gain in Percent of Weight on Day 6 P.C.
*/** : Dunnett-Test based on pooled variance significant at level 5% (*) or 1% (**)
Reason for Exclusion from Evaluation :
<NP> Non-Pregnant

CORRECTED BODY WEIGHT GAIN OF DAMS
GROUP 3 (3 MG/KG)

FEMALE	WEIGHT ON DAY 6 P.C.	WEIGHT ON DAY OF SECTION	WEIGHT OF UTERUS	CORRECTED WEIGHT GAIN GRAM<1>	PERCENT<2>
51	229.0	307.1	46.8	31.4	13.7
52	249.0	370.3	104.8	16.4	6.6
53	206.7	300.2	64.6	28.9	14.0
54	219.3	295.9	71.9	4.8	2.2
55	210.3	318.0	86.9	20.8	9.9
56	225.4	316.8	85.1	6.4	2.8
57	206.2	290.8	74.3	10.4	5.0
58	222.7	321.5	83.1	15.7	7.1
59	236.0	351.3	101.8	13.5	5.7
60	223.9	325.7	90.9	10.9	4.9
61	203.2	290.1	70.8	16.1	7.9
62	233.3	337.7	88.3	16.2	6.9
63	222.3	315.7	91.6	1.8	0.8
64	214.3	317.1	87.1	15.8	7.4
65	242.1	350.4	97.0	11.3	4.7
66	235.5	324.5	80.5	8.5	3.6
67	236.2	347.0	86.1	24.6	10.4
68	238.0	350.2	105.6	6.5	2.7
69 <OI>	223.7	230.6			
70	253.0	352.8	105.2	-5.3	-2.1
71	206.7	283.6	70.9	6.1	2.9
72	238.7	324.4	90.6	-4.9	-2.0
73	211.2	315.9	79.3	25.4	12.0
74	231.1	331.6	74.6	25.9	11.2
75	237.9	320.2	65.2	17.2	7.2
		N	24	24	24
		MEAN	83.4	13.5	6.1
		ST.DEV.	14.5	9.7	4.4

<1> : (Weight on Day of Section) - (Weight on Day 6 P.C.) - (Weight Uterus)
<2> : Corrected Weight Gain in Percent of Weight on Day 6 P.C.
*/** : Dunnett-Test based on pooled variance significant at level 5% (*) or 1% (**)
Reason for Exclusion from Evaluation :
<OI> Implantation Sites only

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DIFFERENCES IN BODY WEIGHT GAIN OF DAMS, MEAN

Group (mg/kg)	Days post coitum 0 - 6 g (%)	6 - 11 g (%)	11 - 16 g (%)	6 - 16* g (%)
1 (0)	17 (+8.3)	17 (+7.7)	24 (+10.1)	41 (+18.6)
2 (1)	16 (+7.8)	15 (+6.8)	23 (+9.8)	38 (+17.3)
3 (3)	20 (+9.7)	17 (+7.5)	27 (+11.1)	44 (+19.5)

* = The calculations of food consumption and body weight gain during the treatment period started on day 6 post coitum (immediately prior to the first administration) and ended on day 16 post coitum (approximately 24 hours after the last administration).

Group (mg/kg)	Days post coitum 16 - 21 g (%)	6 - 21 g (%)	Corrected body weight gain % (see pp. 36-38)
1 (0)	49 (+18.7)	90 (+40.7)	8.7
2 (1)	48 (+18.6)	86 (+39.1)	6.9
3 (3)	53 (+19.6)	97 (+42.9)	6.1

REPRODUCTION DATA SUMMARY

	GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
NUMBER OF DAMS	25	24	24
CORPORA LUTEA	332	305	333
MEAN (+)	13.3	12.7	13.9
ST.DEV.	2.0	1.8	2.1
PRE-IMPLANTATION LOSS	28	30	23
% OF CORP. LUTEA (#)	8.4	9.8	6.9
MEAN (+)	1.1	1.3	1.0
ST.DEV.	1.2	1.5	1.5
NUMBER OF DAMS AFFECTED	16	14	12
IMPLANTATION SITES	304	275	310
% OF CORP. LUTEA (#)	91.6	90.2	93.1
MEAN (+)	12.2	11.5	12.9
ST.DEV.	2.0	2.4	2.4
POST-IMPLANTATION LOSS	29	23	12
% OF IMPL. SITES (#)	9.5	8.4	3.9 ##
MEAN (+)	1.2	1.0	0.5
ST.DEV.	2.1	1.2	0.5
NUMBER OF DAMS AFFECTED	11	13	12
IMPLANTATION SITE SCARS	0	0	0
EMBRYONIC DEATHS : TOTAL	29	23	12
EMBRYONIC RESORPTIONS	29	22	12
% OF IMPL. SITES (#)	9.5	8.0	3.9 ##
MEAN (+)	1.2	0.9	0.5
ST.DEV.	2.1	1.1	0.5
NUMBER OF DAMS AFFECTED	11	13	12
FETAL RESORPTIONS	0	1	0
% OF IMPL. SITES (#)		0.4	
MEAN (+)		0.0	
ST.DEV.		0.2	
NUMBER OF DAMS AFFECTED		1	
FETUSES			
TOTAL FETUSES	275	252	298
% OF IMPL. SITES (#)	90.5	91.6	96.1 ##
MEAN (+)	11.0	10.5	12.4
ST.DEV.	2.8	2.3	2.4
LIVE FETUSES	275	252	298
DEAD FETUSES	0	0	0
ABNORMAL FETUSES	0	0	0
SEX OF FETUSES			
TOTAL MALES	138	132	154
% OF FETUSES (#)	50.2	52.4	51.7
MEAN	5.5	5.5	6.4
ST.DEV.	1.7	2.2	2.6
TOTAL FEMALES	137	120	144
% OF FETUSES (#)	49.8	47.6	48.3
MEAN	5.5	5.0	6.0
ST.DEV.	2.2	2.5	2.0

*/** : Dunnett-Test based on pooled variance significant at level 5% (*) or 1% (**)
#/## : Fisher's Exact Test significant at level 5% (#) or 1% (##)
+ : Steel Test significant at level 5%

REPRODUCTION DATA SUMMARY

	GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
NUMBER OF DAMS	25	24	24
SEX OF FETUSES (CONT.)			
LIVE MALES	138	132	154
LIVE FEMALES	137	120	144
WEIGHTS OF LIVE FETUSES (LITTER BASIS)			
TOTAL FETUSES			
N (LITTERS)	25	24	24
MEAN (*)	4.7	4.9 *	4.9 **
ST.DEV.	0.3	0.3	0.2
MALES			
N (LITTERS)	25	24	24
MEAN (*)	4.8	5.0 *	5.0 **
ST.DEV.	0.3	0.3	0.2
FEMALES			
N (LITTERS)	25	23	24
MEAN (*)	4.6	4.7	4.8 *
ST.DEV.	0.3	0.2	0.2
WEIGHTS OF LIVE FETUSES (INDIVIDUAL BASIS)			
TOTAL FETUSES			
N (FETUSES)	275	252	298
MEAN	4.7	4.8	4.9
ST.DEV.	0.4	0.4	0.3
MALES			
N (FETUSES)	138	132	154
MEAN	4.8	5.0	5.0
ST.DEV.	0.4	0.4	0.3
FEMALES			
N (FETUSES)	137	120	144
MEAN	4.6	4.7	4.8
ST.DEV.	0.4	0.3	0.3

*/** : Dunnett-Test based on pooled variance significant at level 5% (*) or 1% (**)
#/## : Fisher's Exact Test significant at level 5% (#) or 1% (##)
+ : Steel Test significant at level 5%

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REPRODUCTION DATA
GROUP 1 (0 MG/KG)

FEMALE	CORP. LUTEA	IMPL.	-EMBRYONIC DEATHS-- TOTAL	EMBR. STAGE	FETAL STAGE	FETUSES TOTAL	LIVE MALE	LIVE FEM.	DEAD MALE	DEAD FEM.	MALF. MALE	MALF. FEM.
1	14	13	2	2	0	11	7	4	0	0	0	0
2	13	13	0	0	0	13	8	5	0	0	0	0
3	11	11	1	1	0	10	4	6	0	0	0	0
4	12	12	0	0	0	12	5	7	0	0	0	0
5	15	13	1	1	0	12	5	7	0	0	0	0
6	14	14	0	0	0	14	5	9	0	0	0	0
7	11	11	0	0	0	11	7	4	0	0	0	0
8	8	8	0	0	0	8	5	3	0	0	0	0
9	12	11	2	2	0	9	5	4	0	0	0	0
10	12	11	0	0	0	11	4	7	0	0	0	0
11	15	13	0	0	0	13	8	5	0	0	0	0
12	16	15	0	0	0	15	6	9	0	0	0	0
13	16	15	0	0	0	15	6	9	0	0	0	0
14	13	12	1	1	0	11	8	3	0	0	0	0
15	13	11	0	0	0	11	7	4	0	0	0	0
16	16	16	2	2	0	14	8	6	0	0	0	0
17	14	13	0	0	0	13	5	8	0	0	0	0
18	15	13	0	0	0	13	5	8	0	0	0	0
19	10	10	2	2	0	8	4	4	0	0	0	0
20	12	11	2	2	0	9	6	3	0	0	0	0
21	14	14	0	0	0	14	7	7	0	0	0	0
22	13	11	6	6	0	5	3	2	0	0	0	0
23	16	14	9	9	0	5	3	2	0	0	0	0
24	13	8	1	1	0	7	2	5	0	0	0	0
25	14	11	0	0	0	11	5	6	0	0	0	0
TOTAL	332	304	29	29	0	275	138	137	0	0	0	0
MEAN	13.3	12.2	1.2	1.2		11.0	5.5	5.5				
ST.DEV.	2.0	2.0	2.1	2.1		2.8	1.7	2.2				

REPRODUCTION DATA
GROUP 2 (1 MG/KG)

FEMALE	CORP. LUTEA	IMPL.	-EMBRYONIC DEATHS-- TOTAL	EMBR. STAGE	FETAL STAGE	FETUSES TOTAL	LIVE MALE	LIVE FEM.	DEAD MALE	DEAD FEM.	MALF. MALE	MALF. FEM.
26	12	10	0	0	0	10	6	4	0	0	0	0
27	11	11	0	0	0	11	9	2	0	0	0	0
28	13	12	3	3	0	9	5	4	0	0	0	0
29	10	10	1	1	0	9	7	2	0	0	0	0
30	12	12	1	1	0	11	6	5	0	0	0	0
31	11	10	1	1	0	9	7	2	0	0	0	0
32	10	5	0	0	0	5	1	4	0	0	0	0
33	16	14	1	1	0	13	5	8	0	0	0	0
34	14	12	0	0	0	12	5	7	0	0	0	0
35	13	10	0	0	0	10	5	5	0	0	0	0
36	14	13	0	0	0	13	3	10	0	0	0	0
37	10	9	2	2	0	7	3	4	0	0	0	0
38	15	15	1	1	0	14	5	9	0	0	0	0
39	15	15	2	2	0	13	4	9	0	0	0	0
40	15	15	1	1	0	14	8	6	0	0	0	0
41	14	14	0	0	0	14	9	5	0	0	0	0
42	12	9	0	0	0	9	5	4	0	0	0	0
43	13	12	1	1	0	11	11	0	0	0	0	0
44	14	14	4	3	1	10	4	6	0	0	0	0
45	14	12	3	3	0	9	6	3	0	0	0	0
46	14	9	0	0	0	9	6	3	0	0	0	0
47	12	12	0	0	0	12	5	7	0	0	0	0
48	11	10	2	2	0	8	3	5	0	0	0	0
49 <NP>												
50	10	10	0	0	0	10	4	6	0	0	0	0
TOTAL	305	275	23	22	1	252	132	120	0	0	0	0
MEAN	12.7	11.5	1.0	0.9	0.0	10.5	5.5	5.0				
ST.DEV.	1.8	2.4	1.2	1.1	0.2	2.3	2.2	2.5				

Reason for Exclusion from Evaluation :
<NP> Non-Pregnant

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REPRODUCTION DATA
GROUP 3 (3 MG/KG)

FEMALE	CORP. LUTEA	IMPL.	-EMBRYONIC DEATHS-- TOTAL	EMBR. STAGE	FETAL STAGE	FETUSES TOTAL	LIVE MALE	LIVE FEM.	DEAD MALE	DEAD FEM.	MALF. MALE	MALF. FEM.
51	14	7	0	0	0	7	3	4	0	0	0	0
52	17	16	0	0	0	16	8	8	0	0	0	0
53	11	11	1	1	0	10	3	7	0	0	0	0
54	11	11	0	0	0	11	4	7	0	0	0	0
55	16	14	1	1	0	13	6	7	0	0	0	0
56	16	14	1	1	0	13	5	8	0	0	0	0
57	11	11	0	0	0	11	5	6	0	0	0	0
58	12	12	0	0	0	12	7	5	0	0	0	0
59	16	16	0	0	0	16	8	8	0	0	0	0
60	14	14	0	0	0	14	8	6	0	0	0	0
61	12	10	0	0	0	10	4	6	0	0	0	0
62	16	14	1	1	0	13	8	5	0	0	0	0
63	14	14	1	1	0	13	11	2	0	0	0	0
64	13	13	1	1	0	12	11	1	0	0	0	0
65	16	16	1	1	0	15	4	11	0	0	0	0
66	13	12	1	1	0	11	6	5	0	0	0	0
67	13	13	1	1	0	12	8	4	0	0	0	0
68	16	16	0	0	0	16	10	6	0	0	0	0
69 <OI>	2	2										
70	18	17	0	0	0	17	11	6	0	0	0	0
71	12	11	1	1	0	10	3	7	0	0	0	0
72	15	14	0	0	0	14	7	7	0	0	0	0
73	12	11	0	0	0	11	5	6	0	0	0	0
74	12	12	1	1	0	11	5	6	0	0	0	0
75	13	11	1	1	0	10	4	6	0	0	0	0
TOTAL	333	310	12	12	0	298	154	144	0	0	0	0
MEAN	13.9	12.9	0.5	0.5		12.4	6.4	6.0				
ST.DEV.	2.1	2.4	0.5	0.5		2.4	2.6	2.0				

Reason for Exclusion from Evaluation :
<OI> Implantation Sites only

EXTERNAL EXAMINATION OF FETUSES

Group (mg/kg)	No. of fetuses examined	Type of abnormal finding	Individual data of fetus(es)*	Fetus(es) of litter number
1 (0)	275	No abnormal findings		
2 (1)	252	No abnormal findings		
3 (3)	298	No abnormal findings		

* = Fetus number / body weight in grams / sex (M = male; F = female)

VISCERAL EXAMINATION OF FETUSES (WILSON TECHNIQUE)

Group (mg/kg)	No. of fetuses examined	Type of abnormal finding	Individual data of fetus(es)*	Fetus(es) of litter number
1 (0)	129	No abnormal findings		
2 (1)	119	No abnormal findings		
3 (3)	143	No abnormal findings		

* = Fetus number / body weight in grams / sex (M = male; F = female)

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SKELETAL EXAMINATION OF FETUSES (ABNORMAL FINDINGS)

Group (mg/kg)	No. of fetuses examined	Type of abnormal finding	Individual data of fetus(es)*	Fetus(es) of litter number
1 (0)	146	Wavy ribs, nos. 11-13 left side and nos. 8-13 right side; 11th thoracic vertebral centrum dumbbell shaped	69/4.8/M	6
		Wavy ribs, nos. 11-13 left side and nos. 6-13 right side	94/4.3/M	9
		10th thoracic vertebral centrum dumbbell shaped	120/4.3/F	11
		Wavy ribs, nos. 7-13 left side and nos. 5-13 right side	124/4.6/M	11
		Wavy ribs, nos. 4-13 left side and nos. 9-13 right side	332/3.5/F	21
		11th-13th left ribs fused, 7th, 10th-12th thoracic and 1st lumbar vertebral centra dumbbell shaped, 1st-3rd sternebrae fused	346/2.6/M	22
2 (1)	133	Wavy ribs, nos. 6-13 left side and right sides	161/5.2/M	26
		Wavy ribs, nos. 8-13 right side	163/5.5/M	26
		Wavy ribs, nos. 8-13 left side and nos. 6-13 right side	361/5.6/M	32
		12th thoracic vertebral centrum dumbbell shaped	365/5.0/F	32
		Wavy ribs, nos. 9-13 left side and nos. 7-13 right side	399/4.8/F	35
		10th thoracic vertebral centrum dumbbell shaped	757/4.9/F	46
3 (3)	155	12th thoracic vertebral centrum dumbbell shaped	531/4.6/F	56
		Wavy ribs, nos. 10-13 right side	534/5.2/M	57
		Wavy ribs, nos. 10-13 left side and nos. 9-13 right side	726/4.4/M	72

* = Fetus number / body weight in grams / sex (M = male; F = female)

SKELETAL EXAMINATION SUMMARY

—	GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
NUMBER OF LITTERS EXAMINED	25	24	24
UNLISTED FINDING(S) (SHOWN ON PREVIOUS PAGE(S))	5 20%	4 17%	3 13%
CRANIUM			
INCOMPLETELY OSSIFIED			
OS OCCIPITALE	5 20%	3 13%	0 *
OS PARIETALE, BILATERAL	7 28%	3 13%	1 4% *
OS INTERPARIETALE	10 40%	6 25%	1 4% **
CERVICAL VERTEBRAE			
NON-OSSIFIED			
CERVICAL VERTEBRA 1	12 48%	13 54%	11 46%
CERVICAL VERTEBRA 2	13 52%	7 29%	8 33%
CERVICAL VERTEBRA 3	11 44%	1 4% **	4 17% *
CERVICAL VERTEBRA 4	5 20%	0 *	2 8%
CERVICAL VERTEBRA 5	3 12%	0	0
CERVICAL VERTEBRA 6	2 8%	0	0
CERVICAL VERTEBRA 7	1 4%	0	0
DUMBBELL SHAPE			
CERVICAL VERTEBRA 1	21 84%	22 92%	23 96%
BIPARTITE			
CERVICAL VERTEBRA 1	1 4%	6 25% *	2 8%
STERNUM			
INCOMPLETELY OSSIFIED			
STERNEBRA 1	2 8%	0	0
STERNEBRA 2	7 28%	8 33%	6 25%
STERNEBRA 3	3 12%	2 8%	1 4%
STERNEBRA 4	9 36%	7 29%	7 29%
STERNEBRA 5	25 100%	23 96%	24 100%
STERNEBRA 6	2 8%	1 4%	1 4%
NON-OSSIFIED			
STERNEBRA 5	0	1 4%	1 4%
STERNEBRA 6	1 4%	0	0
ABNORMALLY OSSIFIED			
STERNEBRA 4	0	3 13%	0
STERNEBRA 5	1 4%	0	0
RIB(S), LEFT			
SUPERNUMERARY, ONE			
RIB(S), LEFT	11 44%	12 50%	15 63%
RIB(S), RIGHT			
SUPERNUMERARY, ONE			
RIB(S), RIGHT	11 44%	11 46%	15 63%
LEFT FORELIMB			
NON-OSSIFIED			
DIGIT 1 DISTAL PHALANX, LEFT	8 32%	2 8% *	0 **
DIGIT 2 PROXIMAL PHALANX, LEFT	19 76%	11 46% *	7 29% **
DIGIT 2 DISTAL PHALANX, LEFT	15 60%	9 38%	5 21% **
DIGIT 3 PROXIMAL PHALANX, LEFT	6 24%	1 4%	0 *
DIGIT 3 DISTAL PHALANX, LEFT	4 16%	1 4%	0
DIGIT 4 PROXIMAL PHALANX, LEFT	9 36%	4 17%	2 8% *
DIGIT 4 DISTAL PHALANX, LEFT	9 36%	4 17%	3 13%
METACARPALIA 5, LEFT	2 8%	0	0
DIGIT 5 PROXIMAL PHALANX, LEFT	23 92%	22 92%	19 79%
DIGIT 5 DISTAL PHALANX, LEFT	24 96%	23 96%	20 83%

* / ** : Fisher's Exact test significant at 5% (*) or 1% (**) level

SKELETAL EXAMINATION SUMMARY

—	GROUP 1 0 MG/KG	GROUP 2 1 MG/KG	GROUP 3 3 MG/KG
NUMBER OF LITTERS EXAMINED	25	24	24
RIGHT FORELIMB			
NON-OSSIFIED			
DIGIT 1 DISTAL PHALANX, RIGHT	8 32%	2 8% *	0 **
DIGIT 2 PROXIMAL PHALANX, RIGHT	19 76%	11 46% *	8 33% **
DIGIT 2 DISTAL PHALANX, RIGHT	13 52%	10 42%	7 29%
DIGIT 3 PROXIMAL PHALANX, RIGHT	5 20%	1 4%	0 *
DIGIT 3 DISTAL PHALANX, RIGHT	3 12%	1 4%	0
DIGIT 4 PROXIMAL PHALANX, RIGHT	9 36%	4 17%	0 **
DIGIT 4 DISTAL PHALANX, RIGHT	10 40%	3 13% *	2 8% *
METACARPALIA 5, RIGHT	2 8%	0	0
DIGIT 5 PROXIMAL PHALANX, RIGHT	23 92%	21 88%	18 75%
DIGIT 5 DISTAL PHALANX, RIGHT	24 96%	22 92%	19 79%
LEFT HIND LIMB			
NON-OSSIFIED			
TALUS LEFT	24 96%	22 92%	23 96%
METATARSALIA 1, LEFT	13 52%	7 29%	1 4% **
TOE 1 DISTAL PHALANX, LEFT	4 16%	0	0
TOE 2 PROXIMAL PHALANX, LEFT	22 88%	22 92%	22 92%
TOE 2 DISTAL PHALANX, LEFT	3 12%	0	0
TOE 3 PROXIMAL PHALANX, LEFT	21 84%	16 67%	16 67%
TOE 3 DISTAL PHALANX, LEFT	3 12%	0	0
TOE 4 PROXIMAL PHALANX, LEFT	21 84%	16 67%	11 46% **
TOE 4 DISTAL PHALANX, LEFT	3 12%	0	0
TOE 5 PROXIMAL PHALANX, LEFT	25 100%	24 100%	24 100%
TOE 5 DISTAL PHALANX, LEFT	4 16%	0	0
RIGHT HIND LIMB			
NON-OSSIFIED			
TALUS RIGHT	24 96%	22 92%	23 96%
METATARSALIA 1, RIGHT	14 56%	7 29%	1 4% **
TOE 1 DISTAL PHALANX, RIGHT	3 12%	0	0
TOE 2 PROXIMAL PHALANX, RIGHT	22 88%	22 92%	22 92%
TOE 2 DISTAL PHALANX, RIGHT	2 8%	0	0
TOE 3 PROXIMAL PHALANX, RIGHT	21 84%	18 75%	18 75%
TOE 3 DISTAL PHALANX, RIGHT	2 8%	0	0
TOE 4 PROXIMAL PHALANX, RIGHT	21 84%	18 75%	14 58% *
TOE 4 DISTAL PHALANX, RIGHT	2 8%	0	0
TOE 5 PROXIMAL PHALANX, RIGHT	25 100%	24 100%	24 100%
TOE 5 DISTAL PHALANX, RIGHT	3 12%	0	0

* / ** : Fisher's Exact test significant at 5% (*) or 1% (**) level

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SKELETAL EXAMINATION SUMMARY

—	GROUP 1 0 MG/KG		GROUP 2 1 MG/KG		GROUP 3 3 MG/KG	
NUMBER OF FETUSES EXAMINED	146		133		155	
UNLISTED FINDING(S) (SHOWN ON PREVIOUS PAGE(S))	6	4%	6	5%	3	2%
CRANIUM						
INCOMPLETELY OSSIFIED						
OS OCCIPITALE	6	4%	7	5%	0	*
OS PARIETALE, BILATERAL	8	5%	8	6%	1	1% *
OS INTERPARIETALE	17	12%	12	9%	1	1% **
CERVICAL VERTEBRAE						
NON-OSSIFIED						
CERVICAL VERTEBRA 1	22	15%	20	15%	21	14%
CERVICAL VERTEBRA 2	28	19%	13	10% *	11	7% **
CERVICAL VERTEBRA 3	15	10%	3	2% **	5	3% *
CERVICAL VERTEBRA 4	5	3%	0	*	2	1%
CERVICAL VERTEBRA 5	3	2%	0		0	
CERVICAL VERTEBRA 6	2	1%	0		0	
CERVICAL VERTEBRA 7	1	1%	0		0	
DUMBBELL SHAPE						
CERVICAL VERTEBRA 1	54	37%	50	38%	56	36%
BIPARTITE						
CERVICAL VERTEBRA 1	1	1%	6	5% *	3	2%
STERNUM						
INCOMPLETELY OSSIFIED						
STERNEBRA 1	2	1%	0		0	
STERNEBRA 2	10	7%	12	9%	6	4%
STERNEBRA 3	3	2%	2	2%	1	1%
STERNEBRA 4	11	8%	8	6%	8	5%
STERNEBRA 5	76	52%	82	62%	89	57%
STERNEBRA 6	2	1%	1	1%	1	1%
NON-OSSIFIED						
STERNEBRA 5	0		1	1%	1	1%
STERNEBRA 6	1	1%	0		0	
ABNORMALLY OSSIFIED						
STERNEBRA 4	0		3	2%	0	
STERNEBRA 5	1	1%	0		0	
RIB(S), LEFT						
SUPERNUMERARY, ONE						
RIB(S), LEFT	16	11%	16	12%	39	25% **
RIB(S), RIGHT						
SUPERNUMERARY, ONE						
RIB(S), RIGHT	17	12%	18	14%	40	26% **
LEFT FORELIMB						
NON-OSSIFIED						
DIGIT 1 DISTAL PHALANX, LEFT	8	5%	3	2%	0	**
DIGIT 2 PROXIMAL PHALANX, LEFT	57	39%	31	23% **	15	10% **
DIGIT 2 DISTAL PHALANX, LEFT	30	21%	17	13%	9	6% **
DIGIT 3 PROXIMAL PHALANX, LEFT	6	4%	1	1%	0	*
DIGIT 3 DISTAL PHALANX, LEFT	4	3%	1	1%	0	
DIGIT 4 PROXIMAL PHALANX, LEFT	11	8%	8	6%	2	1% **
DIGIT 4 DISTAL PHALANX, LEFT	11	8%	4	3%	3	2% *
METACARPALIA 5, LEFT	2	1%	0		0	
DIGIT 5 PROXIMAL PHALANX, LEFT	84	58%	65	49%	45	29% **
DIGIT 5 DISTAL PHALANX, LEFT	94	64%	75	56%	69	45% **

* / ** : Fisher's Exact test significant at 5% (*) or 1% (**) level

SKELETAL EXAMINATION SUMMARY

—	GROUP 1 0 MG/KG		GROUP 2 1 MG/KG			GROUP 3 3 MG/KG		
NUMBER OF FETUSES EXAMINED	146		133			155		
RIGHT FORELIMB								
NON-OSSIFIED								
DIGIT 1 DISTAL PHALANX, RIGHT	8	5%	3	2%		0		**
DIGIT 2 PROXIMAL PHALANX, RIGHT	53	36%	26	20%	**	15	10%	**
DIGIT 2 DISTAL PHALANX, RIGHT	24	16%	14	11%		9	6%	**
DIGIT 3 PROXIMAL PHALANX, RIGHT	5	3%	1	1%		0		*
DIGIT 3 DISTAL PHALANX, RIGHT	3	2%	1	1%		0		
DIGIT 4 PROXIMAL PHALANX, RIGHT	10	7%	7	5%		0		**
DIGIT 4 DISTAL PHALANX, RIGHT	11	8%	3	2%	*	3	2%	*
METACARPALIA 5, RIGHT	2	1%	0			0		
DIGIT 5 PROXIMAL PHALANX, RIGHT	82	56%	60	45%	*	43	28%	**
DIGIT 5 DISTAL PHALANX, RIGHT	89	61%	71	53%		66	43%	**
LEFT HIND LIMB								
NON-OSSIFIED								
TALUS LEFT	123	84%	92	69%	**	107	69%	**
METATARSALIA 1, LEFT	25	17%	10	8%	*	1	1%	**
TOE 1 DISTAL PHALANX, LEFT	4	3%	0			0		
TOE 2 PROXIMAL PHALANX, LEFT	102	70%	90	68%		79	51%	**
TOE 2 DISTAL PHALANX, LEFT	3	2%	0			0		
TOE 3 PROXIMAL PHALANX, LEFT	70	48%	53	40%		45	29%	**
TOE 3 DISTAL PHALANX, LEFT	3	2%	0			0		
TOE 4 PROXIMAL PHALANX, LEFT	67	46%	45	34%	*	33	21%	**
TOE 4 DISTAL PHALANX, LEFT	3	2%	0			0		
TOE 5 PROXIMAL PHALANX, LEFT	132	90%	112	84%		127	82%	*
TOE 5 DISTAL PHALANX, LEFT	4	3%	0			0		
RIGHT HIND LIMB								
NON-OSSIFIED								
TALUS RIGHT	124	85%	92	69%	**	109	70%	**
METATARSALIA 1, RIGHT	27	18%	11	8%	**	1	1%	**
TOE 1 DISTAL PHALANX, RIGHT	3	2%	0			0		
TOE 2 PROXIMAL PHALANX, RIGHT	102	70%	91	68%		80	52%	**
TOE 2 DISTAL PHALANX, RIGHT	2	1%	0			0		
TOE 3 PROXIMAL PHALANX, RIGHT	75	51%	63	47%		52	34%	**
TOE 3 DISTAL PHALANX, RIGHT	2	1%	0			0		
TOE 4 PROXIMAL PHALANX, RIGHT	76	52%	56	42%		40	26%	**
TOE 4 DISTAL PHALANX, RIGHT	2	1%	0			0		
TOE 5 PROXIMAL PHALANX, RIGHT	130	89%	116	87%		131	85%	
TOE 5 DISTAL PHALANX, RIGHT	3	2%	0			0		

* / ** : Fisher's Exact test significant at 5% (*) or 1% (**) level

BODY WEIGHTS OF LIVE FETUSES SUMMARY (PER DAM)
GROUP 1 (0 MG/KG)

LITTER	- MALES AND FEMALES - N	MEAN	ST.DEV.	------- MALES ------- N	MEAN	ST.DEV.	------ FEMALES ------ N	MEAN	ST.DEV.
1	11	4.6	0.3	7	4.7	0.3	4	4.4	0.2
2	13	4.6	0.2	8	4.6	0.2	5	4.5	0.2
3	10	4.8	0.3	4	4.9	0.5	6	4.8	0.2
4	12	5.0	0.3	5	5.3	0.2	7	4.9	0.3
5	12	4.6	0.5	5	4.8	0.2	7	4.4	0.6
6	14	4.5	0.2	5	4.6	0.2	9	4.5	0.2
7	11	4.4	0.3	7	4.5	0.4	4	4.3	0.1
8	8	4.7	0.1	5	4.8	0.1	3	4.7	0.1
9	9	4.7	0.3	5	4.8	0.3	4	4.6	0.2
10	11	4.9	0.1	4	5.0	0.1	7	4.9	0.1
11	13	4.6	0.3	8	4.8	0.2	5	4.4	0.1
12	15	4.4	0.3	6	4.7	0.1	9	4.1	0.1
13	15	4.4	0.3	6	4.5	0.3	9	4.3	0.2
14	11	4.8	0.2	8	4.8	0.2	3	4.8	0.2
15	11	4.6	0.4	7	4.6	0.5	4	4.5	0.1
16	14	4.8	0.2	8	4.9	0.2	6	4.7	0.2
17	13	4.7	0.2	5	4.8	0.1	8	4.6	0.2
18	13	4.6	0.5	5	4.8	0.4	8	4.5	0.5
19	8	5.2	0.3	4	5.2	0.3	4	5.1	0.3
20	9	4.2	0.4	6	4.3	0.4	3	4.0	0.5
21	14	4.5	0.3	7	4.6	0.2	7	4.4	0.4
22	5	3.9	1.2	3	4.1	1.3	2	3.6	1.5
23	5	5.3	0.3	3	5.5	0.1	2	5.0	0.2
24	7	4.8	0.1	2	4.9	0.3	5	4.7	0.1
25	11	5.1	0.2	5	5.2	0.3	6	5.0	0.2
N	275	25		138	25		137	25	
MEAN	11.0	4.7		5.5	4.8		5.5	4.6	
ST.DEV.	2.8	0.3		1.7	0.3		2.2	0.3	

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BODY WEIGHTS OF LIVE FETUSES SUMMARY (PER DAM)
GROUP 2 (1 MG/KG)

LITTER	MALES AND FEMALES N	MEAN	ST.DEV.	MALES N	MEAN	ST.DEV.	FEMALES N	MEAN	ST.DEV.
26	10	5.1	0.3	6	5.3	0.2	4	4.9	0.2
27	11	4.7	0.4	9	4.8	0.3	2	4.2	0.3
28	9	4.8	0.3	5	4.8	0.2	4	4.7	0.4
29	9	4.9	0.4	7	5.0	0.3	2	4.6	0.4
30	11	4.3	0.4	6	4.5	0.4	5	4.1	0.2
31	9	5.3	0.4	7	5.4	0.3	2	4.9	0.6
32	5	5.2	0.2	1	5.6		4	5.1	0.1
33	13	4.7	0.4	5	4.9	0.5	8	4.6	0.3
34	12	5.0	0.2	5	5.1	0.2	7	5.0	0.3
35	10	5.0	0.2	5	5.2	0.1	5	4.9	0.2
36	13	4.6	0.3	3	4.8	0.4	10	4.5	0.3
37	7	5.0	0.5	3	5.4	0.2	4	4.8	0.5
38	14	4.5	0.3	5	4.7	0.3	9	4.4	0.3
39	13	4.7	0.1	4	4.7	0.1	9	4.7	0.1
40	14	4.6	0.2	8	4.7	0.2	6	4.4	0.2
41	14	4.7	0.3	9	4.7	0.4	5	4.7	0.2
42	9	5.1	0.3	5	5.3	0.2	4	4.9	0.0
43	11	5.2	0.2	11	5.2	0.2	0		
44	10	5.2	0.3	4	5.4	0.3	6	5.0	0.3
45	9	5.0	0.2	6	5.1	0.2	3	4.8	0.2
46	9	4.7	0.3	6	4.8	0.3	3	4.6	0.3
47	12	4.8	0.1	5	4.9	0.1	7	4.7	0.0
48	8	4.9	0.3	3	5.1	0.4	5	4.7	0.2
49 <NP>									
50	10	4.8	0.2	4	4.8	0.1	6	4.9	0.3
N	252	24		132	24		120	23	
MEAN	10.5	4.9		5.5	5.0		5.0	4.7	
ST.DEV.	2.3	0.3		2.2	0.3		2.5	0.2	

Reason for Exclusion from Evaluation :
<NP> Non-Pregnant

BODY WEIGHTS OF LIVE FETUSES SUMMARY (PER DAM)
GROUP 3 (3 MG/KG)

LITTER	- MALES AND FEMALES - N	MEAN	ST.DEV.	------- MALES ------- N	MEAN	ST.DEV.	------ FEMALES ------ N	MEAN	ST.DEV.
51	7	5.0	0.2	3	5.1	0.4	4	4.9	0.1
52	16	5.0	0.2	8	5.1	0.2	8	4.8	0.2
53	10	4.7	0.3	3	5.0	0.2	7	4.5	0.3
54	11	5.0	0.3	4	5.0	0.4	7	5.0	0.2
55	13	4.8	0.2	6	4.9	0.1	7	4.7	0.2
56	13	4.8	0.3	5	4.9	0.2	8	4.7	0.2
57	11	5.0	0.3	5	5.2	0.2	6	4.9	0.2
58	12	4.9	0.2	7	5.0	0.2	5	4.7	0.1
59	16	4.7	0.3	8	4.8	0.3	8	4.7	0.2
60	14	4.8	0.3	8	4.9	0.2	6	4.6	0.4
61	10	5.2	0.2	4	5.3	0.1	6	5.1	0.1
62	13	4.8	0.3	8	4.9	0.2	5	4.6	0.2
63	13	4.9	0.3	11	4.9	0.3	2	4.6	0.3
64	12	5.3	0.2	11	5.3	0.2	1	4.9	
65	15	4.8	0.2	4	5.0	0.2	11	4.7	0.2
66	11	5.2	0.4	6	5.4	0.4	5	5.0	0.3
67	12	5.1	0.2	8	5.2	0.2	4	4.8	0.1
68	16	4.9	0.2	10	5.0	0.2	6	4.7	0.2
69 <OI>									
70	17	4.6	0.4	11	4.6	0.4	6	4.5	0.2
71	10	5.1	0.3	3	5.1	0.2	7	5.1	0.3
72	14	4.7	0.2	7	4.8	0.2	7	4.6	0.2
73	11	5.0	0.4	5	5.1	0.4	6	4.9	0.3
74	11	4.9	0.3	5	5.2	0.3	6	4.7	0.2
75	10	4.7	0.3	4	4.9	0.3	6	4.6	0.1
N	298	24		134	24		144	24	
MEAN	12.4	4.9		6.4	5.0		6.0	4.8	
ST.DEV.	2.4	0.2		2.6	0.2		2.0	0.2	

Reason for Exclusion from Evaluation :
<OI> Implantation Sites only

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DISTRIBUTION WITHIN UTERUS
GROUP 1 (0 MG/KG)

LEFT HORN						POSITION	RIGHT HORN					
IMPLAN-TATIONS	EMPTY SITES	RESORPTIONS EMBR.	RESORPTIONS FETAL	FETUSES DEAD	FETUSES LIVE	IN UTERUS	FETUSES LIVE	FETUSES DEAD	RESORPTIONS FETAL	RESORPTIONS EMBR.	EMPTY SITES	IMPLAN-TATIONS
25	.	2	.	.	23	< 1>	24	.	.	1	.	25
25	.	4	.	.	21	< 2>	22	.	.	3	.	25
24	.	2	.	.	22	< 3>	20	.	.	2	.	22
24	.	2	.	.	22	< 4>	18	.	.	2	.	20
22	.	1	.	.	21	< 5>	16	.	.	.	.	16
19	.	4	.	.	15	< 6>	12	.	.	.	.	12
11	.	3	.	.	8	< 7>	9	.	.	.	.	9
8	.	1	.	.	7	< 8>	6	.	.	.	.	6
5	.	1	.	.	4	< 9>	3	.	.	.	.	3
2	.	.	.	.	2	<10>	.	.	.	1	.	1

IMPLANTATION SITES

```
25 ========================= < 1> ========================= 25
25 ========================= < 2> ========================= 25
 24 ========================= < 3> ======================= 22
 24 ========================= < 4> ====================== 20
   22 ======================= < 5> ================ 16
      19 ===================== < 6> ============ 12
              11 ============ < 7> ========= 9
                  8 ========= < 8> ====== 6
                     5 ===== < 9> === 3
                       2 == <10> = 1
```

LIVE FETUSES

```
23 ======================= < 1> ========================= 24
  21 ======================= < 2> ======================= 22
 22 ======================= < 3> ====================== 20
 22 ======================= < 4> ================== 18
  21 ======================= < 5> ================ 16
        15 ================ < 6> ============ 12
                  8 ========= < 8> ====== 6
                   7 ======== < 9> === 3
                     4 ==== < 9> ===
                       2 == <10>
```

RESORPTIONS

```
  2 == < 1> = 1
4 ==== < 2> === 3
  2 == < 3> == 2
  2 == < 4> == 2
   1 = < 5>
4 ==== < 6>
 3 === < 7>
   1 = < 8>
   1 = < 9>
       <10> = 1
```

DISTRIBUTION WITHIN UTERUS
GROUP 2 (1 MG/KG)

LEFT HORN						POSITION	RIGHT HORN					
IMPLAN-TATIONS	EMPTY SITES	RESORPTIONS EMBR.	RESORPTIONS FETAL	FETUSES DEAD	FETUSES LIVE	IN UTERUS	FETUSES LIVE	FETUSES DEAD	RESORPTIONS FETAL	RESORPTIONS EMBR.	EMPTY SITES	IMPLAN-TATIONS
24	.	1	.	.	23	< 1>	19	.	.	4	.	23
24	.	3	.	.	21	< 2>	21	.	1	1	.	23
23	.	4	.	.	19	< 3>	22	.	.	1	.	23
22	.	.	.	.	22	< 4>	21	.	.	1	.	22
19	.	1	.	.	18	< 5>	19	.	.	.	.	19
12	.	1	.	.	11	< 6>	12	.	.	1	.	13
6	.	.	.	.	6	< 7>	9	.	.	.	.	9
3	.	.	.	.	3	< 8>	3	.	.	2	.	5
2	.	.	.	.	2	< 9>	.	.	.	1	.	1
1	.	1	.	.	.	<10>	1	.	.	.	.	1

IMPLANTATION SITES

```
24 ======================== < 1> ========================  23
24 ======================== < 2> ========================  23
 23 ======================= < 3> ========================  23
  22 ======================= < 4> ========================  22
     19 ===================== < 5> ====================  19
            12 ============ < 6> ============  13
                   6 ====== < 7> ========= 9
                      3 === < 8> ===== 5
                       2 == < 9> = 1
                        1 = <10> = 1
```

LIVE FETUSES

```
23 ======================= < 1> ====================  19
  21 ======================= < 2> ========================  21
    19 ===================== < 3> ========================  22
 22 ======================= < 4> ========================  21
     18 ==================== < 5> ====================  19
            11 =========== < 6> ============  12
                   6 ====== < 7> ========= 9
                      3 === < 8> === 3
                       2 == < 9>
                            <10> = 1
```

RESORPTIONS

```
 1 = < 1> ==== 4
3 === < 2> == 2
4 ==== < 3> = 1
       < 4> = 1
 1 = < 5>
 1 = < 6> = 1
       < 7>
       < 8> == 2
       < 9> = 1
 1 = <10>
```

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DISTRIBUTION WITHIN UTERUS
GROUP 3 (3 MG/KG)

LEFT HORN						POSITION	RIGHT HORN				
IMPLAN-TATIONS	EMPTY SITES	RESORPTIONS EMBR.	RESORPTIONS FETAL	FETUSES DEAD	FETUSES LIVE	IN UTERUS	FETUSES LIVE	FETUSES DEAD	RESORPTIONS FETAL	RESORPTIONS EMBR.	EMPTY SITES	IMPLAN-TATIONS
24	.	.	.	.	24	< 1>	22	.	.	1	.	23
24	.	1	.	.	23	< 2>	19	.	.	4	.	23
24	.	2	.	.	22	< 3>	23	.	.	.	.	23
22	.	.	.	.	22	< 4>	22	.	.	1	.	23
20	.	1	.	.	19	< 5>	20	.	.	1	.	21
19	.	.	.	.	19	< 6>	14	.	.	1	.	15
14	.	.	.	.	14	< 7>	12	.	.	.	.	12
4	.	.	.	.	4	< 8>	9	.	.	.	.	9
2	.	.	.	.	2	< 9>	4	.	.	.	.	4
1	.	.	.	.	1	<10>	2	.	.	.	.	2
1	.	.	.	.	1	<11>						

IMPLANTATION SITES

```
24 ======================== < 1> ======================== 23
24 ======================== < 2> ======================== 23
24 ======================== < 3> ======================== 23
  22 ======================= < 4> ======================= 23
    20 ====================== < 5> ====================== 21
     19 ===================== < 6> ================ 15
          14 =============== < 7> ============ 12
                       4 ==== < 8> ========= 9
                         2 == < 9> ==== 4
                          1 = <10> == 2
                          1 = <11>
```

LIVE FETUSES

```
24 ======================== < 1> ======================= 22
 23 ======================= < 2> ================== 19
  22 ======================= < 3> ======================== 23
  22 ======================= < 4> ======================= 22
     19 ===================== < 5> ===================== 20
     19 ===================== < 6> ================ 14
          14 =============== < 7> ============ 12
                       4 ==== < 8> ========= 9
                         2 == < 9> ==== 4
                          1 = <10> == 2
                          1 = <11>
```

RESORPTIONS

```
          < 1> = 1
        1 = < 2> ==== 4
        2 == < 3>
          < 4> = 1
        1 = < 5> = 1
          < 6> = 1
          < 7>
          < 8>
          < 9>
          <10>
          <11>
```

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 1 (0 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES (POS. IN UTERUS)	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 1											
7/7	1	M	4.8		A	LIVE <1> LIVE	6	F	4.1		W
						E.RES <2> LIVE	7	M	5.0		A
						E.RES <3> LIVE	8	M	4.6		W
	2	M	4.9		W	LIVE <4> LIVE	9	F	4.6		A
	3	F	4.6		A	LIVE <5> LIVE	10	M	4.2		W
	4	F	4.3		W	LIVE <6> LIVE	11	M	4.7		A
	5	M	4.5		A	LIVE <7>					
FEMALE 2											
9/4	12	F	4.7		A	LIVE <1> LIVE	21	M	4.5		W
	13	M	4.6		W	LIVE <2> LIVE	22	M	4.6		A
	14	M	4.4		A	LIVE <3> LIVE	23	M	4.9		W
	15	F	4.5		W	LIVE <4> LIVE	24	M	4.9		A
	16	F	4.7		A	LIVE <5>					
	17	M	4.7		W	LIVE <6>					
	18	F	4.4		A	LIVE <7>					
	19	F	4.2		W	LIVE <8>					
	20	M	4.6		A	LIVE <9>					
FEMALE 3											
6/5	25	F	4.8		A	LIVE <1> LIVE	30	F	4.9		W
	26	M	5.4		W	LIVE <2> LIVE	31	F	5.0		A
	27	M	4.9		A	LIVE <3> LIVE	32	F	4.8		W
	28	M	4.3		W	LIVE <4> LIVE	33	M	5.1		A
	29	F	4.6		A	LIVE <5> LIVE	34	F	4.4		W
						E.RES <6>					
FEMALE 4											
10/2	35	M	5.4		A	LIVE <1> LIVE	45	F	4.9		A
	36	M	5.0		W	LIVE <2> LIVE	46	F	4.9		W
	37	M	5.3		A	LIVE <3>					
	38	F	5.1		W	LIVE <4>					
	39	M	5.2		A	LIVE <5>					
	40	F	4.7		W	LIVE <6>					
	41	F	4.9		A	LIVE <7>					
	42	F	5.3		W	LIVE <8>					
	43	M	5.4		A	LIVE <9>					
	44	F	4.3		W	LIVE <10>					
FEMALE 5											
6/9	47	F	4.4		A	LIVE <1> LIVE	52	F	5.0		W
	48	F	4.6		W	LIVE <2> LIVE	53	F	4.5		A
	49	M	5.0		A	LIVE <3> E.RES					
	50	F	4.4		W	LIVE <4> LIVE	54	M	4.9		W
	51	F	4.9		A	LIVE <5> LIVE	55	M	4.7		A
						<6> LIVE	56	M	4.6		W
						<7> LIVE	57	F	3.1		A
						<8> LIVE	58	M	4.8		W
FEMALE 6											
9/5	59	F	4.3		A	LIVE <1> LIVE	68	F	4.9		W
	60	F	4.2		W	LIVE <2> LIVE	69	M	4.8		A
	61	F	4.3		A	LIVE <3> LIVE	70	F	4.9		W
	62	M	4.5		W	LIVE <4> LIVE	71	F	4.4		A
	63	F	4.5		A	LIVE <5> LIVE	72	F	4.3		W
	64	F	4.7		W	LIVE <6>					
	65	M	4.8		A	LIVE <7>					
	66	M	4.6		W	LIVE <8>					
	67	M	4.4		A	LIVE <9>					

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 1 (0 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES <POS. IN UTERUS>			FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 7													
8/3	73	M	4.7		A	LIVE	<1>	LIVE	81	F	4.4		A
	74	M	5.0		W	LIVE	<2>	LIVE	82	F	4.2		W
	75	M	4.8		A	LIVE	<3>	LIVE	83	F	4.3		A
	76	F	4.5		W	LIVE	<4>						
	77	M	4.0		A	LIVE	<5>						
	78	M	4.5		W	LIVE	<6>						
	79	M	4.1		A	LIVE	<7>						
	80	M	4.2		W	LIVE	<8>						
FEMALE 8													
2/6	84	F	4.8		A	LIVE	<1>	LIVE	86	F	4.6		A
	85	M	4.8		W	LIVE	<2>	LIVE	87	M	4.8		W
							<3>	LIVE	88	M	4.8		A
							<4>	LIVE	89	M	4.9		W
							<5>	LIVE	90	F	4.7		A
							<6>	LIVE	91	M	4.6		W
FEMALE 9													
7/5	92	F	4.8		A	LIVE	<1>	LIVE	97	M	5.0		W
	93	M	5.0		W	LIVE	<2>	LIVE	98	F	4.3		A
	94	M	4.3		A	LIVE	<3>	LIVE	99	M	5.0		W
						E.RES	<4>	LIVE	100	F	4.6		A
	95	M	4.9		W	LIVE	<5>						
						E.RES	<6>						
	96	F	4.6		A	LIVE	<7>						
FEMALE 10													
7/5	101	F	5.0		A	LIVE	<1>	LIVE	107	F	4.9		A
	102	M	4.9		W	LIVE	<2>	LIVE	108	F	5.1		W
	103	F	4.9		A	LIVE	<3>	LIVE	109	F	4.8		A
	104	M	4.9		W	LIVE	<4>	LIVE	110	F	4.9		W
	105	M	4.9		A	LIVE	<5>	LIVE	111	M	5.1		A
	106	F	4.8		W	LIVE	<6>						
FEMALE 11													
9/6	112	F	4.4		A	LIVE	<1>	LIVE	119	M	4.6		W
	113	M	4.5		W	LIVE	<2>	LIVE	120	F	4.3		A
	114	M	4.9		A	LIVE	<3>	LIVE	121	F	4.4		W
	115	M	4.7		W	LIVE	<4>	LIVE	122	M	5.2		A
	116	M	4.9		A	LIVE	<5>	LIVE	123	M	5.0		W
	117	F	4.5		W	LIVE	<6>	LIVE	124	M	4.6		A
	118	F	4.4		A	LIVE	<7>						
FEMALE 12													
6/10	125	M	4.6		A	LIVE	<1>	LIVE	131	F	4.3		A
	126	F	4.3		W	LIVE	<2>	LIVE	132	M	4.8		W
	127	F	4.0		A	LIVE	<3>	LIVE	133	F	4.2		A
	128	F	4.2		W	LIVE	<4>	LIVE	134	M	4.9		W
	129	M	4.7		A	LIVE	<5>	LIVE	135	F	4.0		A
	130	M	4.7		W	LIVE	<6>	LIVE	136	F	4.3		W
							<7>	LIVE	137	M	4.5		A
							<8>	LIVE	138	F	4.2		W
							<9>	LIVE	139	F	3.9		A

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 1 (0 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES (POS. IN UTERUS)			FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 13													
6/10	140	M	4.8		A	LIVE	<1>	LIVE	146	M	4.8		A
	141	F	4.5		W	LIVE	<2>	LIVE	147	F	4.6		W
	142	M	4.2		A	LIVE	<3>	LIVE	148	F	4.6		A
	143	M	4.5		W	LIVE	<4>	LIVE	149	M	4.6		W
	144	M	4.3		A	LIVE	<5>	LIVE	150	F	4.1		A
	145	F	4.0		W	LIVE	<6>	LIVE	151	F	4.2		W
							<7>	LIVE	152	F	4.1		A
							<8>	LIVE	153	F	4.0		W
							<9>	LIVE	154	F	4.4		A
FEMALE 14													
9/4	249	F	5.1		A	LIVE	<1>	LIVE	257	M	5.1		A
	250	M	4.6		W	LIVE	<2>	LIVE	258	F	4.7		W
	251	M	4.8		A	LIVE	<3>	LIVE	259	M	4.8		A
	252	M	4.7		W	LIVE	<4>	E.RES					
	253	M	5.3		A	LIVE	<5>						
	254	F	4.7		W	LIVE	<6>						
	255	M	4.7		A	LIVE	<7>						
	256	M	4.7		W	LIVE	<8>						
FEMALE 15													
5/8	260	F	4.6		A	LIVE	<1>	LIVE	264	M	5.0		A
	261	M	4.2		W	LIVE	<2>	LIVE	265	M	4.5		W
	262	M	4.8		A	LIVE	<3>	LIVE	266	F	4.6		A
	263	F	4.3		W	LIVE	<4>	LIVE	267	F	4.6		W
							<5>	LIVE	268	M	5.3		A
							<6>	LIVE	269	M	4.8		W
							<7>	LIVE	270	M	3.8		A
FEMALE 16													
6/10	271	M	4.8		A	LIVE	<1>	LIVE	277	M	5.3		A
	272	M	4.8		W	LIVE	<2>	E.RES					
	273	F	4.9		A	LIVE	<3>	LIVE	278	F	4.6		W
	274	F	4.9		W	LIVE	<4>	LIVE	279	M	4.8		A
	275	M	4.9		A	LIVE	<5>	LIVE	280	M	4.9		W
	276	F	4.5		W	LIVE	<6>	LIVE	281	M	5.1		A
							<7>	LIVE	282	F	4.6		W
							<8>	LIVE	283	F	4.8		A
							<9>	LIVE	284	M	4.7		W
							<10>	E.RES					
FEMALE 17													
6/8	285	M	4.9		A	LIVE	<1>	LIVE	291	F	4.7		A
	286	F	4.8		W	LIVE	<2>	LIVE	292	M	4.7		W
	287	M	4.7		A	LIVE	<3>	LIVE	293	M	4.8		A
	288	F	4.9		W	LIVE	<4>	LIVE	294	F	4.4		W
	289	F	4.7		A	LIVE	<5>	LIVE	295	F	4.7		A
	290	F	4.4		W	LIVE	<6>	LIVE	296	M	4.8		W
							<7>	LIVE	297	F	4.4		A
FEMALE 18													
5/10/	298	F	4.8		A	LIVE	<1>	LIVE	303	M	4.6		W
	299	M	5.0		W	LIVE	<2>	LIVE	304	M	5.4		A
	300	F	4.5		A	LIVE	<3>	LIVE	305	F	4.7		W
	301	F	4.0		W	LIVE	<4>	LIVE	306	F	5.0		A
	302	M	4.3		A	LIVE	<5>	LIVE	307	F	4.9		W
							<6>	LIVE	308	F	3.6		A
							<7>	LIVE	309	M	4.9		W
							<8>	LIVE	310	F	4.4		A

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 1 (0 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W
FEMALE 19											
5/5						E.RES <1> LIVE	314	F	5.3		W
						E.RES <2> LIVE	315	F	5.4		A
	311	F	4.9		A	LIVE <3> LIVE	316	M	5.3		W
	312	M	5.0		W	LIVE <4> LIVE	317	M	5.6		A
	313	F	4.8		A	LIVE <5> LIVE	318	M	4.9		W
FEMALE 20											
9/3	319	M	4.8		A	LIVE <1> LIVE	325	M	3.8		A
	320	F	3.5		W	LIVE <2> LIVE	326	M	4.4		W
	321	M	4.2		A	LIVE <3> LIVE	327	F	4.5		A
	322	M	4.7		W	LIVE <4>					
	323	M	4.0		A	LIVE <5>					
						E.RES <6>					
						E.RES <7>					
	324	F	4.0		W	LIVE <8>					
FEMALE 21											
6/8	328	F	4.7		A	LIVE <1> LIVE	334	F	4.5		A
	329	M	4.7		W	LIVE <2> LIVE	335	F	4.4		W
	330	M	4.7		A	LIVE <3> LIVE	336	M	5.0		A
	331	F	4.6		W	LIVE <4> LIVE	337	M	4.6		W
	332	F	3.5		A	LIVE <5> LIVE	338	M	4.5		A
	333	M	4.4		W	LIVE <6> LIVE	339	F	4.7		W
						<7> LIVE	340	M	4.7		A
						<8> LIVE	341	F	4.4		W
FEMALE 22											
10/3						E.RES <1> LIVE	346	M	2.6		A
						E.RES <2> E.RES					
						E.RES <3>					
						E.RES <4>					
	342	M	4.9		A	LIVE <5>					
	343	F	4.6		W	LIVE <6>					
						E.RES <7>					
	344	M	4.9		A	LIVE <8>					
	345	F	2.6		W	LIVE <9>					
FEMALE 23											
12/4	347	M	5.3		A	LIVE <1> E.RES					
	348	F	4.9		W	LIVE <2> E.RES					
	349	M	5.6		A	LIVE <3> E.RES					
	350	M	5.5		W	LIVE <4> E.RES					
						E.RES <5>					
						E.RES <6>					
						E.RES <7>					
						E.RES <8>					
						E.RES <9>					
	351	F	5.1		A	LIVE <10>					
FEMALE 24											
6/7	728	F	4.7		A	LIVE <1> LIVE	733	M	5.1		W
						E.RES <2> LIVE	734	F	4.7		A
	729	F	4.9		W	LIVE <3>					
	730	M	4.7		A	LIVE <4>					
	731	F	4.8		W	LIVE <5>					
	732	F	4.7		A	LIVE <6>					

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 1 (0 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES <POS. IN UTERUS>			FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 25													
6/8	735	F	5.2		A	LIVE	<1>	LIVE	739	F	5.0		A
	736	M	5.2		W	LIVE	<2>	LIVE	740	M	5.5		W
	737	F	5.1		A	LIVE	<3>	LIVE	741	F	5.0		A
	738	F	4.8		W	LIVE	<4>	LIVE	742	F	5.2		W
							<5>	LIVE	743	M	5.2		A
							<6>	LIVE	744	M	5.4		W
							<7>	LIVE	745	M	4.8		A

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LIVE - LIVE FETUS
DEAD - DEAD FETUS
E.RES - EMBRYONIC RESORPTION
F.RES - FETAL RESORPTION
W - WILSON SLICING TECHNIQUE
A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 2 (1 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W	IMPLANTATION SITES (POS. IN UTERUS)	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W
FEMALE 26											
8/4	155	F	5.2		A	LIVE <1> LIVE	162	M	5.2		W
	156	M	5.5		W	LIVE <2> LIVE	163	M	5.5		A
	157	F	4.8		A	LIVE <3> LIVE	164	F	4.7		W
	158	M	5.1		W	LIVE <4>					
	159	F	4.9		A	LIVE <5>					
	160	M	5.2		W	LIVE <6>					
	161	M	5.2		A	LIVE <7>					
FEMALE 27											
6/5	165	M	4.8		A	LIVE <1> LIVE	171	M	5.2		A
	166	M	5.0		W	LIVE <2> LIVE	172	F	4.5		W
	167	M	5.0		A	LIVE <3> LIVE	173	M	5.2		A
	168	M	4.4		W	LIVE <4> LIVE	174	M	4.5		W
	169	M	4.6		A	LIVE <5> LIVE	175	M	4.6		A
	170	F	4.0		W	LIVE <6>					
FEMALE 28											
5/8	176	M	5.0		A	LIVE <1> LIVE	180	M	4.6		A
	177	M	5.1		W	LIVE <2> LIVE	181	F	5.0		W
	178	M	4.9		A	LIVE <3> LIVE	182	F	4.9		A
	179	F	4.2		W	LIVE <4> E.RES					
						<5> LIVE	183	F	4.9		W
						<6> E.RES					
						<7> LIVE	184	M	4.6		A
						<8> E.RES					
FEMALE 29											
3/7	185	M	4.8		A	LIVE <1> LIVE	187	F	4.9		A
	186	M	5.2		W	LIVE <2> LIVE	188	F	4.4		W
						E.RES <3> LIVE	189	M	5.0		A
						<4> LIVE	190	M	5.3		W
						<5> LIVE	191	M	5.3		A
						<6> LIVE	192	M	4.8		W
						<7> LIVE	193	M	4.3		A
FEMALE 30											
7/5	194	F	4.3		A	LIVE <1> LIVE	200	M	4.5		A
						E.RES <2> LIVE	201	F	3.9		W
	195	F	4.2		W	LIVE <3> LIVE	202	M	4.8		A
	196	F	4.2		A	LIVE <4> LIVE	203	M	4.7		W
	197	F	3.9		W	LIVE <5> LIVE	204	M	4.9		A
	198	M	4.4		A	LIVE <6>					
	199	M	3.7		W	LIVE <7>					
FEMALE 31											
7/4	352	M	5.5		A	LIVE <1> LIVE	357	F	5.3		W
	353	M	5.4		W	LIVE <2> LIVE	358	M	5.8		A
	354	M	5.5		A	LIVE <3> LIVE	359	M	5.3		W
	355	M	5.7		W	LIVE <4> LIVE	360	M	4.9		A
	356	F	4.4		A	LIVE <5>					
						E.RES <6>					
FEMALE 32											
5/5	361	M	5.6		A	LIVE <1>					
	362	F	5.3		W	LIVE <2>					
	363	F	5.1		A	LIVE <3>					
	364	F	5.2		W	LIVE <4>					
	365	F	5.0		A	LIVE <5>					

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 2 (1 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W
FEMALE 33											
7/9	366	M	5.4		A	LIVE <1> E.RES					
	367	M	4.9		W	LIVE <2> LIVE	372	F	4.9		A
	368	F	4.8		A	LIVE <3> LIVE	373	F	4.5		W
	369	M	4.0		W	LIVE <4> LIVE	374	F	4.9		A
	370	F	4.7		A	LIVE <5> LIVE	375	M	5.1		W
	371	M	5.0		W	LIVE <6> LIVE	376	F	4.1		A
						<7> LIVE	377	F	4.7		W
						<8> LIVE	378	F	4.6		A
FEMALE 34											
7/7	379	M	5.2		A	LIVE <1> LIVE	384	M	5.1		W
	380	M	4.8		W	LIVE <2> LIVE	385	F	4.9		A
	381	M	5.1		A	LIVE <3> LIVE	386	F	5.1		W
	382	F	5.2		W	LIVE <4> LIVE	387	F	4.9		A
	383	M	5.2		A	LIVE <5> LIVE	388	F	5.3		W
						<6> LIVE	389	F	4.5		A
						<7> LIVE	390	F	5.1		W
FEMALE 35											
4/9	391	F	5.1		A	LIVE <1> LIVE	393	M	5.2		A
	392	M	5.1		W	LIVE <2> LIVE	394	M	5.1		W
						<3> LIVE	395	F	5.0		A
						<4> LIVE	396	M	5.1		W
						<5> LIVE	397	M	5.2		A
						<6> LIVE	398	F	5.1		W
						<7> LIVE	399	F	4.8		A
						<8> LIVE	400	F	4.8		W
FEMALE 36											
7/7	401	F	4.8		A	LIVE <1> LIVE	407	M	5.3		A
	402	M	4.9		W	LIVE <2> LIVE	408	M	4.4		W
	403	F	4.5		A	LIVE <3> LIVE	409	F	4.6		A
	404	F	4.2		W	LIVE <4> LIVE	410	F	4.7		W
	405	F	4.6		A	LIVE <5> LIVE	411	F	4.1		A
	406	F	4.2		W	LIVE <6> LIVE	412	F	4.7		W
						<7> LIVE	413	F	4.4		A
FEMALE 37											
6/4	414	M	5.2		A	LIVE <1> LIVE	418	M	5.6		A
	415	F	4.2		W	LIVE <2> LIVE	419	F	5.2		W
						E.RES <3> E.RES					
	416	F	5.0		A	LIVE <4> LIVE	420	M	5.3		A
	417	F	4.8		W	LIVE <5>					
FEMALE 38											
9/6	421	F	4.8		A	LIVE <1> LIVE	429	F	4.5		A
						E.RES <2> LIVE	430	M	5.0		W
	422	M	4.4		W	LIVE <3> LIVE	431	M	4.7		A
	423	F	3.8		A	LIVE <4> LIVE	432	M	4.9		W
	424	F	4.6		W	LIVE <5> LIVE	433	F	4.3		A
	425	F	4.4		A	LIVE <6> LIVE	434	F	4.6		W
	426	F	4.3		W	LIVE <7>					
	427	M	4.5		A	LIVE <8>					
	428	F	4.5		W	LIVE <9>					

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DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 2 (1 MG/KG)

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CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 39											
10/5	435	F	4.9		A	LIVE <1> E.RES					
	436	F	4.8		W	LIVE <2> LIVE	444	F	4.6		W
	437	F	4.6		A	LIVE <3> LIVE	445	M	4.9		A
	438	F	4.6		W	LIVE <4> LIVE	446	F	4.7		W
	439	M	4.9		A	LIVE <5> LIVE	447	F	4.8		A
	440	F	4.6		W	LIVE <6>					
	441	M	4.6		A	LIVE <7>					
	442	F	4.6		W	LIVE <8>					
	443	M	4.6		A	LIVE <9>					
						E.RES<10>					
FEMALE 40											
7/8	448	M	4.8		A	LIVE <1> LIVE	455	F	4.6		W
	449	M	5.0		W	LIVE <2> E.RES					
	450	F	4.3		A	LIVE <3> LIVE	456	F	4.2		A
	451	F	4.6		W	LIVE <4> LIVE	457	M	4.5		W
	452	F	4.4		A	LIVE <5> LIVE	458	M	4.5		A
	453	F	4.4		W	LIVE <6> LIVE	459	M	4.7		W
	454	M	4.6		A	LIVE <7> LIVE	460	M	4.5		A
						<8> LIVE	461	M	4.9		W
FEMALE 41											
8/6	462	M	4.9		A	LIVE <1> LIVE	470	F	5.0		A
	463	F	4.7		W	LIVE <2> LIVE	471	M	5.2		W
	464	F	4.4		A	LIVE <3> LIVE	472	F	4.7		A
	465	M	4.2		W	LIVE <4> LIVE	473	M	5.1		W
	466	M	4.6		A	LIVE <5> LIVE	474	F	4.7		A
	467	M	4.8		W	LIVE <6> LIVE	475	M	5.2		W
	468	M	4.3		A	LIVE <7>					
	469	M	4.3		W	LIVE <8>					
FEMALE 42											
6/6	476	M	5.2		A	LIVE <1> LIVE	481	F	4.9		W
	477	M	5.2		W	LIVE <2> LIVE	482	M	5.1		A
	478	M	5.7		A	LIVE <3> LIVE	483	M	5.2		W
	479	F	4.9		W	LIVE <4> LIVE	484	F	4.9		A
	480	F	4.9		A	LIVE <5>					
FEMALE 43											
6/7	485	M	5.5		A	LIVE <1> E.RES					
	486	M	5.1		W	LIVE <2> LIVE	491	M	5.7		A
	487	M	5.4		A	LIVE <3> LIVE	492	M	5.2		W
	488	M	5.2		W	LIVE <4> LIVE	493	M	5.1		A
	489	M	4.9		A	LIVE <5> LIVE	494	M	5.3		W
	490	M	5.1		W	LIVE <6> LIVE	495	M	5.3		A
FEMALE 44											
4/10	496	F	4.8		A	LIVE <1> LIVE	499	M	5.8		W
						E.RES <2> F.RES					
	497	F	5.2		W	LIVE <3> LIVE	500	F	4.7		A
	498	M	5.4		A	LIVE <4> LIVE	501	M	5.2		W
						<5> LIVE	502	F	5.3		A
						<6> LIVE	503	M	5.2		W
						<7> LIVE	504	F	4.9		A
						<8> E.RES					
						<9> E.RES					
						<10> LIVE	505	F	5.2		W

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 2 (1 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 45											
6/8						E.RES <1> E.RES					
	746	M	5.3		A	LIVE <2> LIVE	749	M	5.0		W
						E.RES <3> LIVE	750	F	5.0		A
	747	M	5.3		W	LIVE <4> LIVE	751	M	4.9		W
	748	F	4.8		A	LIVE <5> LIVE	752	M	4.9		A
						<6> LIVE	753	M	5.2		W
						<7> LIVE	754	F	4.6		A
FEMALE 46											
7/7	755	M	5.2		A	LIVE <1> LIVE	759	F	4.6		A
	756	M	4.8		W	LIVE <2> LIVE	760	F	4.4		W
	757	F	4.9		A	LIVE <3> LIVE	761	M	5.1		A
	758	M	4.5		W	LIVE <4> LIVE	762	M	4.6		W
						<5> LIVE	763	M	4.8		A
FEMALE 47											
6/6	764	F	4.8		A	LIVE <1> LIVE	770	M	5.0		A
	765	F	4.7		W	LIVE <2> LIVE	771	F	4.7		W
	766	M	5.0		A	LIVE <3> LIVE	772	M	4.9		A
	767	F	4.8		W	LIVE <4> LIVE	773	F	4.7		W
	768	F	4.7		A	LIVE <5> LIVE	774	F	4.8		A
	769	M	4.6		W	LIVE <6> LIVE	775	M	4.9		W
FEMALE 48											
6/5	776	M	5.3		A	LIVE <1> LIVE	779	F	4.8		W
	777	F	4.7		W	LIVE <2> LIVE	780	F	5.1		A
						E.RES <3> LIVE	781	M	5.3		W
	778	F	4.6		A	LIVE <4> LIVE	782	M	4.7		A
						E.RES <5> LIVE	783	F	4.6		W
FEMALE 49	(Non-Pregnant)										
FEMALE 50											
5/5	784	M	5.0		A	LIVE <1> LIVE	789	M	4.7		W
	785	F	5.1		W	LIVE <2> LIVE	790	F	4.5		A
	786	M	4.8		A	LIVE <3> LIVE	791	F	5.1		W
	787	M	4.7		W	LIVE <4> LIVE	792	F	4.9		A
	788	F	4.5		A	LIVE <5> LIVE	793	F	5.1		W

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 3 (3 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/ W
FEMALE 51											
9/5	205	M	5.4		A	LIVE <1>					
	206	M	5.3		W	LIVE <2>					
	207	F	4.9		A	LIVE <3>					
	208	F	4.9		W	LIVE <4>					
	209	F	4.9		A	LIVE <5>					
	210	M	4.7		W	LIVE <6>					
	211	F	5.1		A	LIVE <7>					
FEMALE 52											
11/6	212	F	5.0		A	LIVE <1> LIVE	223	M	5.3		W
	213	F	4.9		W	LIVE <2> LIVE	224	F	4.8		A
	214	M	4.9		A	LIVE <3> LIVE	225	M	5.1		W
	215	F	4.6		W	LIVE <4> LIVE	226	M	5.4		A
	216	F	4.5		A	LIVE <5> LIVE	227	M	5.2		W
	217	F	5.0		W	LIVE <6>					
	218	F	5.0		A	LIVE <7>					
	219	F	4.7		W	LIVE <8>					
	220	M	4.9		A	LIVE <9>					
	221	M	5.3		W	LIVE <10>					
	222	M	5.1		A	LIVE <11>					
FEMALE 53											
5/6	228	F	5.0		A	LIVE <1> LIVE	233	M	5.2		W
	229	F	4.6		W	LIVE <2> E.RES					
	230	F	4.3		A	LIVE <3> LIVE	234	M	4.9		A
	231	F	4.7		W	LIVE <4> LIVE	235	F	4.0		W
	232	F	4.6		A	LIVE <5> LIVE	236	F	4.6		A
						<6> LIVE	237	M	4.9		W
FEMALE 54											
7/4	238	F	5.1		A	LIVE <1> LIVE	245	F	4.9		W
	239	M	4.6		W	LIVE <2> LIVE	246	F	5.2		A
	240	M	5.2		A	LIVE <3> LIVE	247	F	4.6		W
	241	M	5.5		W	LIVE <4> LIVE	248	F	5.1		A
	242	F	4.9		A	LIVE <5>					
	243	F	4.9		W	LIVE <6>					
	244	M	4.7		A	LIVE <7>					
FEMALE 55											
8/8	506	M	4.9		A	LIVE <1> LIVE	513	M	4.8		W
	507	M	4.8		W	LIVE <2> LIVE	514	F	4.9		A
	508	F	4.7		A	LIVE <3> LIVE	515	M	5.0		W
	509	M	4.8		W	LIVE <4> LIVE	516	F	4.9		A
						E.RES <5> LIVE	517	M	5.0		W
	510	F	4.7		A	LIVE <6> LIVE	518	F	4.5		A
	511	F	4.5		W	LIVE <7>					
	512	F	4.5		A	LIVE <8>					
FEMALE 56											
7/9	519	F	4.8		A	LIVE <1> LIVE	526	M	5.1		W
	520	F	4.6		W	LIVE <2> LIVE	527	F	4.7		A
	521	M	4.9		A	LIVE <3> LIVE	528	F	5.1		W
	522	F	4.8		W	LIVE <4> E.RES					
	523	M	4.7		A	LIVE <5> LIVE	529	M	5.1		A
	524	F	4.5		W	LIVE <6> LIVE	530	F	4.3		W
	525	M	5.0		A	LIVE <7> LIVE	531	F	4.6		A

LIVE - LIVE FETUS E.RES - EMBRYONIC RESORPTION W - WILSON SLICING TECHNIQUE
DEAD - DEAD FETUS F.RES - FETAL RESORPTION A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 3 (3 MG/KG)

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CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W	IMPLANTATION SITES (POS. IN UTERUS)			FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W
FEMALE 57													
6/5	532	F	4.5		A	LIVE	<1>	LIVE	538	F	5.2		A
	533	M	5.4		W	LIVE	<2>	LIVE	539	M	5.3		W
	534	M	5.2		A	LIVE	<3>	LIVE	540	F	5.1		A
	535	F	4.8		W	LIVE	<4>	LIVE	541	M	5.1		W
	536	F	4.7		A	LIVE	<5>	LIVE	542	M	4.9		A
	537	F	4.8		W	LIVE	<6>						
FEMALE 58													
7/5	543	F	4.6		A	LIVE	<1>	LIVE	550	F	4.8		W
	544	M	5.0		W	LIVE	<2>	LIVE	551	M	5.2		A
	545	F	4.7		A	LIVE	<3>	LIVE	552	M	5.1		W
	546	F	4.6		W	LIVE	<4>	LIVE	553	M	5.2		A
	547	M	5.1		A	LIVE	<5>	LIVE	554	M	5.0		W
	548	M	4.6		W	LIVE	<6>						
	549	F	4.8		A	LIVE	<7>						
FEMALE 59													
7/9	555	M	5.1		A	LIVE	<1>	LIVE	562	F	5.0		W
	556	F	4.5		W	LIVE	<2>	LIVE	563	M	4.6		A
	557	M	4.6		A	LIVE	<3>	LIVE	564	F	4.7		W
	558	M	4.2		W	LIVE	<4>	LIVE	565	F	4.7		A
	559	M	5.1		A	LIVE	<5>	LIVE	566	M	4.8		W
	560	M	5.3		W	LIVE	<6>	LIVE	567	F	4.6		A
	561	F	4.7		A	LIVE	<7>	LIVE	568	F	4.8		W
							<8>	LIVE	569	M	4.6		A
							<9>	LIVE	570	F	4.6		W
FEMALE 60													
4/10	571	M	5.1		A	LIVE	<1>	LIVE	575	M	5.1		A
	572	M	4.8		W	LIVE	<2>	LIVE	576	M	4.7		W
	573	F	5.0		A	LIVE	<3>	LIVE	577	F	4.6		A
	574	F	4.7		W	LIVE	<4>	LIVE	578	F	4.0		W
							<5>	LIVE	579	F	4.7		A
							<6>	LIVE	580	M	5.0		W
							<7>	LIVE	581	M	5.1		A
							<8>	LIVE	582	M	4.7		W
							<9>	LIVE	583	M	4.9		A
							<10>	LIVE	584	F	4.2		W
FEMALE 61													
3/9	585	F	5.3		A	LIVE	<1>	LIVE	588	F	5.2		W
	586	M	5.4		W	LIVE	<2>	LIVE	589	M	5.4		A
	587	M	5.2		A	LIVE	<3>	LIVE	590	M	5.3		W
							<4>	LIVE	591	F	5.1		A
							<5>	LIVE	592	F	5.1		W
							<6>	LIVE	593	F	5.1		A
							<7>	LIVE	594	F	4.9		W
FEMALE 62													
7/9	595	F	4.6		A	LIVE	<1>	LIVE	601	M	5.3		A
	596	M	4.8		W	LIVE	<2>	E.RES					
	597	F	4.3		A	LIVE	<3>	LIVE	602	F	4.9		W
	598	M	4.9		W	LIVE	<4>	LIVE	603	M	5.1		A
	599	M	4.9		A	LIVE	<5>	LIVE	604	F	4.6		W
	600	F	4.6		W	LIVE	<6>	LIVE	605	M	5.1		A
							<7>	LIVE	606	M	4.8		W
							<8>	LIVE	607	M	4.6		A

LIVE - LIVE FETUS
DEAD - DEAD FETUS

E.RES - EMBRYONIC RESORPTION
F.RES - FETAL RESORPTION

W - WILSON SLICING TECHNIQUE
A - ALIZARIN RED S SKELETAL STAINING TECHN.

CONTENTS OF UTERUS (PLAN VIEW)
GROUP 3 (3 MG/KG)

CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. A/ MALF. W	IMPLANTATION SITES <POS. IN UTERUS>	FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. A/ MALF. W
FEMALE 63 7/7	608	M	5.3	A	LIVE <1> LIVE	615	M	4.9	W
	609	M	4.9	W	LIVE <2> E.RES				
	610	M	5.0	A	LIVE <3> LIVE	616	M	4.8	A
	611	F	4.9	W	LIVE <4> LIVE	617	M	4.7	W
	612	M	5.4	A	LIVE <5> LIVE	618	M	5.1	A
	613	F	4.4	W	LIVE <6> LIVE	619	M	4.9	W
	614	M	4.4	A	LIVE <7> LIVE	620	M	4.8	A
FEMALE 64 4/9	621	M	5.4	A	LIVE <1> LIVE	625	M	5.3	A
	622	M	5.1	W	LIVE <2> LIVE	626	M	5.5	W
	623	M	5.4	A	LIVE <3> LIVE	627	M	5.0	A
	624	M	5.8	W	LIVE <4> LIVE	628	M	5.1	W
					<5> E.RES				
					<6> LIVE	629	M	5.2	A
					<7> LIVE	630	F	4.9	W
					<8> LIVE	631	M	5.4	A
					<9> LIVE	632	M	5.3	W
FEMALE 65 6/10	633	M	5.1	A	LIVE <1> LIVE	639	F	4.3	A
	634	F	4.7	W	LIVE <2> LIVE	640	M	4.8	W
	635	F	4.6	A	LIVE <3> LIVE	641	F	4.7	A
	636	F	5.1	W	LIVE <4> LIVE	642	F	4.5	W
	637	M	5.2	A	LIVE <5> LIVE	643	F	4.7	A
	638	F	4.8	W	LIVE <6> E.RES				
					<7> LIVE	644	F	4.9	W
					<8> LIVE	645	M	4.9	A
					<9> LIVE	646	F	4.6	W
					<10> LIVE	647	F	4.7	A
FEMALE 66 8/5	648	M	5.8	A	LIVE <1> LIVE	654	F	4.7	A
	649	F	5.3	W	LIVE <2> LIVE	655	M	5.2	W
	650	F	5.0	A	E.RES <3> LIVE	656	M	5.8	A
	651	M	5.5	W	LIVE <4> LIVE	657	M	4.9	W
	652	M	5.3	A	LIVE <5> LIVE	658	F	5.0	A
	653	F	4.9	W	LIVE <6>				
					LIVE <7>				
FEMALE 67 7/6	659	F	5.0	A	LIVE <1> LIVE	665	M	5.3	A
	660	F	4.8	W	LIVE <2> LIVE	666	M	5.1	W
	661	M	5.4	A	E.RES <3> LIVE	667	M	5.2	A
	662	F	4.7	W	LIVE <4> LIVE	668	F	4.7	W
	663	M	5.4	A	LIVE <5> LIVE	669	M	5.0	A
	664	M	5.2	W	LIVE <6> LIVE	670	M	4.9	W
					LIVE <7>				
FEMALE 68 8/8	671	F	4.5	A	LIVE <1> LIVE	679	M	5.2	A
	672	F	4.6	W	LIVE <2> LIVE	680	M	4.6	W
	673	F	4.7	A	LIVE <3> LIVE	681	M	5.0	A
	674	M	5.3	W	LIVE <4> LIVE	682	M	4.9	W
	675	M	4.9	A	LIVE <5> LIVE	683	F	4.9	A
	676	M	5.2	W	LIVE <6> LIVE	684	F	4.9	W
	677	M	5.0	A	LIVE <7> LIVE	685	F	4.9	A
	678	M	5.0	W	LIVE <8> LIVE	686	M	5.0	W
FEMALE 69 0/2	(Implantation Sites only)								
					<1> EMPTY				
					<2> EMPTY				

LIVE - LIVE FETUS
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F.RES - FETAL RESORPTION
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CONTENTS OF UTERUS (PLAN VIEW)
GROUP 3 (3 MG/KG)

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CORPORA LUTEA L/R	FETUSES LEFT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W	IMPLANTATION SITES (POS. IN UTERUS)			FETUSES RIGHT HORN IDENT	SEX	WEIGHT (GRAM)	ANOM. MALF.	A/W
FEMALE 70													
9/9	687	M	5.1		A	LIVE	<1>	LIVE	696	M	4.9		W
	688	M	5.0		W	LIVE	<2>	LIVE	697	F	4.3		A
	689	F	4.9		A	LIVE	<3>	LIVE	698	M	4.7		W
	690	M	4.6		W	LIVE	<4>	LIVE	699	M	5.0		A
	691	F	4.3		A	LIVE	<5>	LIVE	700	M	4.9		W
	692	F	4.6		W	LIVE	<6>	LIVE	701	F	4.5		A
	693	M	4.8		A	LIVE	<7>	LIVE	702	M	3.8		W
	694	F	4.4		W	LIVE	<8>	LIVE	703	M	4.0		A
	695	M	4.3		A	LIVE	<9>						
FEMALE 71													
3/9	704	M	4.9		A	LIVE	<1>	E.RES					
	705	F	5.7		W	LIVE	<2>	LIVE	707	F	5.2		W
	706	M	5.2		A	LIVE	<3>	LIVE	708	F	4.7		A
							<4>	LIVE	709	F	5.0		W
							<5>	LIVE	710	F	4.9		A
							<6>	LIVE	711	M	5.4		W
							<7>	LIVE	712	F	5.0		A
							<8>	LIVE	713	F	5.0		W
FEMALE 72													
6/9	714	M	4.7		A	LIVE	<1>	LIVE	720	F	4.4		A
	715	F	4.6		W	LIVE	<2>	LIVE	721	M	4.7		W
	716	F	4.5		A	LIVE	<3>	LIVE	722	M	4.9		A
	717	M	5.1		W	LIVE	<4>	LIVE	723	M	4.8		W
	718	F	4.8		A	LIVE	<5>	LIVE	724	F	4.6		A
	719	F	4.6		W	LIVE	<6>	LIVE	725	F	4.7		W
							<7>	LIVE	726	M	4.4		A
							<8>	LIVE	727	M	4.9		W
FEMALE 73													
8/4	794	M	5.5		A	LIVE	<1>	LIVE	801	F	4.8		W
	795	M	5.2		W	LIVE	<2>	LIVE	802	F	5.1		A
	796	M	5.3		A	LIVE	<3>	LIVE	803	M	5.3		W
	797	F	5.0		W	LIVE	<4>	LIVE	804	F	5.1		A
	798	M	4.5		A	LIVE	<5>						
	799	F	4.3		W	LIVE	<6>						
	800	F	5.0		A	LIVE	<7>						
FEMALE 74													
7/5	815	F	4.9		A	LIVE	<1>	LIVE	822	F	4.9		W
	816	M	5.5		W	LIVE	<2>	E.RES					
	817	F	4.5		A	LIVE	<3>	LIVE	823	F	4.6		A
	818	F	4.6		W	LIVE	<4>	LIVE	824	M	4.9		W
	819	M	5.3		A	LIVE	<5>	LIVE	825	M	4.9		A
	820	M	5.3		W	LIVE	<6>						
	821	F	4.6		A	LIVE	<7>						
FEMALE 75													
7/6	805	F	4.6		A	LIVE	<1>	LIVE	810	F	4.6		W
	806	F	4.8		W	E.RES	<2>	LIVE	811	M	5.2		A
	807	M	4.6		A	LIVE	<3>	LIVE	812	M	5.1		W
	808	F	4.4		W	LIVE	<4>	LIVE	813	F	4.7		A
	809	M	4.9		A	LIVE	<5>	LIVE	814	F	4.7		W
						LIVE	<6>						

LIVE - LIVE FETUS
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E.RES - EMBRYONIC RESORPTION
F.RES - FETAL RESORPTION
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MATING/NECROPSY SCHEDULE AND INDIVIDUAL NECROPSY FINDINGS

Group 1 (0 mg/kg)

Female No.	Male No.*	Day 0 p.c.	Date of necropsy	Necropsy findings
1	1	September 6, 1990	September 27, 1990	No abnormal findings
2	4	September 6, 1990	September 27, 1990	No abnormal findings
3	7	September 6, 1990	September 27, 1990	No abnormal findings
4	15	September 6, 1990	September 27, 1990	No abnormal findings
5	21	September 6, 1990	September 27, 1990	No abnormal findings
6	32	September 6, 1990	September 27, 1990	No abnormal findings
7	54	September 6, 1990	September 27, 1990	No abnormal findings
8	65	September 6, 1990	September 27, 1990	No abnormal findings
9	68	September 6, 1990	September 27, 1990	No abnormal findings
10	85	September 6, 1990	September 27, 1990	No abnormal findings
11	86	September 6, 1990	September 27, 1990	No abnormal findings
12	88	September 6, 1990	September 27, 1990	No abnormal findings
13	93	September 6, 1990	September 27, 1990	No abnormal findings
14	26	September 7, 1990	September 28, 1990	Right kidney enlarged
15	31	September 7, 1990	September 28, 1990	No abnormal findings
16	59	September 7, 1990	September 28, 1990	No abnormal findings
17	62	September 7, 1990	September 28, 1990	No abnormal findings
18	66	September 7, 1990	September 28, 1990	No abnormal findings
19	70	September 7, 1990	September 28, 1990	No abnormal findings
20	73	September 7, 1990	September 28, 1990	No abnormal findings
21	78	September 7, 1990	September 28, 1990	No abnormal findings
22	95	September 7, 1990	September 28, 1990	No abnormal findings
23	96	September 7, 1990	September 28, 1990	No abnormal findings
24	7	September 10, 1990	October 1, 1990	No abnormal findings
25	17	September 10, 1990	October 1, 1990	No abnormal findings

* = Number of male mated with the female.

MATING/NECROPSY SCHEDULE AND INDIVIDUAL NECROPSY FINDINGS

Group 2 (1 mg/kg)

Female No.	Male No.*	Day 0 p.c.	Date of necropsy	Necropsy findings
26	19	September 6, 1990	September 27, 1990	No abnormal findings
27	27	September 6, 1990	September 27, 1990	No abnormal findings
28	30	September 6, 1990	September 27, 1990	No abnormal findings
29	42	September 6, 1990	September 27, 1990	No abnormal findings
30	78	September 6, 1990	September 27, 1990	No abnormal findings
31	8	September 7, 1990	September 28, 1990	No abnormal findings
32	17	September 7, 1990	September 28, 1990	No abnormal findings
33	18	September 7, 1990	September 28, 1990	No abnormal findings
34	48	September 7, 1990	September 28, 1990	No abnormal findings
35	52	September 7, 1990	September 28, 1990	No abnormal findings
36	55	September 7, 1990	September 28, 1990	No abnormal findings
37	56	September 7, 1990	September 28, 1990	No abnormal findings
38	61	September 7, 1990	September 28, 1990	No abnormal findings
39	64	September 7, 1990	September 28, 1990	No abnormal findings
40	69	September 7, 1990	September 28, 1990	No abnormal findings
41	71	September 7, 1990	September 28, 1990	No abnormal findings
42	72	September 7, 1990	September 28, 1990	No abnormal findings
43	82	September 7, 1990	September 28, 1990	No abnormal findings
44	85	September 7, 1990	September 28, 1990	No abnormal findings
45	4	September 10, 1990	October 1, 1990	No abnormal findings
46	11	September 10, 1990	October 1, 1990	No abnormal findings
47	13	September 10, 1990	October 1, 1990	No abnormal findings
48	35	September 10, 1990	October 1, 1990	No abnormal findings
49	38	September 10, 1990	October 1, 1990	Non-pregnant, fluid in uterus
50	51	September 10, 1990	October 1, 1990	No abnormal findings

* = Number of male mated with the female.

MATING/NECROPSY SCHEDULE AND INDIVIDUAL NECROPSY FINDINGS

Group 3 (3 mg/kg)

Female No.	Male No.*	Day 0 p.c.	Date of necropsy	Necropsy findings
51	8	September 6, 1990	September 27, 1990	No abnormal findings
52	9	September 6, 1990	September 27, 1990	No abnormal findings
53	60	September 6, 1990	September 27, 1990	No abnormal findings
54	79	September 6, 1990	September 27, 1990	No abnormal findings
55	3	September 7, 1990	September 28, 1990	No abnormal findings
56	7	September 7, 1990	September 28, 1990	No abnormal findings
57	11	September 7, 1990	September 28, 1990	No abnormal findings
58	22	September 7, 1990	September 28, 1990	No abnormal findings
59	24	September 7, 1990	September 28, 1990	No abnormal findings
60	28	September 7, 1990	September 28, 1990	No abnormal findings
61	37	September 7, 1990	September 28, 1990	No abnormal findings
62	46	September 7, 1990	September 28, 1990	No abnormal findings
63	51	September 7, 1990	September 28, 1990	No abnormal findings
64	57	September 7, 1990	September 28, 1990	No abnormal findings
65	74	September 7, 1990	September 28, 1990	No abnormal findings
66	76	September 7, 1990	September 28, 1990	No abnormal findings
67	80	September 7, 1990	September 28, 1990	No abnormal findings
68	83	September 7, 1990	September 28, 1990	No abnormal findings
69	86	September 7, 1990	September 28, 1990	Two implantations detected after staining (Salewski technique)
70	91	September 7, 1990	September 28, 1990	No abnormal findings
71	92	September 7, 1990	September 28, 1990	No abnormal findings
72	98	September 7, 1990	September 28, 1990	No abnormal findings
73	19	September 10, 1990	October 1, 1990	No abnormal findings
74	42	September 10, 1990	October 1, 1990	No abnormal findings
75	47	September 10, 1990	October 1, 1990	No abnormal findings

* = Number of male mated with the female.

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ATTACHMENTS

WATER ANALYSES -
BACTERIOLOGICAL AND CHEMICAL ASSAYS

CONTAMINANT ANALYSES OF FEED

REPORT OF THE DETERMINATION OF THE CONCENTRATION, THE HOMOGENEITY AND STABILITY OF SXX 0665 TECHNICAL IN BI-DISTILLED WATER WITH 0.5 % CREMOPHOR EL

HISTORICAL CONTROL DATA AND SPONTANEOUS ABNORMAL FINDINGS OF WISTAR RATS (SPF QUALITY) FROM 1987, 1988 AND 1989

RCC PROJECT 281518
SXX 0665 TECHNICAL

BACTERIOLOGICAL ASSAY OF DRINKING WATER, ITINGEN

Official Laboratory
Basel-Landschaft

Liestal, 24.09.90
Ref.no. 90090138
90090139
90090141

Sampling points:
1) 59.1.AU, source water, UV-irradiated
2) 59.70.N, water from Sissach
3) 59.A.1, Pumping station "Gstaadmatt"

Sampled on: 13.09.90

Sample:	1)	2)	3)
Time of Sampling	08.00	08.30	09.00
Water temperature (°C)	9.8	14.9	11.4
Air temperature (°C)	15.0	15.0	15.0

Weather condition prior to sampling sunny

Weather condition during sampling sunny

BACTERIOLOGICAL TEST:

Aerobic mesophilic bacteria /ml	173	5	5
E.coli /100 ml	0	0	0
Enterococci /100 ml	0	0	0
Nitrate			23.5
Chloride			20.7

ASSESSMENT:

At the time of sampling, the tested bacteriological parameters were flawless, and met the requirements for drinking water according to article 260 of the "Eidg. Lebensmittelverordnung".

Official Laboratory
The Official Chemist
(signed Dr. W. Stutz)

RCC PROJECT 281518
SXX 0665 TECHNICAL

CHEMICAL WATER ANALYSIS, ITINGEN

Official Laboratory
Basel-Landschaft

Liestal, 14.06.90
Ref.No. 90060086

Location:	59.A.1, Pumping station "Gstaadmatt"
Date of sampling	11.06.90
Time of sampling	08.15 a.m.
Water temperature (°C)	11.3
Air temperature (°C)	19.0
Weather condition prior to sampling	rain
Weather condition during sampling	cloudy
Appearance	clear, colorless
Odor	not remarkable
Taste	not remarkable

Total hardness		fr.H°	41.8
Alkaline hardness		fr.H°	28.0
Non carbonate hardness		fr.H°	13.8
Conductivity at 20 °C		µS/cm	655.0
Oxygen demand (KMnO4 cons.)		mg/l	2.1
Free ammonia	NH4+	mg/l	<0.0100
Nitrite	NO2-	mg/l	<0.0050
Nitrate	NO3-	mg/l	21.7
Chloride	Cl-	mg/l	19.8
Sulphate	SO4--	mg/l	112.8
Calcium	Ca++	mg/l	145.5
Magnesium	Mg++	mg/l	13.2
Dry residue		mg/l	588
pH electrometrically			7.12
Free carbonic acid CO2 potentiometric			35.0
Free carbonic acid CO2		mg/l	52.3
Excess carbonic acid CO2		mg/l	0.0
Oxygen		mg/l	6.74
Oxygen % saturation			62.4
Phosphate		mg/l	<0.005

The water sample meets the chemical requirements for drinking water according to article 260 of the "Eidg. Lebensmittelverordnung". The values for nitrate and chloride exceed the recommended limits slightly.

Official Laboratory
The Official Chemist
(signed Dr. W. Stutz)

RCC PROJECT 281518
SXX 0665 TECHNICAL

CONTAMINANT ANALYSIS OF DRINKING WATER, ITINGEN

RCC Project: 278010

Date of sampling: 27.06.90

Sample: Tap water RCC Itingen, Room U 10

Parameter	Assay level mg/kg
Lindane	<0.005
Heptachlor	<0.005
Malathion	<0.5
DDT, total	<0.025
Dieldrin	<0.005
PCB's	<0.025
Cadmium	<0.02
Arsenic	<0.15
Lead	<0.25
Mercury	<0.05
Selenium	<0.15
Copper	<0.15
Nitrosamines (DMN, DEN, NPIP, NMORPH), total	<0.01

< 0.001 = less than 0.001 milligram per kilogram

July 11, 1990
signed K.Biedermann

i.A. W. Vogel

W. Vogel

RCC PROJECT 281518
SXX 0665 TECHNICAL

ANALYTICAL TEST REPORT

Project 281452
10.08.1990

Prepared for	: Klingentalmühle AG CH-4303 Kaiseraugst
Attention of	: Dr. A. Oharek
Materials tested	: Kliba 343, Batch 73/90 09.08.1990
Tests performed	: AAS, GC, GC-MS, HPLC
Test results	: See attached Table 1
Submitted	: J. Walker
Issued by	: K. Riedermann

K. Riedermann
August 24, 1990/sad

The undersigned confirms that analysis of KLIBA-feed (number 343, Batch 73/90, manufactured 09.08.1990) was performed, and that this certificate represents accurately the analysis results of the feed delivered.

Date: 27.08.1990

KLINGENTALMUEHLE AG
Oharek

CH-4452 Itingen/Basel Switzerland Telephone 061/98 52 52 Telex 966136 rcc ch Telefax 061/98 52 66

RCC

RCC PROJECT 281518
SXX 0665 TECHNICAL

Attachment

Project 281452
10.08.1990 —

Table 1 - Test Results Kliba 343, Batch 73/90
09.08.1990

Parameter	Assay level mg/kg
Aflatoxins (B1, B2, G1, G2), total	<0.001
Estrogens (DES, Hexestrol, Dienestrol), total	<0.001
Lindane	0.007
Heptachlor	<0.005
Malathion	<0.5
DDT, total	<0.025
Dieldrin	<0.005
Cadmium	0.04
Arsenic	<0.15
Lead	0.97
Mercury	<0.05
Selenium	<0.15
Copper	15
PCBs	<0.025
Nitrosamines (DMN, DEN, NPIP, NMORPH), total	<0.01

<0.001 = less than 0.001 milligram per kilogram

The original certificate of analysis has been archived by KLIBA of Kaiseraugst.

Date: 27.08.1990

KLINGENTALMUEHLE AG

R C C

U-M W E L T C H E M I E A G

RCC PROJECT 281518

DETERMINATION OF THE CONCENTRATION, THE HOMOGENEITY AND STABILITY OF SXX 0665 TECHNICAL IN BIDISTILLED WATER WITH 0.5 % CREMOPHOR EL

SUPPLEMENTARY STUDY TO THE

EMBRYOTOXICITY STUDY (INCLUDING TERATOGENICITY)

IN THE RAT

REPORT

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CONTENTS

		Page
PREFACE		3
	General	3
	Project Staff	3
	Archiving	3
ABSTRACT		4
1	INTRODUCTION	5
2	MATERIALS AND METHODS	5
2.1	Test Article	5
2.2	Sample Storage	5
2.3	Analytical Procedure	6
2.3.1	Standard Solutions	6
2.3.2	Analysis of Samples	6
2.3.3	HPLC-Conditions	6
2.3.4	Evaluation of Results	7
3	RESULTS	8
	TABLES	9/10
	FIGURES	11/12

PREFACE

GENERAL

RCC Project No.	281518
Bayer Project No.	T 9034679
Sponsor	BAYER AG Institut für Toxikologie Landwirtschaft Friedrich-Ebert-Strasse 217 D-W-5600 Wuppertal 1
Study Monitor	Dr. B. Holzum
Test Article	SXX 0665 TECHNICAL
Testing Facility	R C C UMWELTCHEMIE AG Department of Chemistry CH-4452 Itingen / Switzerland

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Date: April 22, 1991/sad

ARCHIVING

R C C, CH-4452 Itingen	Raw data, report and duplicate of report for at least 10 years.

ABSTRACT

This study determined the concentration, the homogeneity and stability of SXX 0665 TECHNICAL in bidistilled water with 0.5 % Cremophor EL.

The mean concentration of the 0.1 mg/ml dose group samples was found to be 93.0 % of the nominal concentration; moreover, the homogeneity varied from - 5 % to + 3 % of the mean concentration.

The mean concentration of the 0.3 mg/ml dose group samples was found to be 96.5 % of the nominal concentration; moreover, the homogeneity varied from - 5 % to + 3 % of the mean concentration.

SXX 0665 TECHNICAL is stable in bidistilled water with 0.5 % Cremophor EL at room temperature for at least two hours.

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1 INTRODUCTION

This report describes the results obtained for the concentration, the homogeneity and stability of SXX 0665 TECHNICAL in bidistilled water with 0.5 % Cremophor EL.

The analysis of homogeneity was performed by analyzing samples of each dose group from three different segments (top, middle, bottom) of the respective mixing container.

2 MATERIALS AND METHODS

2.1 TEST ARTICLE

Identity:	SXX 0665 TECHNICAL
Batch Number:	17005/89
Description:	light beige powder
Purity:	94.7 % (according to analysis dated 13.6.90)
Storage:	At room temperature, in the dark
Stability of the pure test article:	December 13, 1990
Stability in the vehicle:	Stable for at least 2 hours
Safety precautions:	Goggles and gloves

2.2 SAMPLE STORAGE

Test article/vehicle mixtures were prepared and immediately thereafter deep-frozen until analysis was performed. The samples of the stability test were allowed to stand at room temperature for two hours prior to deep-freezing.

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2.3 ANALYTICAL PROCEDURE

2.3.1 Standard Solutions

A stock solution of the test article in acetonitrile was prepared (1.0 mg/ml). The various standard solutions were prepared by respective dilution of this stock solution with acetonitrile to yield concentrations in the range from 1.0 µg/ml to 100 µg/ml. The standard solutions in the concentration range from 1.0 µg/ml to 10 µg/ml were used to calibrate the HPLC.

2.3.2 Analysis of Samples

About 2 g (weighed to the third decimal) of each test article/vehicle mixture was transferred into a 100 ml volumetric flask. Each sample was dissolved with 20 ml of bidistilled water by treatment in an ultrasonic bath; then, the volumetric flasks were filled to volume with acetonitrile. Finally, an aliquot (20 µl) was analyzed by HPLC.

2.3.3 HPLC-Conditions

Apparatus:	Merck 655A-12 pump Merck 655A-22 photometer Merck D-2000 integrator Merck 655A-40 sampling unit	
Column:	Lichrospher RP-18, 5 µm; 125 x 4.6 mm	
Temperatures:	Room temperature	
Eluent:	Acetonitrile Bidistilled water	70 % 30 %
Flow:	1.0 ml/min.	
Detection:	UV, 215 nm	
Injection volume:	20 µl	

2.3.4 Evaluation of Results

Injected samples were quantified by peak height with reference to the calibration curve. The latter was obtained by correlation of the peak height (in counts) of the analytical standards with their corresponding concentration in µg/ml.

The calibration curve is listed in Table 1 and typical chromatograms of standard solutions are shown in Figure 1. From this curve, the concentration Y of SXX 0665 TECHNICAL in µg/ml of an injected sample was calculated from equation 1.

$$Y = a + b \cdot X \qquad (1)$$

where

Y = µg/ml SXX 0665 TECHNICAL of injected sample

a = y-axis intercept

b = slope

X = peak height of injected sample in counts

The concentration of the tested material in the vehicle was calculated from equation 2.

$$C = \frac{Y \cdot V}{W \cdot 1000} \qquad (2)$$

where

C = Concentration of SXX 0665 TECHNICAL in the vehicle (mg/ml)

Y = µg/ml of injected sample calculated by equation 1

V = Volume used for the dissolution (100 ml)

W = Weight of sample (about 2 g, weighed to the third decimal)

The density of the test article/vehicle mixtures was assumed to be 1.0 g/ml.

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3 RESULTS

The tabulated values represent rounded results obtained by calculations which used the exact raw data.

The results obtained for the concentration, the homogeneity and stability of SXX 0665 TECHNICAL in bidistilled water with 0.5 % Cremophor EL are summarized in the attached table on page 10.

The mean concentration of the 0.1 mg/ml dose group samples was found to be 93.0 % of the nominal concentration; moreover, the homogeneity varied from - 5 % to + 3 % of the mean concentration.

The mean concentration of the 0.3 mg/ml dose group samples was found to be 96.5 % of the nominal concentration; moreover, the homogeneity varied from - 5 % to + 3 % of the mean concentration.

SXX 0665 TECHNICAL is stable in bidistilled water with 0.5 % Cremophor EL at room temperature for at least two hours.

The calibration curve is listed in Table 1 and typical chromatograms of standard solutions and samples are presented in the attached figures.

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Table 1: Calibration curve

Standard (µg/ml)	Peak height (counts)	
	before samples	after samples
1.0	1186	1179
2.0	2353	2295
5.0	5788	5825
10	11929	11850

$Y = 4.94\ E\text{-}2 + 8.40\ E\text{-}4 \cdot X \qquad (R^2 = 1.00)$

where

Y = µg/ml SXX 0665 TECHNICAL of injected sample

X = peak height of injected sample in counts

TEST ARTICLE IN VEHICLE
STABILITY, CONTENT AND HOMOGENEITY

DATE OF PREPARATION: 13-SEP-90

Dose Group Time	Nominal mg/ml	Date of analysis		Concentrat. found mg/ml	% of Nom.	Mean % of Nom.	± Dev. in % of Mean
1							
0 Hour	0	18-SEP-90		0.000	---	---	---
2							
0 Hour	0.1	18-SEP-90	T	0.089	88.6	93.0	-5 / +3
0 Hour			M	0.095	95.5		
0 Hour			B	0.095	94.9		
2 Hour[s]			*	0.100	99.9	99.9	
3							
0 Hour	0.3	18-SEP-90	T	0.276	92.0	96.5	-5 / +3
0 Hour			M	0.299	99.8		
0 Hour			B	0.293	97.8		
2 Hour[s]			*	0.365	121.6	121.6	

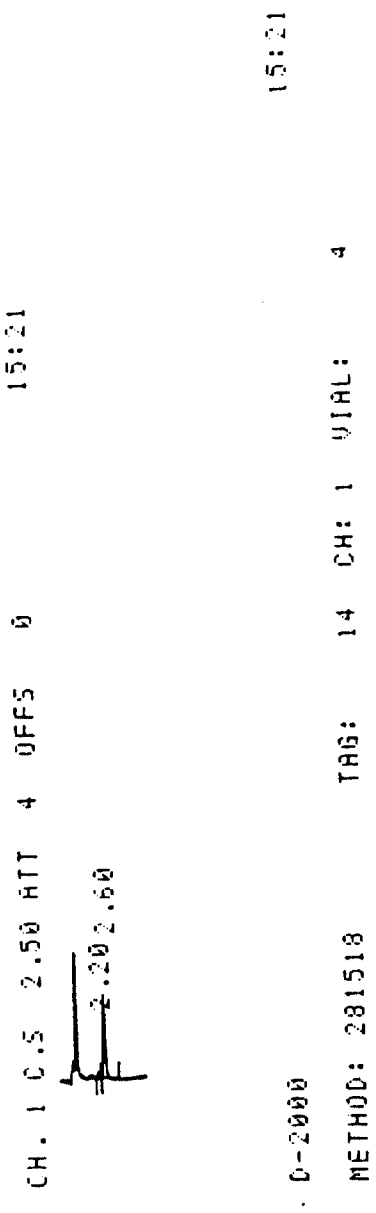
T: Top)
M: Middle) of mixing container
B: Bottom)

* Stability test over two hours at room temperature

Figure 1: Typical Chromatograms

1. Standard solution 1.0 µg/ml, before samples
2. Standard solution 10 µg/ml, before samples

1.



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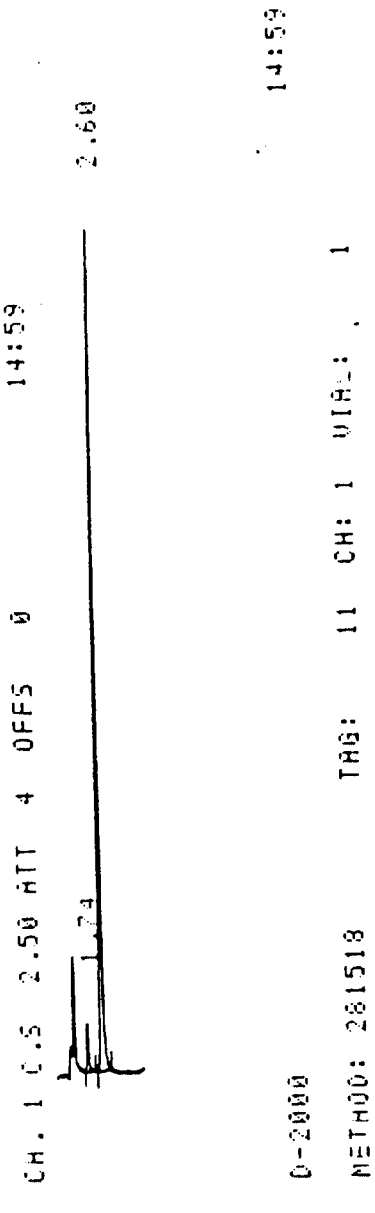
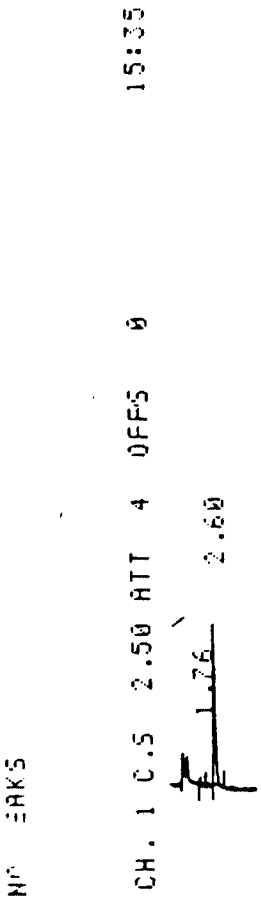


Figure 2: Typical Chromatograms

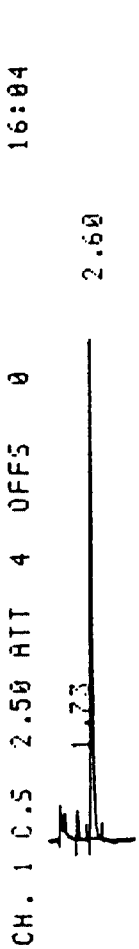
1. Control sample
2. Sample, nominal 0.1 mg/ml
3. Sample, nominal 0.3 mg/ml

1.

2.



3.



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HISTORICAL CONTROL DATA AND SPONTANEOUS ABNORMAL
FINDINGS OF WISTAR RATS (SPF QUALITY) FROM 1987, 1988 AND 1989

The data presented are for dams with live fetuses only. The number of dams with total resorptions or abortion and the incidence of mortalities are given at the head of the tables.

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HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter —	Controls (treated with a vehicle, by gavage)			
	1. STUDY	2. STUDY*	3. STUDY	4. STUDY
DATE	FEB/MAR 87	AUG/SEP 87	MAR/APR 87	JUN/JUL 87
NUMBER OF FEMALES MATED	25	25	25	25
PREGNANT	24	25	25	24
USED FOR CALCULATION	24	25	25	24
CORPORA LUTEA	333	335	334	345
MEAN	13.9	13.4	13.4	14.4
ST.DEV.	1.7	1.7	1.5	1.4
PRE-IMPLANTATION LOSS	35	27	43	21
% OF CORP. LUTEA	10.5	8.1	12.9	6.1
MEAN	1.5	1.1	1.7	0.9
IMPLANTATION SITES	298	308	291	324
MEAN	12.4	12.3	11.6	13.5
ST.DEV.	2.1	1.5	1.8	1.6
POST-IMPLANTATION LOSS	22	26	22	15
% OF IMPL. SITES	7.4	8.4	7.6	4.6
MEAN	0.9	1.0	0.9	0.6
EMBRYONIC RESORPTIONS	18	26	21	15
% OF IMPL. SITES	6.0	8.4	7.2	4.6
MEAN	0.8	1.0	0.8	0.6
FETAL RESORPTIONS	4	0	1	0
% OF IMPL. SITES	1.3	0.0	0.3	0.0
MEAN	0.2	0.0	0.0	0.0
FETUSES				
TOTAL FETUSES	276	282	269	309
% OF IMPL. SITES	92.6	91.6	92.4	95.4
MEAN	11.5	11.3	10.8	12.9
ST.DEV.	2.2	1.6	2.0	1.6
LIVE FETUSES	276	282	269	309
DEAD FETUSES	0	0	0	0
SEX OF FETUSES				
TOTAL MALES	133	154	135	154
% OF FETUSES	48.2	54.6	50.2	49.8
TOTAL FEMALES	143	128	134	155
% OF FETUSES	51.8	45.4	49.8	50.2
WEIGHTS OF LIVE FETUSES				
MALES AND FEMALES				
MEAN	4.7	4.8	4.7	4.8
ST.DEV	0.4	0.4	0.3	0.3

* = Supplementary study to the 1st study.

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HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter —	Controls (treated with a vehicle, by gavage)			
	5. STUDY	6. STUDY	7. STUDY	8. STUDY
DATE	JUN/JUL 87	JUL/AUG 87	SEP 87	NOV/DEC 87
NUMBER OF FEMALES MATED	25	25	25	25
PREGNANT	25	25	23	24
USED FOR CALCULATION	25	25	23	24
CORPORA LUTEA	331	363	316	330
MEAN	13.2	14.5	13.7	13.8
ST.DEV.	1.8	1.7	1.5	1.9
PRE-IMPLANTATION LOSS	30	24	42	27
% OF CORP. LUTEA	9.1	6.6	13.3	8.2
MEAN	1.2	1.0	1.8	1.1
IMPLANTATION SITES	301	339	274	303
MEAN	12.0	13.6	11.9	12.6
ST.DEV.	1.5	1.7	2.0	1.6
POST-IMPLANTATION LOSS	20	25	18	10
% OF IMPL. SITES	6.6	7.4	6.6	3.3
MEAN	0.8	1.0	0.8	0.4
EMBRYONIC RESORPTIONS	17	24	18	10
% OF IMPL. SITES	5.6	7.1	6.6	3.3
MEAN	0.7	1.0	0.8	0.4
FETAL RESORPTIONS	3	1	0	0
% OF IMPL. SITES	1.0	0.3	0.0	0.0
MEAN	0.1	0.0	0.0	
FETUSES				
TOTAL FETUSES	281	314	256	293
% OF IMPL. SITES	93.4	92.6	93.4	96.7
MEAN	11.2	12.6	11.1	12.2
ST.DEV.	1.4	1.7	2.1	1.4
LIVE FETUSES	281	314	256	293
DEAD FETUSES	0	0	0	0
SEX OF FETUSES				
TOTAL MALES	145	160	127	136
% OF FETUSES	51.6	51.0	49.6	46.4
TOTAL FEMALES	136	154	129	157
% OF FETUSES	48.4	49.0	50.4	53.6
WEIGHTS OF LIVE FETUSES				
MALES AND FEMALES				
MEAN	4.8	4.8	4.7	4.6
ST.DEV	0.4	0.4	0.4	0.3

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HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter —	Controls (treated with a vehicle, by gavage)
	9. STUDY
DATE	NOV/DEC 87
NUMBER OF FEMALES MATED	25
PREGNANT	25
USED FOR CALCULATION	25
CORPORA LUTEA	369
MEAN	14.8
ST.DEV.	1.7
PRE-IMPLANTATION LOSS	50
% OF CORP. LUTEA	13.6
MEAN	2.0
IMPLANTATION SITES	319
MEAN	12.8
ST.DEV.	1.7
POST-IMPLANTATION LOSS	21
% OF IMPL. SITES	6.6
MEAN	0.8
EMBRYONIC RESORPTIONS	21
% OF IMPL. SITES	6.6
MEAN	0.8
FETAL RESORPTIONS	0
% OF IMPL. SITES	0
MEAN	0
FETUSES	
TOTAL FETUSES	298
% OF IMPL. SITES	93.4
MEAN	11.9
ST.DEV.	1.7
LIVE FETUSES	100
DEAD FETUSES	0
SEX OF FETUSES	
TOTAL MALES	148
% OF FETUSES	49.7
TOTAL FEMALES	150
% OF FETUSES	50.3
WEIGHTS OF LIVE FETUSES	
MALES AND FEMALES	
MEAN	4.7
ST.DEV	0.4

SPONTANEOUS ABNORMAL FINDINGS OF WISTAR RATS (SPF QUALITY)

	1. STUDY		2. STUDY*		3. STUDY		4. STUDY	
NUMBER OF LITTERS/FETUSES	24/276		25/282		25/269		24/309	
NUMBER OF FETUSES FOR VISCERAL/SKELETAL EXAMINATION	137/139		141/141		133/136		153/156	
DATE	FEB/MAR 87		AUG/SEP 87		MAR/APR 87		JUN/JUL 87	
ABNORMAL FINDINGS	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)
[SK]= Wavy rib(s)	6 (4.3)	4 (16.7)			2 (1.5)	2 (8.0)	2 (1.3)	2 (8.3)
[SK]= Tibia/fibula separate/ shortened/missing	1 (0.7)	1 (4.2)						
[SK]= Thoracic/lumbar vertebral centrum(a) dumbbell shaped/bipartite/ abnormally ossified	3 (2.2)	3 (12.5)	1 (0.7)	1 (4.0)	3 (2.2)	2 (6.0)	4 (2.6)	4 (16.7)
[SK]= 4 or more sternebrae bipartite/fused/ asymmetric/abnormally ossified	1 (0.7)	1 (4.2)			1 (0.7)	1 (4.0)		

* = Supplementary study to the 1st study

[EX] = EXTERNAL EXAMINATION

[VI] = VISCERAL EXAMINATION

[SK] = SKELETAL EXAMINATION

SPONTANEOUS ABNORMAL FINDINGS OF WISTAR RATS (SPF QUALITY)

—	5. STUDY		6. STUDY		7. STUDY		8. STUDY	
NUMBER OF LITTERS/FETUSES	25/281		23/314		23/256		24/293	
NUMBER OF FETUSES FOR VISCERAL/SKELETAL EXAMINATION	139/142		156/158		127/129		146/147	
DATE	JUN/JUL 87		JUL/AUG 87		SEP 87		NOV/DEC 87	
ABNORMAL FINDINGS	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)
[EX]= Missing tail							1 (0.3)	1 (4.2)
[EX]+[VI]= Brachygnathia; visceral examination revealed partial twin, attached dorsally, duplication of liver, kidneys, lungs; dystopia of organs in "host" twin.							1 [EX] (0.3) [VI] (0.7)	1 (4.2) (4.2)
[SK]= Microcephaly; sternebrae nos. 1-6 bipartite and/or incompletely ossified					1 (0.8)	1 (4.4)		
[SK]= Wavy ribs	8 (5.6)	6 (24.0)	2 (1.3)	1 (4.0)	3 (2.3)	2 (8.7)		
[SK]= Thoracic vertebral centrum no.1 incompletely ossified; sternebrae nos. 1, 2, 5 and 6 incompletely ossified	1 (0.7)	1 (4.0)					1 (0.7)	1 (4.2)
[SK]= Thoracic vertebral centrum(a) dumbbell shaped/bipartite			1 (0.6)	1 (4.0)	1 (0.8)	1 (4.4)	4 (2.7)	3 (12.5)
[SK]= Lumbar vertebral centra nos. 1-5 non-ossified, lumbar vertebral arches nos. 2-4 incompletely/non-ossified							1 (0.7)	1 (4.2)
[SK]= 4 or more sternebrae asymmetric/bipartite/incompletely ossified							1 (0.7)	1 (4.2)
[SK]= 4th and 5th left ribs fused at base; 7th left rib branched distally and fused in the middle part with 6th rib; 2nd sternebra non-ossified; 3rd and 4th sternebrae incompletely ossified	1 (0.7)	1 (4.0)						

[EX] = EXTERNAL EXAMINATION
[VI] = VISCERAL EXAMINATION
[SK] = SKELETAL EXAMINATION

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SPONTANEOUS ABNORMAL FINDINGS OF WISTAR RATS (SPF QUALITY)

	9. STUDY		X. STUDY		X. STUDY		X. STUDY	
NUMBER OF LITTERS/FETUSES	25/298							
NUMBER OF FETUSES FOR VISCERAL/SKELETAL EXAMINATION	149/149							
DATE	NOV/DEC 87							
ABNORMAL FINDINGS	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)	NUMBER Fetuses (%)	AFFECTED Litters (%)
[EX]= Palatoschisis	1 (0.3)	1 (4.0)						
[SK] = Wavy ribs	2 (1.3)	2 (8.0)						
[SK]= Thoracic vertebral body dumbbell shaped/bipartite	4 (2.7)	3 (12.0)						

[EX] = EXTERNAL EXAMINATION

[VI] = VISCERAL EXAMINATION

[SK] = SKELETAL EXAMINATION

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HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter	Controls (treated with a vehicle, by gavage)			
	1. STUDY	2. STUDY	3. STUDY	4. STUDY
DATE	FEB/MAR 88	MAR/APR 88	JUL 88	AUG/SEP 88
NUMBER OF FEMALES MATED	25	25	25	25
PREGNANT	25	24	25	24
TOTAL RESORPTION	0	0	1	0
USED FOR CALCULATION	25	24	24	24
CORPORA LUTEA	370	321	305	349
MEAN	14.8	13.4	12.7	14.5
ST.DEV.	1.2	1.3	1.4	1.3
PRE-IMPLANTATION LOSS	36	24	22	60
% OF CORP. LUTEA	9.7	7.5	7.2	17.2
MEAN	1.4	1.0	0.9	2.5
ST.DEV.	1.8	1.0	1.4	2.2
IMPLANTATION SITES	334	297	283	289
% OF CORP. LUTEA	90.3	92.5	92.8	82.8
MEAN	13.4	12.4	11.8	12.0
ST.DEV.	2.1	1.4	1.8	2.0
POST-IMPLANTATION LOSS	17	15	18	18
% OF IMPL. SITES	5.1	5.1	6.4	6.2
MEAN	0.7	0.6	0.8	0.8
ST.DEV.	0.7	0.6	1.1	0.8
IMPLANTATION SITE SCARS	0	0	0	0
EMBRYONIC DEATHS : TOTAL	17	15	18	18
EMBRYONIC RESORPTIONS	17	15	18	18
% OF IMPL. SITES	5.1	5.1	6.4	6.2
MEAN	0.7	0.6	0.8	0.8
ST.DEV.	0.7	0.6	1.1	0.8
FETAL RESORPTIONS	0	0	0	0
% OF IMPL. SITES				
MEAN				
ST.DEV.				
FETUSES				
TOTAL FETUSES	317	282	265	271
% OF IMPL. SITES	94.9	94.9	93.6	93.8
MEAN	12.7	11.8	11.0	11.3
ST.DEV.	2.1	1.5	1.9	2.3
LIVE FETUSES	317	282	265	271
DEAD FETUSES	0	0	0	0
MALFORMED FETUSES	0	0	0	0

HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter —	Controls (treated with a vehicle, by gavage)			
	1. STUDY	2. STUDY	3. STUDY	4. STUDY
DATE	FEB/MAR 88	MAR/APR 88	JUL 88	AUG/SEP 88
NUMBER OF FEMALES MATED	25	25	25	25
PREGNANT	25	24	25	24
TOTAL RESORPTION	0	0	1	0
USED FOR CALCULATION	25	24	24	24
SEX OF FETUSES				
TOTAL MALES	155	136	128	141
% OF FETUSES	48.9	48.2	48.3	52.0
MEAN	6.2	5.7	5.3	5.9
ST.DEV.	2.1	1.5	1.7	2.0
TOTAL FEMALES	162	146	137	130
% OF FETUSES	51.1	51.8	51.7	48.0
MEAN	6.5	6.1	5.7	5.4
ST.DEV.	2.3	1.8	1.7	2.5
WEIGHTS OF LIVE FETUSES (LITTER BASIS)				
MALES AND FEMALES				
N (LITTERS)	25	24	24	24
MEAN	4.8	4.7	4.8	4.6
ST.DEV.	0.3	0.3	0.2	0.2
MALES				
N (LITTERS)	25	24	24	24
MEAN	4.9	4.8	4.9	4.7
ST.DEV.	0.3	0.3	0.3	0.3
FEMALES				
N (LITTERS)	25	24	24	24
MEAN	4.6	4.6	4.7	4.5
ST.DEV.	0.3	0.2	0.3	0.2
WEIGHTS OF LIVE FETUSES (INDIVIDUAL BASIS)				
MALES AND FEMALES				
N (FETUSES)	317	282	265	271
MEAN	4.7	4.7	4.8	4.6
ST.DEV.	0.4	0.4	0.4	0.3
MALES				
N (FETUSES)	155	136	128	141
MEAN	4.9	4.8	4.9	4.7
ST.DEV.	0.4	0.4	0.4	0.3
FEMALES				
N (FETUSES)	162	146	137	130
MEAN	4.6	4.6	4.7	4.5
ST.DEV.	0.3	0.3	0.4	0.3

HISTORICAL REPRODUCTION DATA OF WISTAR RATS (SPF QUALITY)

Parameter —	Controls (treated with a vehicle, by gavage)		
	5. STUDY	6. STUDY	7. STUDY
DATE	SEP/OCT 88	NOV/DEC 88	DEC/JAN 89
NUMBER OF FEMALES MATED	25	25	25
PREGNANT	23	25	25
USED FOR CALCULATION	23	25	25
CORPORA LUTEA	328	366	364
MEAN	14.3	14.6	14.6
ST.DEV.	1.5	2.3	1.7
PRE-IMPLANTATION LOSS	46	50	48
% OF CORP. LUTEA	14.0	13.7	13.2
MEAN	2.0	2.0	1.9
ST.DEV.	1.5	1.4	1.4
IMPLANTATION SITES	282	316	316
% OF CORP. LUTEA	86.0	86.3	86.8
MEAN	12.3	12.6	12.6
ST.DEV.	1.9	2.3	2.1
POST-IMPLANTATION LOSS	16	10	11
% OF IMPL. SITES	5.7	3.2	3.5
MEAN	0.7	0.4	0.4
ST.DEV.	0.9	0.6	0.7
IMPLANTATION SITE SCARS	0	0	0
EMBRYONIC DEATHS : TOTAL	16	10	11
EMBRYONIC RESORPTIONS	16	9	11
% OF IMPL. SITES	5.7	2.8	
MEAN	0.7	0.4	
ST.DEV.	0.9	0.6	
FETAL RESORPTIONS	0	1	0
% OF IMPL. SITES		0.3	
MEAN		0.0	
ST.DEV.		0.2	
FETUSES			
TOTAL FETUSES	266	306	305
% OF IMPL. SITES	94.3	96.8	96.5
MEAN	11.6	12.2	12.2
ST.DEV.	2.1	2.5	2.1
LIVE FETUSES	266	306	305
DEAD FETUSES	0	0	0
MALFORMED FETUSES	0	0	0